Assessment of minimally responsive patients: clinical difficulties of single-case design

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Improved management of very severely central nervous system (CNS) injured individuals has given rise to an increasing number of patients in a minimally responsive state. There is a growing literature stressing the importance of accurately determining these patients’ level of cognitive functioning and its role in appropriate rehabilitation and long term management. The single case design model appears to be the intervention of choice, with its great flexibility and tailored approach to each individual case. The recent literature has focused on the technical aspects of the assessment, offering clear procedural guidelines. Unfortunately, there is a dearth of information about clinical factors such as clinical setting and family involvement, which may interfere with or prevent a planned intervention. The case of MT is presented, who was the subject of a single case intervention 9 months following an extremely severe traumatic brain injury. The planned intervention was to examine the effects of a psychostimulant on MT’s level of arousal, in order to improve his participation in the rehabilitation programme. Beyond the results (which were equivocal), the clinical difficulties in conducting single case study designs in rehabilitation are discussed. Ways to minimize these difficulties are proposed.

Introduction

Developments in medical technology, improved techniques and better understanding of medical conditions have resulted in reduced mortality and better management and outcome following health-related incidents. This is particularly the case for the most severely CNS injured individuals, whose chance of survival has markedly increased in the past 30 years [1]. These very same developments in medical knowledge and management have resulted in an increase in the number of very low functioning patients, who now not only survive their trauma but have seen their life expectancy increase markedly, approaching, in some cases, that of the normal population [2].

These low functioning patients have been variously described as being in ‘persistent’ or ‘permanent vegetative state’ (VS), suffering from ‘appalliac syndrome’ or being ‘minimally responsive’. There have been attempts to classify and differentiate these conditions, however, specific classification and clear diagnostic criteria are lacking, making it difficult to assess their prevalence and current incidence [3–6].
VS and appallic syndrome describe a similar condition, in which the patient is not (or no longer) in a comatose state but remains unaware of the environment. Features generally included in the presentation are a description of minimal cortical activity with preserved sleep/wake cycles, as well as other autonomic functions supported by subcortical structures [3, 4]. The clinical presentation is one of no or very few consistent voluntary movements and with purposeful and consistent communication generally absent.

The term ‘minimal responsive state’ describes a condition which differs from VS in important but subtle ways. Unlike patients in VS, minimally responsive patients appear to respond to external stimulations and exhibit purposeful behaviours, but inconsistently so [6]. These infrequent behaviours suggest some spontaneous activity at a cortical level but with an inability to sustain or replicate these ‘bursts’ of activities on command. They may show little improvement over time despite intensive multi-disciplinary rehabilitation and remain fully dependent in most, if not all, activities of daily living, show inconsistent means of communication and remain severely handicapped.

Healthcare costs, such as provision of adequate long term facilities and services, and social costs (for example, impact of injury on a patient’s family constellation) associated with these conditions are very important [2] and their impact will depend on accurate prognosis and outcome. Therefore, a better understanding of minimally responsive patients’ level of functioning and potential for recovery is crucial, as even some minimal improvement or change in behaviour may signify a dramatic change in quality of life and decreased dependency on support services, together with better resource allocation. In some extreme cases it may also mean the difference between maintaining and withdrawing a life supporting intervention [7].

In addition to maintenance and sensory stimulation programmes, in-depth assessments of cognitive functions are now a very important part of the management of minimally responsive patients. Unfortunately, cognitive tests traditionally used in clinical practice have little relevance to the clinical reality for minimally responsive patients and lack sufficient sensitivity for providing information on cognitive status and cognitive changes. Even scales commonly used, such as the Rancho Los Amigos Scale [8] or the Western Neuro Sensory Stimulation Profile [9] may offer limited sensitivity to subtle changes in functioning in the cognitive domain.

Some authors have overcome this difficulty by using single case design models in the evaluation and management of minimally responsive patients [10, 11]. Single case study is a very flexible model. It can be adapted to evaluate a broad range of interventions and to assess their impact on a patient’s specified behaviours [12–14]. This method has been used to assess the effect of medications such as methylphenidate on the general level of arousal of patients [15, 16] or to evaluate a patient’s understanding of their current condition and their ability to make informed decisions about future treatment [7].

This approach permits clinicians to optimize therapeutic interventions by an examination of a patient’s cognitive or behavioural abilities and limitations and to monitor the impact of a planned intervention on defined target behaviours. Careful planning and implementation of a testing programme, data collection and statistical analyses allow for a more accurate description of the patient’s level of functioning and minimize clinical biases.

The authors’ experience with this type of intervention has revealed clinical issues not discussed in the current literature on traumatic brain injury rehabilitation. For
example, whilst the methodology, patient type and level of intervention are clearly documented, often little is said about the practical aspects of setting up a single case model intervention in a clinical setting (see for example [9, 17–19]). What appears to be a relatively straightforward endeavour at a theoretical level may turn out to be incompatible with the daily clinical demands. Similarly, the impact of aspects such as the importance of the involvement of family members in the intervention programme or a clear understanding of the therapeutic goals from the clinical staff, factors well known in the implementation of behaviour management programmes for example, are not mentioned.

This paper presents the case of MT, who became minimally responsive following a traumatic brain injury, and discusses the difficulties the single case intervention model presented in the context of an intensive rehabilitation setting.

Method

Subject

MT was 31 years old when he fell off his motorbike. He was found unconscious on the side of the road some 6 hours following the accident. He sustained multiple lesions to the head, chest, and abdomen and had a Glasgow Coma Scale (GCS) [20] score of 3 on arrival to hospital. CT scans of the head revealed multiple haemorrhages across both hemispheres and a left cerebellar haemorrhage. There was a previous medical history of idiopathic epilepsy (generalized seizures). He subsequently developed hydrocephalus that required insertion of a ventriculoperitoneal shunt.

At 2 months post-injury, his GCS score was 5 and his Functional Independence Measure (FIM) [21] score was 18 (lowest possible score). At 9 months post-injury, MT was medically stable with a FIM score of 18, despite intensive rehabilitation. He displayed a severe left hemiparesis, pseudobulbar paralysis and showed very limited functional movements on the right side, his right arm being involved in some basic activities of personal hygiene (brushing teeth). He exhibited very little functional communication, responding unreliably to simple verbal commands. Vision was not formally tested but MT appeared to respond to visual stimulations (for example, recognizing family members or catching a soft ball), albeit again inconsistently. He was fed via a nasogastric tube. Medications included 400 mg of Carbamazepine daily; stable dose without evidence of epileptic activity.

At 9 months post-injury, a trial of Ritalin (methylphenidate) was introduced. The hypothesis was that the introduction of an optimal dose of methylphenidate (between 10 and 60 mg/day) would result in an improvement in MT’s arousal and, in turn, participation in therapy [17–19, 22]. This improvement would be indirectly reflected by an increase in frequency and consistency (i.e. reliability) of some specific behaviours (see procedure for targeted behaviours). Advantages of this psychostimulant are its time taken for maximal effect (about 1 hour) and its short half-life (about 2 hours), as well as relatively minor side effects (hypertension, tachycardia and insomnia have been reported in some cases in the initial stage) [22]. The medication was introduced only after it was suggested to the family and the rationale, potential side effects and aims of the intervention were clearly discussed. The family remained actively involved throughout the duration of the intervention.
**Procedure**

A double-blind placebo-controlled design (A-B-A-B design) was used to assess the efficacy of the therapeutic procedure [12–14]. Baseline observations were conducted over 8 days and several low frequency but possible behaviours were identified. Of particular interest were behaviours that would be functionally relevant for the purpose of developing consistent communication tools such as a communication board, as well as developing and maintaining participation in simple tasks of personal hygiene and dressing.

Following the observation period, the identified behaviours were grouped into two categories of five items each. The first category focused on MT’s ability to display appropriate movements following simple verbal commands (for example: ‘Turn your head to the left’) within 30 seconds of the command. The second category focused on his ability to identify and point to visual stimuli within 45 seconds. These stimuli varied in complexity and included simple geometric figures, line drawings, coloured disks, black and white photos and colour photos (see table 1). Each stimulus was 10 × 10 cm in size and presented side by side with a foil on an A4 sheet of cardboard. The location of each stimulus on the sheet (i.e. left versus right) was randomized across sessions. Each item was presented in MT’s midline field of vision to minimize interference due to possible visual field defects, and within easy reach of his right arm.

For the two categories, all items were rated on a 3-point ordinal scale: no response or delayed response, partial or incorrect response, complete or correct response. The time limits (30 and 45 seconds) were set after determining the frequency of spontaneous occurrence of the target behaviours, in order to avoid spontaneous, random responses unrelated to the command.

Two daily sessions (one in the morning and one in the afternoon) took place, approximately 60–90 minutes after administration of the medication or the placebo. The order of presentation for each category was randomized across sessions, as well as the order of presentation for the items within the two categories. Each session was recorded on video and rated by two judges (O.P. and D.P.H.) blind to the stage of the experiment, based on the specific classification criteria described above and agreed upon prior to the beginning of the experiment. There was a complete agreement between the judges for 97% of the measures. When a disagreement occurred, the lowest rating was chosen as a conservative measure. Behaviours likely to represent possible side effects such as increase in blood pressure, sleep disturbance, and increase in muscle spasticity were also monitored daily by medical and nursing staff.

**Table 1. Description of items for each behaviour category**

<table>
<thead>
<tr>
<th>Verbal commands</th>
<th>Identification of visual stimuli</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ‘Touch your shoulder’</td>
<td>‘Point to the . . . (item in bold)’</td>
</tr>
<tr>
<td>2. ‘Turn your head to the left (or right depending on the initial position of the head)’</td>
<td>1. <em>Square</em> v circle (geometric figures)</td>
</tr>
<tr>
<td>3. ‘Poke out your tongue’</td>
<td>2. <em>Cup</em> v toothbrush (line drawings)</td>
</tr>
<tr>
<td>4. ‘Raise your hand’</td>
<td>3. <em>Red</em> v blue (coloured disks)</td>
</tr>
<tr>
<td>5. ‘Close your mouth’</td>
<td>4. <em>Person</em> v dog (black &amp; white photos)</td>
</tr>
<tr>
<td></td>
<td>5. <em>Bike</em> v car (colour photos)</td>
</tr>
</tbody>
</table>
The structure and organization of clinical and non-clinical services within the rehabilitation unit impacted on the implementation of the original design, which became an [A-B]-[C-B]-A-B-[C-B] design rather than a pure A-B-A-B one. A and C were the randomized medication or placebo phases respectively, and were of 3 days duration, and B was a no-medication phase of 4 days duration. The duration of each [A-B] or [C-B] pair was, therefore, 1 week. The treatment was discontinued in the 4th week, when a bed in an appropriate nursing home became unexpectedly available. In total, 28 sessions were administered and recorded, each session lasting approximately 30–45 minutes.

Results

Visual inspection of the results indicated a difference in response frequency between the medication and placebo conditions for some of the items in both categories (see figure 1). Non-parametric statistical analysis using Mann–Whitney U revealed an overall significant difference for the category ‘verbal commands’ between conditions \( z = -3.4595; p = 0.0005 \), indicating an improvement in performance under the methylphenidate trial condition compared to the placebo condition. Between condition difference was non-significant for the ‘identification of visual stimuli’ category \( z = -0.0857; p = 0.9317 \). Further, within group analysis on individual items revealed significant differences between conditions for two items from the ‘verbal commands’ category: ‘poke out your tongue’ and ‘touch your shoulder’ \( z = -2.3607; p = 0.02 \) and \( z = -2.1654; p = 0.03 \), respectively. The differences between conditions for the remaining individual items failed to reach statistical significance at the 0.05 level. The intervention being explorative in nature, no correction for multiple measures was applied, as it was felt that a correction would result in an overly conservative approach and would limit the value of the procedure.

Discussion

This case exemplifies the use of a single-case study design in the assessment of a minimally responsive patient. It raises a number of important clinical questions. The primary issue is how clinically significant are these findings? In other words, is a significant difference for all items between the conditions necessary to accept a positive treatment effect or not? If not, what is acceptable and at what level? In the case presented, MT was showing a significant change between the methylphenidate and placebo conditions for the ‘verbal commands’ category but not for the ‘identification of visual stimuli’ category. However, analyses conducted on individual items within each category showed that a significant difference between conditions existed for two items only; i.e. ‘poke out your tongue’ and ‘touch your shoulder’.

A reasonable statistical interpretation is that the results indicate that MT was showing potential for responding positively to verbal commands requiring simple motor responses under the methylphenidate condition, compared to the placebo condition, and that he responded less so for commands requiring more complex decision making processes. From a clinical perspective, however, this result was obtained with only two out of the five items showing a significant change in the
Figure 1. Types of responses within categories between conditions (sq = square; cu = cup; re = red; pe = person; bi = bike; sh = shoulder; he = head; to = tongue; ha = hand; mo = mouth; p = placebo condition; r = ritalin condition).
‘verbal command’ category, which makes the clinical significance doubtful. Obviously, in clinical settings, therapists are more interested in clinical rather than statistical significance and, for this reason, the overall outcome of the intervention is difficult to interpret. Perhaps additional sessions, different time limits or a different design with more items in each category may have provided clearer results. These findings also show that variation in responses in minimally responsive patients is the rule rather than the exception [19, 23].

The second issue related to this type of intervention is that the appropriateness and success of such protocols depend not only on the patient or the subject of the design but are also heavily dependent on the environment. This has been long recognized, particularly for behaviour management interventions (see for example [24]). Environment includes an interdisciplinary team approach, a consistent method of intervention and regular update meetings on the programme for all therapists and family members involved with the patient. The importance of these factors is rarely emphasized in the literature on the management of minimally responsive patients (but, see [25] for a good example).

For a greater chance of success, questions to be addressed by the clinical team involved must include whether or not the implementation of such designs complements the team culture (i.e. can it be implemented without disturbing established programmes); whether or not it is perceived as an integral part of the treatment (i.e. it is a ‘valuable’ intervention within current resources), and whether or not it is technically feasible within a reasonable time frame. It is interesting to note that the team involved in MT’s management went through similar phases with most noticeably, and most surprisingly, an initial lack of interest and clinical support for the intervention. The reasons were probably twofold: limited knowledge regarding this type of intervention leading to a lack of understanding of the purpose of the intervention and the tendency for ‘ownership’ of patient by some therapists (‘what I do with this patient is more valuable than what you do’).

Other important aspects worth mentioning, which may have a detrimental effect on single case design procedures, include coordination of the intervention with clinical and non-clinical services. For example, therapeutic intervention times may frequently and unexpectedly be disrupted in order for other daily activities, such as showering or meal times, to be completed. It can also become extremely difficult to organize and coordinate an intervention programme with half the staff on a 5-day week, 8am to 5pm timetables and the other on 7-day, 24-hour shift work. In this case, an additional difficulty was the limited access to services external to the unit, preventing the implementation of a strict A-B-A-B design.

Cost is another significant parameter to consider, particularly in a climate where there is an increasingly strong emphasis on outcome measures and increased productivity. In this case, MT was receiving 1 hour of therapy/intervention each day from two therapists (not including the rating of the videotape). It may be argued that such intense involvement is at the expense of other patients’ treatments and, consequently, the programme may encounter resistance from other therapists, from the administration or funding bodies.

Finally, as for any therapeutic intervention, but more particularly so for unusual intervention, resistance by family members may prevent a successful implementation. In this case, this was avoided with careful explanations and education of the mechanisms of the medication, potential side effects and reasons for the intervention plan. Optimal cooperation was maintained, with regular meetings as part of the
usual interdisciplinary rehabilitation programme. As a general rule, cooperation from family members will require education and regular updates on the treatment, particularly when results do not meet initial expectations.

In conclusion, whilst assessment of cognitive functions of minimally responsive patients is possible with intervention models easily available in the current literature, clinicians must be aware of additional clinical issues not currently addressed appropriately. In this case, these issues did not prevent the introduction of the experimental design as such, but delayed its introduction and limited the findings and their applicability.

Perhaps the most crucial component of such intervention is education; education not only for the family of the patient involved in the programme but also education of the team members, as well as other services indirectly involved in patient management. Ideally, this education process will take place in the initial planning stage, prior to the implementation of the programme and will also be available during the intervention until its completion. Shiel and Wilson [23] point out that recovery from VS or from a minimal responsive state may occur at different rates for different areas of function. This means that it may be necessary to repeat a procedure at regular intervals, despite initial negative results. Without the full collaboration and understanding of those involved in the management and care of a client, this may become very difficult or even impossible.

References

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