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Sensory stimulation for brain injured individuals in coma or vegetative state (Review)

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[Intervention Review]

Sensory stimulation for brain injured individuals in coma or vegetative state

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ABSTRACT

Background

Coma and vegetative state follow traumatic brain injury in about one out of eight patients, and in patients with non traumatic injury the prognosis is worse. The use of sensory stimulation for coma and vegetative state has gained popularity during the 1980's but beliefs and opinions about its effectiveness vary substantially among health professionals.

Objectives

To assess the effectiveness of sensory stimulation programmes in patients in coma or vegetative state.

Search methods

We searched the Injuries Group specialised register, the Cochrane Controlled trials register, EMBASE, MEDLINE, CINAHL and PSYCHLIT from 1966 to January 2002, without language restriction. Reference lists of articles were scanned and we contacted experts in the area to find other relevant studies.

Selection criteria

Randomised or controlled trials that compared sensory stimulation programmes with standard rehabilitation in patients in coma or vegetative state.

Data collection and analysis

Abstracts and papers found were screened by one reviewer. Three reviewers independently identified relevant studies, extracted data and assessed study quality resolving disagreement by consensus.

Main results

Three studies were identified with 68 patients in total. The overall methodological quality was poor and studies differed widely in terms of outcomes measures, study design and conduct. We therefore did not carry out any quantitative synthesis but reviewed results of available studies qualitatively.

Authors' conclusions

This systematic review indicates that there is no reliable evidence to support, or rule out, the effectiveness of multisensory programmes in patients in coma or vegetative state.

PLAIN LANGUAGE SUMMARY

No strong evidence about the effects of sensory stimulation for a brain-injured person in a coma

About half of people in a coma (deep unconsciousness) because of traumatic brain injury will wake within a year of the accident. Speeding recovery to allow people to wake sooner is a priority for them and their family. One type of treatment uses sensory stimulation to try to keep the person's brain working normally. Sensory stimulation methods vary greatly, from one or two hourly sessions of a day, through to shorter sessions every hour for 12 to 14 hours a day. The review found there is no strong evidence to determine whether sensory stimulation benefits people in comas.

BACKGROUND

Prolonged coma and vegetative state follow severe traumatic brain injury in about one of eight patients with severe closed-head injury assessed at discharge from a Trauma Centre (Levin 1991). According to the Traumatic Coma Data Bank, 52 per cent of the vegetative survivors from severe head trauma regain consciousness within one year post-injury and 40 per cent improve to a higher Glasgow Outcome Scale within six months (Task Force on PVS). The remaining individuals die or remain in a vegetative state for months or years.

The outcome for individuals in coma or vegetative state with non-traumatic brain injury is worse than that for those with traumatic brain injury (Sazbon 1993). In one trial, of 100 patients, 20 recovered consciousness within five months, 31 had died by six months after onset, and 49 remained unconscious for the remainder of their lives. Only seven individuals were alive after 72 months of follow-up (Sazbon 1993).

In the early 1950's researchers at the Institute for the Achievement of Human Potential (I.A.H.P.) proposed the idea that programmes of environmental sensory input, at a frequency, intensity, and duration far greater than those in the usual hospital setting, could enhance the speed and degree of recovery from coma. They stated that "in comatose patients, although the problem is primarily cerebral, there is a condition of environmental deprivation that could lead to widespread impairment of intellectual and perceptual processes accompanied by changes in cerebral electrical activity" (Le Winn 1978). The use of sensory stimulation for coma and vegetative state gained popularity in the western world, despite a lack of scientific evidence (Wood 1991, Zasler 1991, Andrews 1996, Giacino 1997).

The intensity of sensory stimulation treatment proposed by different authors has varied considerably. Ranging from one or two cycles of stimulation daily, of approximately one hour each (Mitchell 1990), to one session of multimodal stimulation and one session of unimodal stimulation a day for 10 minutes each (Wilson 1991), to hourly stimulatory cycles, lasting approximately 15-20 minutes, for 12-14 hours per day, six days a week (Doman 1993). Yet another approach has been proposed by Wood, who in 1991, performed a critical analysis of the concept of sensory stimulation (Wood 1991). He outlined that "clinical experience has shown that patients exposed to an undifferentiated bombardment of sensory information lose the ability to process information due to the background noise (habituation)". Wood introduced the 'Sensory Regulation' approach, based on the concept of regulating the way in which stimulations are delivered (i.e. create a quiet environment, regulate the way in which staff communicate with patient, etc.) (Wood 1992).

Owing to the severe impact on the life of many individuals, both those with a brain injury and their relatives, it is urgent to know whether these treatments are more effective than a standard rehabilitation programme in promoting recovery from coma and vegetative state. Moreover, as randomised control trials do not seem to be easily accepted in the rehabilitation community we will discuss potential problem in designing and conducting RCTs in this area.

OBJECTIVES

To compare the effectiveness of Intense Multisensory Stimulation (IMS) Programme, Formalised Not-Intensive Stimulation Programme and Sensory Regulation Programme ,to standard rehabilitation treatments in patients with traumatic or non-traumatic brain injury.

In particular, we wish to test the following hypotheses:

- IMS and Sensory Regulation programmes are more effective than standard rehabilitation treatment in arousing patients from coma.
- IMS and Sensory Regulation programmes are more effective than standard rehabilitation treatment in reducing time to recovery from coma.

In addition we will assess the methodological quality of relevant studies to identify their major drawbacks and suggest appropriate directions for future research.

METHODS

Criteria for considering studies for this review

Types of studies

All Randomised Controlled Trials (RCT) that compared effectiveness of Intense Multisensory Stimulation (IMS) programme, Formalised Not-Intensive Stimulation Programme or Sensory Regulation Programmes with a usual rehabilitation treatment.
If no RCTs were found we intended to perform an analysis of available controlled studies describing their main design characteristics together with selected aspects of their conduct (i.e. length and completeness of follow-up, type of end point and method of ascertainment, etc.). Controlled trials with historical controls, case series and case reports without a control group were not eligible for this review.

Types of participants

Patients diagnosed as brain injured with traumatic and non-traumatic etiology (i.e. anoxic), of any age and gender. Patients are defined in different ways in original studies. For the purpose of this review we accepted two definitions. The first, proposed by the American Congress of Rehabilitation Medicine (ACRM 1995), classified patients in two sub-categories:

- a) Coma: unarousable with absence of sleep/wake cycles on electroencephalogram and loss of the ability of environmental interaction. Major neurobehavioral criteria: the patient's eyes do not open either spontaneously or to external stimulation, the patient does not follow any commands.
- b) Vegetative State: loss of the ability to interact with the environment despite the capacity for spontaneous or stimulus-induced arousal, sleep/wake cycles may be present on EEG and subcortical reflexes are partially or fully preserved. Major neurobehavioral criteria: the patient's eyes open spontaneously or after stimulation; the patient does not follow any commands.

The second classification is based on the Glasgow Coma Scale (GCS) where coma is defined when GSC is equal to, or less than, eight (Teasdale 1974).

Types of interventions

Comparison of

- 'Intense Multisensory Stimulation Programme' (IMS) - e.g Doman's programme defined as stimulatory cycles lasting approximately 15 - 20 minutes, repeated every hour for 12-14 hours per day, six days a week
- 'Formalised Not-Intensive Stimulation Programme' - e.g. Mitchell and Wilson's programme, defined as cycles of stimulation 10-60 minutes twice a day
- 'Sensory Regulation Programme' - e.g. 'Wood programme' defined as single brief sessions of stimulation in a quiet environment completely free of noise

Versus

- Standard rehabilitation treatment, aimed at reducing behavioural, cognitive and motor complications, with usual nursing interventions, swallowing treatment, nutrition, hydration, physical therapy, and neuro-pharmachological interventions.

Types of outcome measures

- Duration of unconsciousness (including coma and vegetative state) defined as the time between trauma and objective recovery of the ability to respond to verbal commands.
- Level of consciousness, as measured by the Glasgow Coma Scale (GCS).
- Level of Cognitive Functioning (LCF) (Hagen 1979).
- Functional outcomes, as measured by Glasgow Outcome Scale (GOS) (Jennett 1975) or by Disability Rating Scale (Rappaport 1982).
- Adverse effects i.e. increased intracranial pressure.

Search methods for identification of studies

Electronic searches

Studies were identified by searching:

- the Cochrane Injuries Group's specialised register
- the Cochrane Controlled Trial register
- MEDLINE
- EMBASE
- CINAHL
- PSYCHLIT (1966-January 2002).

The search strategy can be found in Appendix 1.

Searching other resources

In addition we scanned the reference lists of relevant articles and contacted experts in the area for further relevant studies that they may have been aware of. We did not apply any language restriction.

Data collection and analysis

Selection of studies

To identify relevant studies abstracts were screened by one reviewer (FL). Studies for inclusion were then independently selected by three reviewers (FL, ADT, MT) and disagreement resolved by consensus. For studies that met the inclusion criteria data was independently extracted by three reviewers using a pre-specified data extraction sheet. Information extracted included types of patients and interventions, outcomes measured and timing of assessments, method of randomisation, selection criteria for patients, number of patients lost to follow-up and blinding of outcome assessors. We relied on what was reported in the paper and did not seek additional information from the authors.

Assessment of risk of bias in included studies

Since there is evidence that the quality of allocation concealment particularly affects the results of studies (Schulz 1995), two reviewers scored this quality on the scale used by Schulz (Schulz 1995) as shown below, assigning C to poorest quality and A to best quality:

- A=trials deemed to have taken adequate measures to conceal allocation (i.e. central randomization; numbered or coded bottles or containers; drugs prepared by the pharmacy; serially numbered, opaque, sealed envelopes; or other description that contained elements convincing of concealment).
- B=trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories.
- C=trials in which concealment was inadequate (such as alternation or reference to case record numbers or to dates of birth).

We compared the scores allocated and resolved differences by discussion.

RESULTS

Description of studies

The searching identified 25 potential studies. Of these, three studies met the inclusion criteria.

The main characteristics of the eligible studies are reported in the table of included studies.

Johnson 1993
This was a randomised controlled trial including 14 male coma patients with GCS equal to or less than eight who suffered acute brain injury due to a road traffic accident and were admitted within 24 hours to an Intensive Care Unit. Patients were randomly assigned into two groups. Seven patients (mean age 27.7, mean GCS 4.8) were allocated to the active intervention group who underwent therapeutic sessions where all five senses (olfactory, visual, auditory, gustatory, tactile) were vigorously stimulated. The sessions lasted 20 minutes a day throughout the patients stay in ICU. The other seven patients (mean age 31.4, mean GCS 4.8) in the control group, received usual care without any specified sensory stimulation programme. The outcome measures, which were assessed daily, were GCS, state of ventilation, spontaneous eye movements, oculocephalic response and oculovestibular response. Skin conductance, heart rate and blood test were assessed 20 minutes before and after treatment.

Kater 1989
This was a controlled clinical trial (CCT) with 30 head injured patients at least two weeks after the trauma. There were 18 male and 12 female participants, (mean age 28 years) with GCS ranging from three to 14 and length of coma ranging from six hours

to six months. The study compared a multisensory stimulation programme with usual rehabilitation. The two groups (active intervention and usual rehabilitation), with 15 patients each, were matched for age, sex, type of injury, GCS and length of time from injury each selected from two different health care facilities. Within the two groups, patients were further classified into three subgroups on the basis of GCS score: Deep (GCS 3-6), Moderate (7-10) and Light (11-14). The experimental treatment consisted of a section of stimulation of six modalities: visual, auditory, olfactory, cutaneous, kinestesic and oral, that lasted 45 minutes, twice a day, six days per week until the patients were aroused from coma. Maximum duration of treatment was three months. The outcome measure assessed was 'Level of Cognitive Functioning' (LCF) at two weeks and six months after injury.

Mitchell 1990
The third study was a CCT comparing a coma arousal procedure (CAP) in 12 patients with severe head injury with a matched group of 12 participants receiving usual rehabilitation. The two groups were comparable in terms of demographic characteristics, type and location of head injury, surgical intervention and GCS on admission to hospital. The trial began when patients reached clinical stability (mean 7.9 days). The active intervention group underwent a 'cycle' of sensory stimulation: auditory, tactile, olfactory, taste, visual and kinestesic (60 minutes), one or two times a day, for six days a week, for a maximum of four weeks. Outcomes assessed in this study were GCS score, recorded weekly for four weeks, and total duration of coma.

Risk of bias in included studies

The one randomised controlled trial found (Johnson 1993) did not report details of the method of allocation concealment used. For the two controlled clinical trials (CCTs) (Kater 1989, Mitchell 1990) important details of the methods used to select the groups, (i.e. were patients truly consecutive? Did referral criteria differ from one ward to another? etc.), were not reported. None of the three studies used blinding for outcome assessment. All the studies included all patients originally recruited in the final analysis although for the two CCTs this is more difficult to assess given the nature of the study design.
As far as the appropriateness of the outcome measures used is concerned, two studies used the GCS only without any other indicator of functional status. The study by Kater (Kater 1989) used the LCF scale but analysed results inappropriately considering it a continuous variable rather than a descriptive-nominal one. Only one study presented a functional assessment at a fairly long follow-up (three months). Studies recruited very few patients (range 14-30).

Effects of interventions

As only one study was randomised and studies differed widely in terms of outcomes measured, as well other important aspects of study design and conduct, we did not carry out any quantitative synthesis of data.

Overall none of the three studies provided useful and valid results on outcomes of clinical relevance for coma patients. Johnson (Johnson 1993) did not report information on the main outcome measure (GCS) and only presented data of questionable clinical relevance (i.e. heart rate, skin conductance, cathecholamine, 3-methoxy,4-hydroxyphenylglicol.). The statistical analysis of data in one of the studies (Kater 1989) was flawed because the LCF scale was analysed as a continuous rather than as a qualitative variable. Therefore, the statistically significant difference in favour of the actively treated group reported in the study must be interpreted with caution. Finally, the study by Mitchell (Mitchell 1990) reported a significant difference in the mean length of coma in favour of the experimental group (22 days - SD 9.7 versus 26.9 days - SD 6.6 - control group, p<0,05). However, the clinical relevance of this outcome measure, divorced from any other functional indicator, is questionable.

DISCUSSION

a) Quality and reliability of available studies

We found three studies meeting our inclusion criteria of which only one was a randomised controlled trial. Overall, this review does not provide enough information to allow us to make any conclusions about the effect of sensory stimulation in coma patients. Considering the health care, social and emotional implications that the treatment of coma and vegetative state patients has for patients, family and their carers, the dearth of reliable data and poor quality of the studies is astonishing. Although this review does not support or rule out the effectiveness of this intervention, we still believe that this critical appraisal may provide useful insight for further studies in this area.

One of the major methodological drawbacks in the studies reviewed is the inconsistent use of definitions of coma and vegetative state. This led to important inter-study variation of the criteria used to assess arousal from coma. In the Kater study, for example, patients with GSC values in the 10-14 range have also been included and this raises important questions about the comparability of the results of this study with others. This, together with the unblinded evaluation of the patient status could lead to important biases.

Methodological rigor is also lacking in the definition of the experimental intervention (ie. sensory stimulations). In the Kater study, for example, relatives were asked to deliver stimuli but no information was presented on how they were trained, what they did in practice and whether this was done in addition to the stimulation delivered by therapists during sessions or instead of it. Also relatives were asked to assess patient's reactions to the intervention but again without any information on how this was done and how it was used in the analysis. In the Mitchell study sessions lasted 45 minutes but the study reports that one or two sessions could be delivered without giving details of what criterion, if any, was used to decide on the intensity of treatment.

Two of the three studies included in this review used outcomes of questionable clinical relevance. In the studies we reviewed the use of functional outcomes that could add important clinically relevant information was extremely rare. Johnson used only physiological/ biochemical markers and Mitchell measured the length of coma alone without looking at whether this was associated with a lower score on any disability measure.
It is unfortunate that the study by Kater, the only one that used a functional outcome (Levels of Cognitive function, LCF), used inappropriate statistical analysis that meant the results could not be interpreted reliably.

b) Is the dearth of rigorous studies justifiable?

Randomised controlled trials are still rarely used in this setting and their suitability to evaluate interventions in rehabilitation have been debated (Whyte 1994). In the case of the intervention considered in this review, however, we do not think there are good reasons why randomised controlled trials cannot be conducted. As sensory stimulation represents an intervention that is additional to standard care it is hard to see why patients could not be randomised. Furthermore, as potential bias in outcome assessment may occur it is important to overcome this by having independent assessment of the impact of sensory stimulation on patients. Reservations about the feasibility of conducting RCTs may also arise from the idea that providers' skills in delivering stimuli may bias the results. This may be true but the same objection may be made in many other clinical situations (i.e. surgery, psychosocial interventions etc) where RCTs have been carried out. It is true, however, that an important limitation to the conduct of reliable studies in this area is the lack of sufficiently sensitive and valid tools for outcome assessment.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review indicates that there is no reliable evidence to support, or rule out, the effectiveness of multisensory programmes in patients in a coma or vegetative state.

The need to improve our current knowledge in this field, as well as the dearth of effective treatments in this area, strongly indicates that the delivery of treatment interventions based on the concept of 'sensory stimulation' should be provided only in the context of properly designed and adequately sized randomised controlled trials.

Implications for research

Future studies in this area are needed. As almost 50% of patients have a spontaneous arousal after the acute event, and because of the difficulty of delivering rehabilitation programmes in the intensive care setting (Grosswasser 1990) where patients are often sedated and assessment are usually made on physiological measurments, studies should recruit patients in a stable clinical condition who are discharged from intensive care units. The size of the studies should be sufficient to detect a clinically relevant difference between study groups. To recruit sufficient numbers of patients it may be necessary to organise multi-centre randomised controlled trials.
Outcomes measured should be both related to the impairment but also to functional abilities. The latter should be evaluated at least at an interval of six to 12 months in order to evaluate the consistency of the findings overtime. Due to the potential for bias due to subjectivity and expectations from carers, outcomes should be subject to a rigorous blinded assessment.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Johnson 1993

Methods	Randomised controlled trial. Randomisation method: not specified.
Participants	14 caucasian male adults, affected by traumatic brain injury from road traffic accident, with GCS < = 8, consecutively admitted within 24 hours to the intensive care unit. Experimental group: 7 subjects, mean age 27.7 (12.3), mean GCS: 4.8 (1.9) Control group : 7 subjects, mean age 31.4 (11.2) mean GCS: 4.8 (1.4) Patients with neurological or psychiatric disorders, alcohol or drug abuse, or previous head injuries were excluded.
Interventions	Experimental group: stimulation of five senses for 20-minute a day for all their stay in the ICU (median stay 8.1 days). Order of stimulus presentation was randomized. Control group were not stimulated during the same period (stay medium 3.7 days).
Outcomes	Glasgow Coma Scale (GCS), State of ventilation, Spontaneous eye movements, Oculocephalic response, Oculovestibular response, assessed daily. Catecholamine levels, Serotonin level, Acetylcholinesterase level, 3-methoxy,4-hydroxyphenylglicol, skin conductance, heart rate, assessed 20 minutes pre- and post-treatment period.
Notes	Randomisation method not specified.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kater 1989

Methods	Controlled clinical trial. Two groups were matched for age, sex and type of injury - each selected for two different health care facilities.
Participants	30 patients with traumatic brain injury (mean age 28 y, range 18-47, 18 male and 12 female), at least 2 weeks from the trauma, admitted at 2 different health care facilities. GCS ranged from 3 to 14, length of coma ranged from 6 hours to 6 months. The subjects in the control group (15) were matched with the patients in the experimental group (15) on the basis of age, sex, type of injury, GCS and length of time post-injury.
Interventions	Experimental group: stimulation of 6 modalities: visual, auditory, olfactory, cutaneous, kinestesic, oral. Treatment initiated at least 2 weeks from the trauma, and lasted 45 minutes, twice a day, 6 days per week for a 1 to 3 month period, depending of the subject's length of coma. Relatives were encouraged to apply sensory stimulation whenever they approached or delivered care to the patient. Control group received nursing care without planned, structured sensory stimulation.
Outcomes	Level of Cognitive Functioning (LCF) measured 2 weeks post injury (baseline) and at 3 months post injury.
Notes	In this study the inclusion criteria were broad (e.g. GCS from 3 to 14).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Mitchell 1990

Methods	Controlled clinical trial. The two groups were matched on demographic characteristics, type and location of head injury, surgical intervention and GCS on admission to hospital.
Participants	24 patients with traumatic brain injury divided in 2 groups of 12 patients, treated in the same Neurological Unit. Treatment group: 10 male and 2 female, mean age 22.3 (6.15), range 17-40; range GCS admission 4-6. Control group : 10 male and 12 female, mean age 22.75 (6.77), range 17-42; range GCS admission 4-6. The two groups were matched on the basis of age, sex, type and location of head injury, surgical intervention and GCS on admission to hospital.
Interventions	Experimental group: visual, auditory, olfactory, tactile, gustatory, kinestetic and vestibular stimulation. The stimulation sessions started from 4 to 12 days following injury (mean 7.08 days). Treatment lasted 1 hour for 1or 2 times a day. Control group did not receive arousal procedure at any time while in coma.
Outcomes	Total duration of coma (days). Glasgow Coma Scale (GCS).
Notes	Timing of GCS not specified.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Boyle 1983	Case series.
Cooper 1999	CCT with historical control group and with intervention based on a single stimulation, not multisensory.
De Young 1987	Case series.
Doman 1993	Case series.
Guina 1997	Single case trial.
Hall 1992	Case series.
Johnson 1989	Case series.
Jones 1994	Single case trial.
Le Winn 1978	CCT with historical control group.
Mackay 1992	CCT, the experiemental group underwent other interventions and not only multisensory stimulation.

Study	Reason for exclusion
Pierce 1990	Case series.
Rader 1989	Case series.
Rosadini 1982	Case series.
Schinner 1995	Case series.
Sisson 1990	Case series.
Weber 1984	Case series.
Wilson 1991	Case series.
Wilson 1993	Case series.
Wilson 1996 A	Case series.
Wilson 1996 B	Case series.
Wood 1992	CCT with historical control group.
Wood 1993	CCT with historical control group.

APPENDICES

Appendix 1. Search strategy

The following terms were used (MeSH headings in capital letters):

BRAIN INJURIES OR HEAD INJURIES OR Brain NEAR injur* OR Head NEAR injur*
and
COMA OR COMA, POST HEAD INJURY OR PERSISTENT VEGETATIVE STATE OR UNCONSCIOUSNESS OR Comatos* OR vegetat* OR unconscious*
and
REHABILITATION OR Rehabilitat* OR Enrich* OR depriv* OR Sensor* OR stimulat*

WHAT'S NEW

Date	Event	Description
11 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Lombardi F: Helped to design the protocol, read the original studies, assessed study quality, helped with the interpretation of results and drafted the initial version of the manuscript.
Taricco M: Helped to design the protocol, read the original studies, assessed study quality, provided methodological guidance during the conduct of the review, helped with the interpretation of results, drafted the initial manuscript and reviewed the final version.
De Tanti A : Helped to design the protocol, read the original studies, assessed study quality, helped with the interpretation of results and drafted the initial version of the manuscript.

Telaro E : Helped with the preparation of the study protocol, provided methodological guidance during the entire review process and commented on earlier and final versions of the manuscript.
Liberati A : Helped with the preparation of the study protocol, assisted with the preparation of the manuscript, contributed to the interpretation of the results, reviewed and edited its final version.

DECLARATIONS OF INTEREST

None known.

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External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Sensation; Brain Injuries [complications] [rehabilitation]; Coma, Post-Head Injury [*rehabilitation]; Persistent Vegetative State [*rehabilitation]; Physical Stimulation [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans