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ORIGINAL ARTICLE

Children and young adults in a prolonged unconscious state due to severe brain injury: Outcome after an early intensive neurorehabilitation programme

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Abstract

Primary objective. The Rehabilitation Centre Leijpark in the Netherlands provides an Early Intensive Neurorehabilitation Programme (EINP) to children and young adults in a prolonged unconscious state after severe brain injury. In an extensive research project the effects of EINP were studied. This part of the project focused on the outcome in terms of level of consciousness (LOC) in relation to the specific characteristics of a retrospectively studied cohort.

Research design. This study was executed according to a one-group archived pre-test–post-test design.

Subjects. Subjects were all consecutively admitted patients ($n = 145$, 72% male) between December 1987–January 2001. Inclusion criteria were: age 0–25 years, within 6 months after injury, LOC at admission vegetative state (VS) or minimally conscious state (MCS). One hundred and four patients (72%) suffered a traumatic injury and 41 patients (28%) a non-traumatic injury.

Methods and procedures. All patients had received EINP until they reached consciousness or until it was concluded that no progress was achieved during 3 months after the start of EINP. Medical files were investigated to collect the patients' characteristics and injury data, to determine the LOC at admission and at discharge and to determine the discharge destination.

Results. Almost two-thirds of the patients reached full consciousness. LOC at admission, aetiology and interval since injury were found to be significant prognostic factors. Traumatic patients had a much better outcome than non-traumatic patients. A comparison with earlier outcome studies showed a more favourable outcome than expected. It is argued that a multi-centre study is needed to confirm possible effects of EINP.

Keywords: *Severe brain injury, children, young adults, outcome, early intensive neurorehabilitation, vegetative state, minimally consciousness*

Introduction

Brain injury in children and young adults is frequently encountered in clinical practice. Such injuries can have a huge lifelong impact on the patients [1] and their relatives [2]. In the Netherlands, each year 200–250 children and approximately twice as many young adults suffer from a severe brain injury. The mortality rate of these patients within the first year is high and most survivors suffer from serious physical, cognitive and behavioural consequences. Some patients do not regain full consciousness within the first weeks or months after the injury and remain in a vegetative state (VS) or in a minimally conscious or low awareness state (MCS) [3–5] for months or even years.

Research on outcome after severe brain injury shows that the chance of recovering full consciousness

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and regaining independent functioning is low. In 1994, the Multi-Society Task Force on Persistent Vegetative State (MSTF) used all published reliable outcome studies (all in the US) of children who were in a vegetative state after traumatic brain injury (TBI) for at least 3 months, to compute outcome chances. The results indicate that, at 12 months, the chance is 14% of the patients being deceased, 30% to be still in a vegetative state, 24% of having regained consciousness but with severe disabilities and 32% showing moderate disabilities or a good recovery [6, 7]. Of the children who suffered a non-traumatic brain injury (NTBI), the chance of recovering to a conscious state (albeit minimal) is 3% and the chance of ever being able to function at an independent level is zero.

In the last decade, evidence for human neuroplasticity has been accumulating, including evidence for the development of new neurons from stem cells [8–12]. Furthermore, it is acknowledged that environmental input and exercise can influence the anatomy and physiology of the (human) brain, even when it is injured [11, 13–16].

Ever since the early 1960s, treatment programmes have been developed aimed at restoring consciousness [5, 17–24]. Most of the programmes are based on principles of recovery of brain function by regulated stimulation of the senses. The effectiveness of these programmes has never been demonstrated [25–28]. A major problem in evaluating comprehensive clinical treatment programmes is the control group dilemma [29]. Legal and ethical considerations and practical problems make it difficult to use a randomized control group design. Especially family members can be expected to oppose a random attribution of the patients over the experimental and the control group. Also the complicated character of the treatment programmes makes it difficult to control for all variables. Only a long-lasting nation-wide multi-centre study, in which a sufficient amount of patients can be included and in which it is possible to control for all important treatment variables, may make a control group design feasible.

In 1987, a comprehensive early intensive neurorehabilitation programme (EINP) for children in VS or MCS was developed at the Rehabilitation Centre Leijpark (RCL) in the Netherlands. It was based on a wide set of principles: the principle of effects of sensory deprivation opposite to stimulation [30, 31], the principle of developmental resemblance of recovery processes of all vegetative, sensory, motor and psychological functions [32], the principle of involving families in the treatment process [33] and the principle of centrally steered trans-disciplinary treatment [34, 35].

In 1994, following the recommendations of Ylvisaker [36], a specialized team was formed and EINP was formalized by a written protocol. The retrospective outcome study described here is part of a larger research programme that has been developed in order to evaluate the effects of EINP. This is the first study of this size ever done in Europe. Although this study lacks a control group, the data are of interest, giving insight in the characteristics of a large cohort of consecutively admitted patients and offering the opportunity to compare the outcome data with some earlier outcome studies.

In the present report, first the results of a cohort of 145 patients will be presented in terms of level of consciousness (LOC) at admission and at discharge and their discharge destination. Secondly, it will identify sub-groups (e.g. traumatic or non-traumatic, age) and variables (e.g. LOC at admission, time interval between injury and admission) to determine whether any prognostic variables to the LOC at discharge can be identified. Finally, it will compare the outcome data with some existing data from the literature.

Method

Treatment programme

The Early Intensive Neurorehabilitation Programme (EINP) was applied to children and young adults up to 25 years of age, in VS or MCS, starting as soon as possible after leaving the intensive care unit, but in any case within 6 months after the injury (since September 1995 within 3 months in case of an anoxic cause). The programme was carried out for 3 months or for a shorter period when recovery of consciousness has occurred. In case of signs of recovery of consciousness, the total programme gradually changed into a cognitive learning programme, taking into account the individual needs and possibilities of the patient. The basic philosophy of the programme was that an active approach may induce recovery of brain functions in many severe injured patients, but only when all important health threats are identified and treated [37] and when known principles of development and growth of brain tissue are taken into account [38].

The treatment programme focused on several domains:

- Improving the metabolic state, the state of nourishment, respiration and skin condition, as well as diminishing the risk of infections [39]. The actual treatment activities depended on the individual situation of each patient. Special attention was given to removing invasive devices, like a tracheostomy tube or a bladder catheter.

- Recovery of the normal circadian cycles by offering a homelike environment, that was structured and filled with daily activities [31].
- Improving arousal and awareness by structured stimulation of all sensory modalities (vision, hearing, smell, taste, touch, posture and motion, pain and temperature) in such a way that maximal arousal was generated [30]. As soon as the patient showed any voluntary reactions, reflecting a change from VS into MCS, the programme focused on stimulation and training of cognitive functions, the contents depending on age and cognitive status [19].
- Improvement of normal posture and motor activities by intensive physiotherapy, occupational therapy and oro-facial therapy, using sitting aids, a variety of splints and other appliances [40].
- Improvement of the capabilities of the family to cope with the situation and their own feelings, by giving support, (psycho)education, training in handling the patient and, when needed, treatment [41].

Each day, five treatment activities (sensory stimulation, physiotherapy, occupational therapy, oral therapy or activity therapy) were planned in such a way that these activities were alternated with rest, with moments of personal care and with family visits.

Since September 1994, the programme had been executed by a specialized team, consisting of a rehabilitation physician, a neuropsychologist, a stimulation therapist, physiotherapists, occupational therapists, speech therapists, nursing staff, a social worker and activity therapists. The team worked according to a written protocol, describing all the steps in the programme from admission to discharge and describing the outline of the content of the programme at the different stages of recovery.

Patients' condition and progress were evaluated in a weekly schedule, together with the whole team, resulting in changes in the kind and intensity of parts of the programme. When needed, changes were made on a daily basis.

Procedures and measures

This study was executed according to a one-group archived pre-test–post-test design. The first author investigated the patients' medical files to collect the patients' characteristics and injury data, to determine the LOC at admission and at discharge in the rehabilitation centre and to determine the discharge destination.

The following patient and injury data were collected:

- Gender and birth date.
- Date of injury.
- Aetiology.
- Admission date to EINP.
- Discharge date of EINP.
- Discharge destination.

The aetiology was determined on the basis of the medical note and was classified into two main categories: traumatic and non-traumatic, and further subdivided into 'traffic' or 'other' in the traumatic patients and in 'hypoxia', 'near-drowning', 'encephalitis' or 'other' in non-traumatic patients. It was not always clear what really caused the loss of consciousness, e.g. in case of epileptic seizures.

The LOC of the patients was based on notes and descriptions in the patients' files. First, the admission and discharge reports were analysed. If reports were missing or there was some doubt, all medical, therapists and nursing notes were scanned and analysed.

The LOC was classified into one of the following categories: 1 = conscious (only at discharge), 2 = minimally conscious state (MCS), 3 = vegetative state (VS). The definitions of MCS and VS were based on the descriptions of the International Working Party on the Management of the VS [3] and of the Aspen Neurobehavioural Conference [5].

- *Characterization of the VS*: Patients have a sleep-awake pattern and the vegetative functions are generally recovered. Patients can show delayed reflex activity or generally massive extensor or startle responses. This may progress into flexor withdrawal. Patients can also show single limb responses to stimulation and sometimes withdrawal or intermittent localization. Eventually, roving eye movements or even tracking eye movements may be seen without focusing on people or objects.
- *Characterization of the MCS*: Patients are awake for most of the day. At least they show more definite localization with tracking eye movements following objects or people and they react with emotional responses to the presence of family. Eventually, patients may respond to simple commands, but all have profound cognitive deficits. MCS patients are totally dependent on others.
- *Consciousness is characterized* by continuous alertness with mutual communication in a consistent manner on complex matters (regarding age), albeit with all kinds of possible cognitive disturbances.

Although no studies are known about the reliability and validity of this classification, similar procedures have been described and used in other outcome studies [4, 42].

Scoring in one of the categories was only done when the described key characteristics were reported consistently. In case of doubt, the lowest category was scored. The outcome category 'deceased' was added to classify patients who died during admittance to EINP.

The discharge destination was determined from the discharge report or, in case of absence of this report, from notes and was classified in two main categories: 'regular rehabilitation' indicating further recovery possibilities or 'no rehabilitation', indicating a halt to further recovery. The last category was sub-divided into: 'long-stay home with special services for brain-injured young persons', 'nursing home' or 'back home without treatment'.

Patients

The subjects were all patients ($n = 145$) who were admitted to the EINP between December 1987–January 2001. Patients who were dependent on artificial respiration, on oxygen or on intravenously administered medication were not admitted. Inclusion criteria were: age 0–25 years, within 6 months after injury, LOC at admission VS or MCS. So, by definition, none of the patients was able to communicate at admission. One patient was admitted at 7.57 months after injury because of a long waiting list procedure. Patients were admitted from all over the country, which is rather unusual in the Netherlands, where health care is regionally organized. The EINP was terminated when patients regained consciousness and were admitted to a regular rehabilitation programme or when they were still in VS or MCS 3 months after admission without showing any recovery. When patients showed progress in the recovery of the LOC, but were unable to receive a regular rehabilitation programme, the EINP was prolonged as long as substantial progress was shown.

Seven patients (5%) died before reaching one of the terminating criteria of the EINP.

The initial Glasgow Coma Scale (GCS) [43] score was known for 108 of the patients. One had a score of 9; all the others had a score less than or equal to 8 (mean $= 4.59$; median $= 4.00$; SD 1.45), so almost all patients suffered a severe brain injury.

Of all the patients, 72% ($n = 104$) were males. Most of the patients (104 patients; 72%) had suffered a TBI (traffic accident: 63%) and 41 patients (28%) a NTBI injury (see Table I).

All but one patient were admitted within 6 months after the injury (median $= 2.1$ months; range $= 0.70$–7.57, see Figure 1). The mean age of the patients was 12.4 years (range 0–25). The age distribution between the TBI and the NTBI patients was different (see Figure 2).

The mean age of the TBI patients was 14.2 years (median $= 15.0$ years; range 0–25) and the mean age of the NTBI patients was 7.5 years (median $=$ 4.0 years; range 0–24).

Table I. Cause of injury.

Cause		n	%
Traumatic	Traffic	91	62.8
	Other	13	9
Non-traumatic	Hypoxia	15	10.3
	Near-drowning	12	8.3
	Encephalitis	8	5.5
	Other	6	4.1
Total		145	100

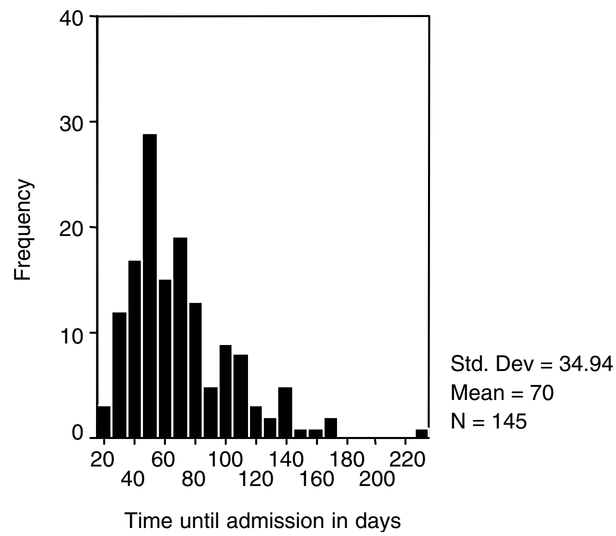

Figure 1. Time interval between injury and admission to EINP.

Analyses

Data were analysed with the Statistical Package for the Social Sciences (SPSS 11.0.1, © SPSS Inc.). Descriptive statistics such as frequency tabulations were used to describe the population and the outcome figures. Association between categorical variables was tested by Chi-square tests and group differences were tested by analysis of variance.

A logistic regression analysis was performed to see whether the level of functioning at discharge could successfully be predicted by the variables 'Level of consciousness at admission', 'Type of trauma', 'Time between injury and admission', 'Age at injury', 'Gender' and 'Admission before or after start of team treatment'. For statistical reasons, LOC at discharge had to be reduced to two categories: conscious or otherwise (MCS, VS or deceased). All variables were first transformed into z-scores.

Results

Admission

There was no relation between aetiology and age on one hand and the time interval until admission on

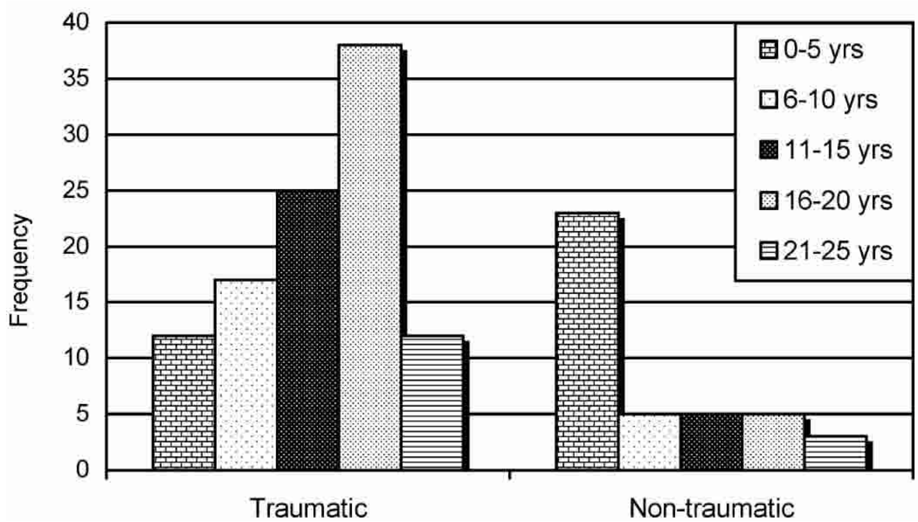

Figure 2. Age distribution of traumatic and non-traumatic patients.

the other hand. The interval between injury and admission was significantly longer for patients admitted before the introduction of the EINP protocol ($n = 49$; $M = 81.63$ days; SD 38.40) compared to the patients admitted after the introduction ($n = 96$; $M = 64.13$ days; SD 31.64). An analysis of variance revealed a significant interaction effect ($F(1, 143) = 8.57$; $p < 0.01$).

Discharge

The mean interval between injury and discharge was 6.60 months (SD 3.50) in the TBI group and 6.95 months (SD 3.10) in the NTBI group. The mean interval between admission and discharge was 4.29 months (SD 3.00) in the TBI group and 4.66 months (SD 2.62) in the NTBI group. When LOC at admission is included in the differentiation, the following cross-table displays the mean treatment duration for each group (Table II).

An analysis of variance revealed a significant interaction effect ($F(1, 141) = 9.55$; $p < 0.01$), indicating that in the TBI group the treatment duration was longer for the VS patients than for the MCS patients. In the NTBI group this was reversed: the treatment duration was longer for the MCS patients than for the VS patients.

There were no significant main effects in this analysis, so neither the LOC nor the aetiology alone contributed to the differences in duration of treatment.

Level of consciousness

At admission, 82 patients (57%) were in MCS and 63 (43%) were in VS. At discharge, 90 patients (62%) were conscious, 39 (27%) were in MCS and nine (6%) were in VS. Seven patients (5%) died before one of the terminating criteria of EINP was reached (see Table III).

Table II. Mean duration of treatment in months, related to aetiology and LOC at admission.

	MCS at admission	VS at admission	All patients
Traumatic	3.37	5.44	4.29
Non-traumatic	5.12	4.06	4.66
All patients	3.86	5.08	4.39

Two Chi-square tests for association were performed, first on a 4×2 table, obtained by combining the MCS-scores and the VS-scores and secondly on a 4×2 table, obtained by combining the traumatic scores and the non-traumatic scores. The tests revealed that patients in MCS at admission had a better chance for recovery than patients in VS at admission ($\chi^2(3) = 31.121$, $p < 0.01$) and traumatic patients had a better chance for recovery than non-traumatic patients ($\chi^2(3) = 12.084$; $p < 0.01$, see also Figure 3).

Discharge destination

Of the 101 surviving traumatic patients, 69 (68%) were referred to a regular rehabilitation facility. Four of them were still in MCS, one infant of 2 years and three young adults who were discharged to a psychiatric rehabilitation centre. Eleven (four of them conscious) were discharged to a long-stay home with special services for brain-injured young persons, 12 (all in VS or MCS) were discharged to a nursing home or hospital and nine (three of them conscious) went back home without further treatment. Of the 37 surviving non-traumatic patients,

Table III. Outcome (including deceased) related to aetiology and LOC at admission.

	Admission				
	Traumatic MCS	Traumatic VS	Non-traumatic MCS	Non-traumatic VS	Total
LOC at Discharge					
Conscious	51 (86%)	22 (49%)	15 (65%)	2 (11%)	90 (62%)
Minimally conscious	7 (12%)	17 (38%)	6 (26%)	9 (50%)	39 (27%)
Vegetative	0	4 (9%)	0	5 (28%)	9 (6%)
Deceased	1 (2%)	2 (4%)	2 (9%)	2 (11%)	7 (5%)
Total	59 (100%)	45 (100%)	23 (100%)	18 (100%)	145 (100%)

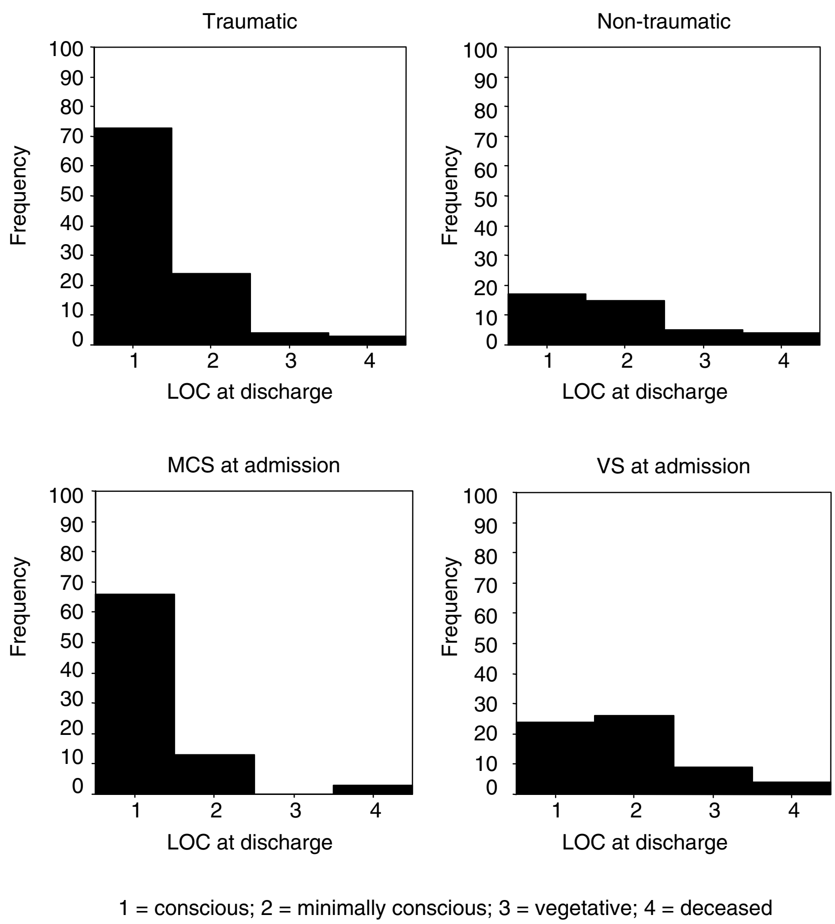

Figure 3. Level of outcome in different groups of patients.

13 (35%) were discharged to a rehabilitation setting (one in MCS: a child of 5 years). Five (14%) patients were discharged to a long-stay home with special services for brain-injured young persons (one conscious). Six (16%) patients were discharged to a nursing home or hospital (one conscious: a young woman who was discharged to a hospital because of complications) and 12 (35%) went back home without further treatment (three of them were conscious). Of the 22 patients who went home, 20 (91%) were under 16 years of age. Of the 44 patients who went to a nursing or long-stay home, 29 (67%) were 16 years or older.

The association between the LOC at discharge (values: 1 = conscious, 2 = MCS, 3 = VS) and the indication for further treatment (values: 1 = rehabilitation, 2 = no rehabilitation) was calculated. The Spearman rho equalled 0.73 ($p < 0.01$), which means there was a strong association between the discharge destination in terms of treatment possibilities and the LOC at discharge.

Prediction of level of functioning at discharge

Based on six predictors (LOC at admission, time between injury and admission, type of trauma, age at injury, team treatment and gender), a logistic regression analysis was performed to predict the LOC at discharge in terms of 'conscious' or 'not conscious'. A test of the regression model containing all six variables against a model containing the constant only revealed a highly significant result: $\chi^2(6) = 56.25$ ($p < 0.001$). Thus, the predictors as a set distinguish successfully between the patients who regained consciousness and those who did not. The proportion of variance explained by the model (Nagelkerke's R^2) was equal to 0.44, while 62% of the cases could be classified correctly for the non-conscious outcome category and 88% for the conscious outcome category. Comparison of this classification with the chance classification of success of 50% was again highly significant ($z = 6.72$; $p < 0.001$). Further analysis revealed that, of the six predictors, three contributed significantly to the prediction of the LOC at discharge. The level of consciousness at admission to the rehabilitation centre clearly was the most important one: the odds of being conscious at discharge were more than nine times higher for those being in MCS at admission as compared to those being in VS ($\chi^2(1) = 29.14$; $p < 0.01$; odds-ratio = 9.54; $CI_{95} =$ 3.85–23.64). The next important variable was 'Type of trauma'. Traumatic patients had a six times better perspective than non-traumatic patients ($\chi^2(1) = 11.77$; $p < 0.01$; odds-ratio = 6.04; $CI_{95} = 2.06$–17.73). 'Time between injury and admission' was the least important predictor. A one-unit increase in time until admission (in terms of z-scores) was associated with a likelihood of becoming conscious that was about half as high ($\chi^2(1) = 13.02$; $p < 0.01$; odds-ratio = 0.43; $CI_{95} = 0.26$–0.71). So, when time until admission increased, the chances of regaining consciousness decreased significantly. The variables 'age at injury', 'team treatment' and 'gender' separately did not contribute to the LOC at discharge.

Discussion

The aims of the present study were two-fold. First, one was interested in the characteristics of the cohort and in the outcome figures in terms of LOC and discharge destination. Secondly, one tried to identify variables that could predict the recovery possibilities.

The distribution between TBI and NTBI and the distribution between male and female in this cohort reflect what is generally found in epidemiological studies [44, 45]. It also is of no surprise that, in the youngest children, non-traumatic injuries were the majority, nor that the adolescents showed a peak of traffic accidents [46]. One can, therefore, conclude that the studied cohort is a representative sample of young persons with a severe brain injury.

The cohort can be considered as having severe brain injury, as shown by the known GCSscores. Although the GCSscore of 37 patients was unknown, it appeared that the percentage of VS patients at admission in this group was higher than in the group with a known GCSscore (51% compared to 41%), indicating an even more severe level of brain injury. In severe brain-injured patients, the outcome is expected to be poor, related to recovery of consciousness [47], as well as to recovery of function [48]. Nevertheless, the outcome figures show that a majority of the patients underwent a substantial recovery, although some patients did not show any recovery at all.

To compare this study with earlier outcome studies, one found one outcome study of Boyer and Edwards [35], describing a similar treatment programme for children and adolescents with TBI. Of the 83 patients in that study who were in VS after 3 months, 43% were still in VS at 1 year. In this study, only 5.4% were in VS at discharge at a mean of 8.66 months (median = 7.85; SD 3.59). Ten years ago, the Multi-Society Task Force (MSTF) [7] computed the outcome chances for different categories of patients who were still in a VS at 3 months after injury, based on all available outcome studies. In this study, 39 TBI patients and 21 NTBI patients were still in a vegetative state 3 months after injury. According to the MSTF, TBI patients have a 14% chance ($CI_{99} = 1$–27) of dying and a 30% chance ($CI_{99} = 13$–47) of staying in VS. In this study, none of the NTBI patients died and 5% ($CI_{99} = 0$–14) remained in VS. The NTBI patients' chance of dying, as calculated by the MSTF, is 3% ($CI_{99} = 0$–11) and the chance of remaining in VS is 97% ($CI_{99} = 89$–100). In this study, 10% ($CI_{99} = 0$–26) died and 19% ($CI_{99} =$ 0–41) remained in VS. As can be seen, the outcome percentages between the MSTF calculations and the results of this study differ significantly in two categories; in one category there is a small overlap in the 99% confidence intervals. Only the percentage of NTBI patients that died corresponds with the computed chances. So, the patients in this study generally had a more favourable outcome than predicted by the MSTF. In a series of studies, Kriel et al. [49–51] described the outcome of a total of 188 children and adolescents with severe brain injury, traumatic and non-traumatic, who had been admitted to an in-patient brain injury rehabilitation service at a regional specialty hospital for children. Sixty (65% TBI) were in VS at least 3 months after injury. Six months after injury, 67% of them were still in VS and only 17% were fully conscious (could communicate). At 12 months after injury, 45% were in VS and 23% were fully conscious. In this study, 42 (64.3% TBI) children and adolescents were still in VS after 3 months. The mean discharge from EINP in this group is at 8.14 months (median = 7.53; SD 3.80) after injury. At discharge, 19% had died or were still in VS and 45% were fully conscious. In some older studies, outcome percentages of children (in TBI) who remained in a VS vary between 11–35% [52, 53]. In one study on NTBI patients, 80% remained in a VS [54]. So, compared to earlier studies and to the computed outcome chances by the MSTF, in this study the outcome seemed to be more favourable. This counts for TBI patients as well as for NTBI patients. One could not find any study with outcome results of comparable patients that surpass this study. One can wonder what caused the more favourable outcome in the study. A possible explanation is the use of the EINP, which has been developed to improve and accelerate recovery possibilities. However, it should be taken into account that the differences in outcome between this study and the other reported studies can be the result of unknown differences in extent of injury, secondary damage, differences in (initial) medical care and finally chance.

The findings in this study are remarkably similar to those reported by Giacino and Kalmar [42], who studied a group of 104 adults with equal proportions of TBI and NTBI patients in VS or MCS. These patients were also admitted to a rehabilitation-based coma intervention programme. Although the authors did not describe the programme, a lot of similarity is assumed between both programmes. In the Giacino and Kalmar study, the outcome was measured by scoring the Disability Rating Scale (DRS) on admission and at 1, 3, 6 and 12 months after injury. At 6 months (comparable to the mean discharge time in this study which is 6.59 months after injury; median = 5.90; range 1.61–17.84), the mean DRS-category scores in the different patient groups are comparable to the LOC scores in this study. The similarities between both studies confirm the conclusion of Giacino and Kalmar that their findings are of clinical importance. 'Prognostic specificity, the importance of accurate differential diagnosis and the end-of-life decision making' are all enhanced by the similarity of the results. Especially the fact that in children and young adults the same trends are visible as in an adult group is of importance.

The comparison with other outcome studies on children and adolescents and with the outcome study by Giacino and Kalmar concerning adults leads to the conclusion that there may exist an indication of a beneficial effect of rehabilitation programmes. Nevertheless, this has to be proven definitively in a future study following a control-group design. This study agrees with Giacino and Kalmar's [42] conclusion that the only way to execute such a study is 'to initiate multi-centre collaborative studies capable of enrolling high numbers of patients' (p. 48).

As could be expected, a strong association was found between the discharge destination in terms of treatment possibilities and the LOC at discharge. Nevertheless, one was surprised to see that some patients in MCS were discharged to a rehabilitation facility, whereas some conscious patients were not. A further analysis revealed that this discrepancy between LOC and discharge destination is present, especially in the younger children. Sometimes children who were determined conscious went home, combined with some day care facility. On the other hand, some infants did get the benefit of the doubt and were referred to a special rehabilitation facility for infants. Perhaps regional differences in the facilities played a role.

Most of the youngest patients who did not receive further rehabilitation went home, whereas the oldest patients generally went to a long-stay facility. These findings are comparable to the findings of Boyer and Edwards [35], who concluded that the combination of older parents and heavier patients makes home care more difficult.

Referral patterns seem to have changed over the years. Before the start of the formal procedures, the majority of patients (67%) stemmed from the immediate vicinity of the hospital, whereas in later years the rehabilitation centre was more known all over the Netherlands. So then, the majority of the patients (66%) stemmed from other parts of the country, sometimes preventing patients from going home at the weekend. This could have an effect on MCS patients, most of whom are more comfortable when they are able to stay at home at weekends.

The interval between injury and admission was not related to aetiology or age. Comparison of the patients who were still in VS at admission to the patients who were already in MCS revealed that the mean interval was slightly shorter in the latter group (66–76 days). It is possible that a longer interval was caused by medical complications, but generally referral to EINP and waiting time were obviously influenced by other more coincidental factors. Introduction of the formalized protocol of EINP, combined with public announcement, reduced the interval substantially. The familiarity with EINP of hospital specialists, the Dutch family organization and other key figures was probably the most important factor.

One can conclude from the mean treatment interval of 4 months that the EINP generally is a relatively short-term therapy, unlike some other recovery stimulation programmes [23, 55].

It was unexpected to see that non-traumatic patients who were in VS at admission had a shorter period of EINP-treatment compared to non-traumatic patients who were in MCS at admission, whereas the figures for traumatic patients show the opposite pattern. As far as is known, this study is the first to reveal this pattern. The underlying mechanism might partly be explained by the far higher chance that vegetative TBI patients have to become minimally conscious and eventually conscious, compared to NTBI patients. When vegetative patients showed any recovery of the LOC, the treatment was continued until full consciousness was reached, thus explaining the long total treatment duration time for this group. It might also be explained by the fact that the non-traumatic MCS patients have fewer possibilities to recover well, because extensive diffuse brain injuries result in a slow recovery pattern [56]. In such cases, the treatment is often continued for a longer period, trying to make use of all recovery possibilities the patient may have, until a certain plateau is reached.

The data analysis revealed that LOC at admission is the most important predictive factor to the LOC at discharge. This is not surprising, assuming that some recovery already had started in these patients. Furthermore, the results showed that traumatic patients who were already in MCS at admission had an almost 90% chance to recover to consciousness, especially when admitted as quickly as possible. As the MSTF calculations have already shown, TBI patients have a much higher chance to recover to a good outcome level than NTBI patients [7]. Underlying pathology is thought to be the main cause: in the case of non-traumatic injuries, the diffuse damage affects all parts of the brain, whereas in traumatic injury large parts of the brain are undamaged and can become functional again. Especially when the sub-cortical white matter or the major relay nuclei of the thalamus are profoundly damaged, recovery seems impossible [57]. This is probably the case more often in NTBI patients than in TBI patients.

Because almost all of these patients needed further intensive rehabilitation to return to some participation in society, early admittance to a rehabilitation centre is important [35, 36]. As has been shown, the shorter the interval between injury and admission, the greater the chances of recovery. Furthermore, the sooner rehabilitation is started, the fewer patients are at risk to develop unwanted behaviours caused by recovery-induced agitation [58] and the better the different treatment goals can be co-ordinated [59]. However, one may wonder about the experienced quality of life of the patients who recover to consciousness but fail to regain full independence. Earlier studies have demonstrated that patients generally have poor quality of life [60], with indications that early treatment with a formalized programme like the EINP can positively contribute to the level of discharge destination [61] and so to the quality of life. When patients are able to live in a (semi-)independent facility, they generally experience better quality of life compared to patients who are fully dependent and live in a facility like a nursing home.

The logistic regression analysis did not show any effect of the team treatment with formal procedures on the outcome, although in earlier publications the importance of a formalized programme was emphasized [35]. Apart from the possibility that this absence of an effect is real, a possible explanation is that the informal procedures and the co-ordination before the formation of the team of specialists were already executed in the same way as after formalization of the procedures. Another possibility is that the patient groups before and after the start of the team programme were not comparable. For instance, no match could be made on medical complications during admission to the hospital because of missing data in the patients' files. It is, therefore, possible that the two groups differed in recovery possibilities because of underlying physical problems.

Finally, no effect of age was found on the LOC at discharge. This seems contrary to some general ideas of better recovery chances for the very youngest children. However, as has been reported, young children with severe brain injury probably have worse chances for good recovery [62, 63]. In both studies, long-term functional outcome measures have been used, while this study only described the LOC at discharge. Consequently, it still is possible that, in further recovery and development, the youngest children in the cohort appear to have fewer possibilities, because of structural damage to brain regions important for learning.

Methodological considerations

The reliability of the procedure of retrospectively determining the LOC at admission and at discharge based on patients' files can be questioned. Information in the files was often incomplete. Not all the signs and symptoms important for the determination of the LOC were always reported. Determining LOC, thus, might have been subject to interpretation errors. In addition, the author who determined the LOC at admission and at discharge was, in most cases, one of the main therapists of the patients and for long periods, the team co-ordinator. Consequently, there is a chance of biased judgement. Nevertheless, some of the recorded information is objective, i.e. the discharge destination. This feature correlated highly with the determined LOC at discharge, indicating a rather reliable judgement of the LOC.

Another issue that has to be taken into consideration is whether the categories used (VS, MCS and consciousness) are well described and clearly distinguishable. In recent history, it has been proven to be very difficult to come to an agreement on the description of terms and levels of (un)consciousness and on recovery patterns when a group of specialists is asked to do so [3, 5]. As far as is known now, no reliability study has been done on this classification of levels of consciousness. Further research on the use of this classification as a clinical scale is needed. Nevertheless, most of the time, therapists do not differ substantially when asked to evaluate patients' LOC in terms of the classification. So, the classification used at this moment is the next-best solution to describe levels of consciousness.

Conclusion and recommendations

In this study, the level of consciousness of severe brain injured patients after receiving an early intensive neurorehabilitation programme exceeded the expectations based on earlier outcome studies. So, despite the methodological shortcomings of this study, there are indications that the described early intensive neurorehabilitation programme contributed to the ultimate level of consciousness of some children and young adults in an unconscious state due to severe brain injury.

Patients who are admitted to a rehabilitation programme within the first 2 months after the injury, who are already in a minimally conscious state and who suffered a traumatic injury have the best chance to make a substantial recovery, even to full independence. Non-traumatic patients still in VS after at least 2 months have little chance to recover to full consciousness.

Further studies are needed to be able to draw firmer conclusions. There is also a need for further research on the reliability of the classification of levels of consciousness used, on the long-term outcome levels and on the perceived quality of life. However, most needed, whenever ethically and technically possible, is a controlled group study to compare treatment programmes for patients in VS or MCS, like the EINP, to non-treatment or a standard treatment.

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