Can electromyography objectively detect voluntary movement in disorders of consciousness?

T A Bekinschtein,1,2,3 M R Coleman,3 J Niklison III,2 J D Pickard,3,4 F F Manes1,2,5

ABSTRACT

Determining conscious processing in unresponsive patients relies on subjective behavioural assessment. Using data from hand electromyography, the authors studied the occurrence of subthreshold muscle activity in response to verbal command, as an objective indicator of awareness in 10 disorders of consciousness patients. One out of eight vegetative state patients and both minimally conscious patients (n = 2) demonstrated an increased electromyography signal specifically linked to command. These findings suggest electromyography could be used to assess awareness objectively in pathologies of consciousness.

In the neurological assessment of patients with disorders of consciousness a reproducible motor response to command is taken as a sign of awareness. Critically, this response is used to distinguish comatose and vegetative state (VS) patients from those who retain inconsistent but reproducible evidence of awareness, namely the minimally conscious state (MCS). Comatose patients are in a state of unarousable unresponsiveness, characterised by no evidence of eye opening or sleep–wake cycles, with partial preservation of basic reflexes and no response to sensory or cognitive stimulation. In contrast, VS patients demonstrate eye opening and sleep–wake cycles. They also show no evidence of sustained, reproducible, purposeful or voluntary behavioural responses to visual, auditory, tactile or noxious stimuli and no evidence of awareness of themselves or their environment.1–4 The MCS differs from the VS by the presence of inconsistent but clearly discernible behavioural evidence of awareness of self or environment; responding purposefully to sensory stimuli (ie, tracking a person moving) and/or responding to command.4 Differentiation between these states is complicated by complex central nervous system changes and also peripheral changes, especially muscle spasticity. The chronic nature of these conditions means patients are bedbound, incurring muscle wastage and often tendon shortening. Combined with the subjective nature of the behavioural assessment it subsequently becomes difficult to attribute an absent behavioural response to command.2–5

In the past decade several assessment methods have been designed and validated carefully to identify subtle signs of awareness,8–11 because the Glasgow Coma Scale12 is not sufficiently sensitive to the behavioural portfolio of these patients and the subtle diagnostic distinction.

To determine objectively whether an unresponsive patient is aware incurs the problem of proving conscious processing without explicit verbal or motor response.13 Such a test has recently been proposed using functional magnetic resonance imaging. In an elegant single case, Owen and colleagues14 asked the patient to perform a mental imagery task to command and showed specific cortical activity to each task.14 The task is, however, cognitively very demanding for severe brain injury patients and requires technology that is not widely available. Consequently, an objective task to determine responses to command is desperately required and should ideally be available at the bedside. We propose to record muscle activity using electromyography to command, which can detect voluntary movement below the behavioural threshold. We hypothesise that electromyography may be used to explore preserved function in VS/MCS and has the potential to become a simple and objective methodology to assess awareness (not detectable by observation) in patients clinically defined as VS or MCS.

METHODS

Ten patients (six women, 19–56 years old) matching the inclusion criteria, either in VS (n = 8) or MCS (n = 2) were selected for investigation from an initial cohort of 24. The inclusion criteria defined the minimal processing capabilities to apply the proposed test, these included relatively preserved auditory evoked potentials (normal or mildly delayed wave V) on at least one side, three months from ictus or more and a preserved withdrawal reflex from at least one of the upper extremities. Signed assent from patients’ next of kin was acquired before investigation. The Cambridge Local Research Ethics Committee and the Buenos Aires Ethics Committee approved this study. All subjects underwent a full and repeated clinical assessment including neurological examination, Coma Recovery Scale (CRS)5 and Wessex Head Injury Matrix (WHIM)⁶ to establish each patient’s behavioural profile, including response to command. Four patients fulfilling the criteria defining VS and two patients the criteria defining MCS had traumatic brain injuries with diffuse axonal injury; the remaining four had non-traumatic injuries including anoxic–ischaemic events (n = 3) and encephalitis–cardiac arrest (n = 1). In addition to the behavioural assessment, all patients underwent magnetic resonance imaging, auditory and somatosensory evoked potentials.

For the proposed objective task surface electromyograms (EMG) were recorded from right and left flexor digitorum superficialis and abductor pollicis brevis muscles. Prerecorded auditory stimuli were presented to one or both ears (75 dB) in...
blocks of 30 seconds using the following commands: “Please try to move your right hand” and “Please try to move your left hand” (at the end of the block the instruction was “Please do not move, stay still”); and two control auditory phrases: “Today is a sunny day” and “It is raining outside today”. All phrases, although different in semantic information, had the same length and approximately the same intonation. Periods of silence were used to separate stimulus blocks. Stimuli were repeated six times in a block, blocks were presented four times in the task. The task was delivered twice to each patient; total task time was 540 seconds. Five minutes of free EMG acquisition before and after the task were used to assess spontaneous muscle activity.

Electromyographic signals were amplified, digitised (sampling rate 250 Hz), filtered with a band pass of 3–10 kHz and rectified. Blocks were separated into 10 subblocks and taken as response units for statistical analysis. EMG was continuously monitored and stored on a computer for subsequent review. Each patient’s EMG data were analysed using one-way analysis of variance and a subsequent post-hoc Tukey test with a 5% global probability level contrast between target (move your hand) and control commands and between command and rest condition, when a difference was detected between means. SPSS 10.0 statistical software was used (SPSS Inc, Chicago, Illinois, USA).

RESULTS
VS patients displayed a limited behavioural portfolio showing low CRS scores ranging from 5 to 9 on a 23-point scale (mean 6.4, SD 1.6) and WHIM ranging from 5 to 16 on a 62-point scale (mean 9.3, SD 3.9). MCS patients scored 14 and 16 (CRS) and 26 and 23 (WHIM) showing more complex behaviours such as sustained visual fixation or pursuit. MCS2 showed inconsistent but repeatable hand movement to command, sustained visual fixation and brief visual pursuit. MCS1 did not show hand or foot movement to command but inconsistently moved his eyes to the left when asked to do so; he could also follow a person from midline to the left visual field but not to the right. None of the patients in the VS group showed any evidence of awareness during the repeated behavioural assessments.

To characterise muscle activity we assessed withdrawal reflexes in the upper extremities and recorded spontaneous muscle activity using video and electromyography. Seven patients (five VS, two MCS) demonstrated preserved withdrawal reflexes in both hands and three in one hand only (VS1, VS2 and VS8). All patients except VS8 showed spontaneous muscle activity on EMG and, to the naked eye, some degree of muscle function.

Two patients (VS3 and MCS1), who did not show suprathreshold behavioural responses (it was not possible to detect voluntary movements in the behavioural assessment), demonstrated significantly higher EMG activity while hearing target versus control commands in one hand but not in the other (Tukey’s HSD post-hoc p<0.05 in both cases, fig 1). MCS2 showed both an increased EMG signal and behavioural suprathreshold activity in response to target commands in both hands. No significant change in EMG activity in response to target commands was found in the remaining seven VS patients despite relatively spared muscle function. All three patients who showed responses to command had incurred a traumatic brain injury and had relatively less brain atrophy than most of the other VS patients.

Auditory and somatosensory evoked potentials were totally or partly preserved in the patients studied. Somatosensory conduction delays were found in a number of patients but did not correlate with spontaneous muscle activity or the degree of hand withdrawal.

DISCUSSION
Many think existing clinical assessment procedures for patients with impaired consciousness sometimes fail to detect the full responsive capacity of those patients. Consequently, the electromyography-based task proposed here provides a first step towards establishing an objective bedside test to: (1) increase the detection of responses to command in daily clinical practice and (2) improve efforts to distinguish VS and MCS patients, as the distinction between these patients is highly subjective, relying upon the patients’ clinical history and doctors’ behavioural observations.

As one would expect, the patient in this study who showed suprathreshold EMG activity to command was diagnosed as...
MCS. One patient fulfilling the behavioural criteria for VS and one patient the criteria for MCS, however, showed sub-behavioural threshold EMG activity to command. The underlying cognitive correlates of this simple task depend on the degree of response obtained. Patients VS3 and MCS1 showed partial motor intention processes suggesting the capacity for movement preparation, selection and initiation (subthreshold muscle activity) but no execution. MCS2 showed suprathreshold muscle activity, fulfilling the criteria for execution although her movement was severely restricted.

Unfortunately, we were unable to detect subthreshold EMG activity to command in the remaining seven VS patients studied and therefore no evidence to suggest they were even able to process semantic information. Kotchoubey and collaborators have previously asserted that only a quarter of VS patients display cortical evidence of semantic differentiation. Moreover, Owen and colleagues asserted that it was likely to be the case that only a small number of patients meeting the behavioural criteria for VS would harbour covert evidence of awareness of self or environment. Nevertheless, the preliminary results reported here suggest that this task may provide a simple bedside method with the potential to assist the clinician and improve the accuracy of diagnosis. This methodology might be used in conjunction with functional imaging tasks to reveal far more about the integrity of cognitive function after brain damage.

Acknowledgements: The authors would like to thank the patients and their families for their participation.

Funding: This research was supported by the following grants: Antorchas Foundation (JDP); Raul Carrea Institute and Cognition and Brain Sciences Unit (FFM) and Smith’s Charity UK (JDP, MRC).

Competing interests: None.

Ethics approval: The Cambridge Local Research Ethics Committee and Buenos Aires Ethics Committee approved this study.

Contributors: The authors declare they have participated in the study: Concept and design: TAB, MRC, JN, FFM and JDP; Acquisition of data: TAB, MRC, JN; Analysis and interpretation of data: TAB, MRC, JN, FFM, JDP; Drafting of the manuscript: TAB, MRC; Critical revision of the manuscript for important intellectual content: TAB, MRC, JN, JDP, FFM;anes; Statistical analysis: TAB, MRC, Obtaining funding: TAB, JDP, FFM; Administrative, technical, and material support: TAB, JN, FFM; Study supervision: TAB, JN, MRC. All authors have seen and approved the final version.

REFERENCES

Dear Author

During the preparation of your manuscript for publication, the questions listed below have arisen. Please attend to these matters and return this form with your proof. Many thanks for your assistance

<table>
<thead>
<tr>
<th>Query Reference</th>
<th>Query</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>You have opted not to pay a fee to make your article free online (Unlocked). If you wish to change your mind, please indicate this clearly when you return your proofs. This is the last point in the production process where you can choose to Unlock your paper; details of the fee etc can be found at <a href="http://jnnp.bmj.com/info/unlocked.dtl">http://jnnp.bmj.com/info/unlocked.dtl</a></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Ref 14 – please provide full page range, or is 1 page only correct?</td>
<td></td>
</tr>
</tbody>
</table>