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REVIEW ARTICLE

COMPREHENSIVE REHABILITATION PROGRAMMES IN THE CHRONIC PHASE AFTER SEVERE BRAIN INJURY: A SYSTEMATIC REVIEW

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Objective: The aim of this study was to perform a systematic review of the effectiveness of comprehensive rehabilitation programmes for adults in the chronic phase after severe acquired brain injury.

Methods: PubMed, PsychINFO and PsychLit were searched for articles published between 1990 and 2008 and a quality assessment was performed. The comprehensive programmes were subdivided into neurobehavioral interventions, residential community reintegration and day-treatment programmes. The extracted data included study characteristics, patient characteristics and intervention characteristics.

Results: Thirteen studies met pre-established criteria. Two studies were randomized controlled trials, 5 were controlled comparative studies and 6 were uncontrolled longitudinal cohort studies. Overall, their methodological quality was limited. The investigated programmes led to substantial improvement in daily life functioning and community integration of severe chronic brain injury patients, with lasting effects at follow-up.

Day-treatment programmes had the highest level of evidence.

Conclusion: Comprehensive rehabilitation programmes appear to be effective in terms of a reduction in psychosocial problems, a higher level of community integration and an increase in employment. Although this is the first review to differentiate between specific programmes, clear-cut clinical recommendations cannot yet be set out due to limited methodological quality and poor description of patient and intervention characteristics. Specific recommendations for future studies are given.

Key words: brain injury; rehabilitation; comprehensive rehabilitation; review; adult; middle-aged.

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INTRODUCTION

Severe acquired brain injury can have a tremendous impact on patients and family members. They must learn to live with a diminished potential for physical, emotional, cognitive, and social functioning (1). Many patients with severe acquired brain injury receive primary rehabilitation after hospital care. Camney et al. (2) consider “functioning as independently as possible in the patient’s own home and in society” to be the main goal of rehabilitation. To reach this goal, the rehabilitation process after brain injury needs to attain optimal community reintegration, including a good balance between social and vocational functioning, taking into account individual limitations (3). The ultimate goal is to gain a satisfying quality of life.

Apart from the direct consequences of injury, such as cognitive, emotional, behavioural problems and an impaired awareness of limitations (4), some patients develop secondary psychosocial problems later in life. These problems encompass anxiety, depression, and even alcohol and drug dependencies (5). These psychosocial problems in the chronic phase often hinder independent functioning and participation in society. The complexity and magnitude of these problems may require specialized comprehensive rehabilitation. Several comprehensive rehabilitation programmes addressing the long-term psychosocial consequences of brain injury have been developed (6). In their review, Malec & Basford (6) classified the comprehensive rehabilitation programmes for chronic sequelae of brain injury into: (i) neurobehavioral programmes: being “residential programmes that provide intensive behavioural treatment to brain injury patients with severe behavioural disturbances”; (ii) residential community reintegration programmes: providing “integrated cognitive, emotional, behavioural, physical, and vocational rehabilitation to patients who cannot participate in outpatient programmes because of either severe cognitive and behavioural impairments or the unavailability of outpatient services”; and (iii) holistic day-treatment programmes: offering “integrated, multimodal rehabilitation”, as defined and described by Ben-Yishay & Prigatano (7).

Cicerone et al. (8, 9) performed 2 literature reviews on the effects of cognitive and psychosocial rehabilitation, including research published up to 2002. They stated that “there is also evidence that gains in community functioning can be achieved by patients one or more years post-injury” and recommended comprehensive rehabilitation as a practice guideline for moderate to severe traumatic brain injury (TBI). However,
they did not distinguish between the above-mentioned types of comprehensive treatment programmes, nor did they systematically address the impact of late rehabilitation.

Turner-Stokes (10) recently combined a Cochrane Review (previously published in 2005) with an approach using less rigorous design demands, yet excluding low-quality studies. She stated that: "although there is encouraging data from non-randomized clinical trials to support the benefits of behavioural management programmes, community rehabilitation and long-term intervention, this evidence is not yet sufficient to support strong recommendations". This review contained only 4 studies concerning late rehabilitation, and the precise period for the inclusion of studies was not indicated. Moreover, the focus was primarily on the comparison of the 2 review approaches, whereas the specific patient characteristics and the content of the different comprehensive treatment programmes were not discussed.

Hence, little is known about the effectiveness of comprehensive treatment programmes for patients in the chronic phase after severe brain injury in view of their specific goals. Indeed, substantial differences between studies can be expected regarding the applied interventions within the various comprehensive programmes (i.e. neurobehavioural, residential community reintegration and holistic day-treatment), based on different patient characteristics. To our knowledge, no systematic review has yet been conducted to address these specific issues. The aim of this review was, therefore, systematically to address the following questions: (i) Are the different comprehensive treatment programmes for the management of long-term psychosocial problems in patients with severe acquired brain injury effective in terms of reducing these problems and improving community integration?, (ii) What are the specific patient characteristics for the various comprehensive treatment programmes?, and (iii) What are the essential intervention characteristics of these programmes?

**METHODS**

**Selection of articles**

A systematic literature search was performed in the primary electronic databases covering this research area: PubMed, PsychINFO and Psyclit, including articles published between 1990 and 2008. The year 1990 was chosen as a starting point because Turner-Stokes (10) and Ciccone et al. (8, 9) covered the period before 1990 and found no high-quality studies concerning comprehensive rehabilitation programmes for patients with chronic brain injury. A quick search performed by the first author confirmed this finding. Details of the search strategies are shown in Appendix 1. Grey literature was identified by additional hand-searching of the reference lists of the review articles on evidence-based cognitive rehabilitation (2, 8–11). Moreover, reference lists from the other identified articles were screened to complete the initial list of references. The first author performed the literature search as well as the primary selection of articles based on their abstracts. The primary selection of articles for this review was performed based on the criteria described in Table I. When selection was not possible based on the abstract alone, or when abstracts were not available, inclusion or exclusion was based on the full text versions.

Studies were included only when they addressed the effect of comprehensive treatment in a randomized controlled trial (RCT), a controlled comparative study or an uncontrolled longitudinal cohort study. Cross-sectional studies or reviews were excluded, because these study designs cannot assess treatment effects or deliver new (original) information on treatment effects, respectively. Furthermore, studies could be included when they addressed the chronic phase of severe acquired brain injury in adult patients, aged 19–64 years. For this specific purpose, "chronic" was operationalized as one year post-onset (6). The majority (>50%) of the patients included in the study had to be in the chronic phase, or the results of the chronic patients had to be described separately.

**Quality assessment**

After the first selection, the methodological quality of the RCTs was assessed using the CONSORT Statement Checklist (12–16). The quality of potentially relevant articles with other study designs was judged using an adaptation of the Consort Statement, which was constructed in a consensus meeting with all authors. A set of minimal criteria for internal validity was established. Studies were definitively included when they fulfilled each of the following criteria: (i) the inclusion criteria were described; (ii) the content of the intervention was described at least globally; (iii) the number of patients was a minimum of 20 for uncontrolled cohort studies and at least 10 patients per treatment condition for controlled comparative studies or RCTs; (iv) effect sizes and statistical significance were reported; (v) at least one brain injury severity measure was described; and (vi) loss to follow-up was less than 20% (17).

**Data extraction**

When the methodological quality was considered sufficient, the first (GJG) and second (CVH) authors reviewed the articles separately and extracted the following data: (i) study characteristics (design, outcome domains/measures, duration of follow-up, and reported effects); (ii) patient characteristics (inclusion and exclusion criteria, number of participants, sex, age, aetiology, severity, time post-onset, baseline functioning); and (iii) intervention characteristics (content, duration, intensity, inpatient or outpatient treatment, rehabilitation team). Consensus was obtained in all instances and no discrepancies had to be settled by an independent third reviewer.

**RESULTS**

**Selection and assessment of studies**

The primary literature search of databases, the hand search of the reference lists of review articles (2, 8–11), and the screen-
ing of the reference lists from all identified articles resulted in 425 potentially relevant studies. The primary selection based on title, abstract, and (when necessary) full text yielded 47 potentially relevant studies. These 47 studies were subjected to quality assessment, after which 13 studies were finally included for review (Fig. 1).

The characteristics of the design, patient population, and the treatment programme of the 13 selected studies are summarized in Tables II–IV. The studies can be categorized based on the applied treatment programme using the definitions set out by Malec & Basford (6): neurobehavioural programmes (n = 1), residential community reintegration programmes (n = 3), and day-treatment programmes (n = 9).

Study outcomes
The applied study designs, measurement instruments and observed treatment effects are described in Table II. Two studies were RCTs (18, 19) and 5 other studies were (non-randomized) controlled comparative studies (20–24). Two of these used matching (22, 24). The remaining 6 studies were uncontrolled longitudinal cohort studies. Study outcomes are discussed on the basis of study design and applied treatment programme.

Randomized controlled trials
Day-treatment programmes. In a RCT by Cicerone et al. (18) the experimental treatment was a comprehensive day-treatment group programme, emphasizing the integration of interventions directed at deficits, emotional difficulties and interpersonal behaviour with feedback from the group on the performance of the patient and active self-evaluation aimed at adaptation to chronic limitations. The control treatment was an interdisciplinary individual day-treatment programme targeting deficits including the retraining of cognitive functions. Both the experimental and control group comprised 34 patients. Treatment duration was 15 h per week for 16 weeks. Validated instruments (Community Integration Questionnaire (CIQ) and the Perceived Quality of Life scale (PQoL)) were used as primary outcome measures and the follow-up period was 6 months. The experimental treatment had a moderate clinical effect on community functioning (assessed with the CIQ) and a small clinical effect on life satisfaction (assessed with the PQoL) compared with the control treatment. The experimental treatment showed significantly greater improvements than the control treatment and these gains were maintained at 6 months follow-up.

The RCT performed by Ruff & Nieman (19) also compared 2 day-treatment programmes. The experimental group received cognitive remediation and problem-solving training, whereas the control group received a programme aimed at enhancing psychosocial functioning and activities of daily living. Both the experimental and control groups comprised 12 patients who received treatment for 12 h per week during 8 weeks. A validated outcome instrument (Katz Adjustment Scale (KAS)) was used, but there was no follow-up. Both treatments appeared equally effective: patients became less socially withdrawn and depressed. Unfortunately, despite randomization, there were baseline differences for coma duration, with a shorter duration in the experimental group. This inequality at baseline was most likely due to the small number of patients. Another drawback of this study was the potential lack of contrast between the experimental and control treatment.

Residential community reintegration programmes. No RCT was identified.

Neurobehavioral programmes. No RCT was identified.

Controlled comparative studies
Day-treatment programmes. In the first comparative study, Rattock et al. (20) compared 3 day-treatment mixes. Their treatment programme was changed over the years and patients undergoing these separate mixes were compared. Differences in treatment were related to the availability and duration of cognitive remediation, the participation in small-group interpersonal exercises and the duration of personal counselling. The treatment groups comprised 18–23 patients. Patients received 400 h of treatment during 20 consecutive weeks. A combination of validated neuropsychological measures (such as the Wechsler Adult Intelligence Scale, Benton Visual Retention Test, etc.) and descriptive non-validated instruments was used. There was a follow-up only with regard to employability at 3 and 9 months. The description of absolute effect sizes was limited. All treatment mixes appeared effective on most neuropsychological measures, behavioural measures,
<table>
<thead>
<tr>
<th>Table II. Treatment programmes</th>
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<tbody>
<tr>
<td>Author, year (Ref)</td>
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<td><strong>Neurobehavioral treatment programmes</strong></td>
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<td>Wood et al., 1999 (30)</td>
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<td><strong>Residential community reintegration treatment programmes</strong></td>
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<td>Wilier et al., 1999 (24)</td>
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<td>Gray &amp; Burnham, 2000 (28)</td>
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<td><strong>Day-treatment programmes</strong></td>
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<tr>
<td>Ruff &amp; Nieman, 1990 (19)</td>
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<td>Christensen et al., 1992 (25)</td>
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<td>Rattok et al., 1992 (20)</td>
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<td>Teasdale et al., 1993</td>
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<td>Malec, 2001</td>
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<td>Malee et al., 2004</td>
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<td>Sarajuuri et al., 2005</td>
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<td>Hashimoto et al., 2006</td>
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<td>Cicerone et al., 2008</td>
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*Results are summarized as reported in the original studies.

+: a positive difference in favour of the experimental group/compared with themselves; 0: no difference between the group/compared with themselves; -: a negative difference in adverse of the experimental group/compared with themselves; C: control; CDT: Comprehensive Day-treatment; CES-D: Centre for Epidemiological Studies-Depression; CIQ: Community Integration Questionnaire; E: experimental; ERS: Employability Rating Scale; ES: effect size; EuroQol: EuroQol group quality of life scale; FAM: Functional Assessment Measure; FIM: Functional Independence Measure; GAS: Goal Attainment Scaling; HALS: Modified Health and Activity Limitation Survey; ICRP: Intensive Cognitive Rehabilitation Programme; ILS: Independent Living Scale; KAS: Katz Adjustment Scale; MPAI: Mayo-Portland Adaptability Inventory; PAI: Portland Adaptability Inventory; PqoL: Perceived Quality of Life; QCIQ: Quality of Community Integration Questionnaire; RCT: randomized controlled trial; RDRS: Rappaport Disability Rating Scale; SRP: Standard Neurorehabilitation; VIS: Vocational Independence Scale.
<table>
<thead>
<tr>
<th>Author, year (Ref)</th>
<th>Inclusion and exclusion criteria</th>
<th>Patients: $n$, M/F, age</th>
<th>Aetiology, time post-onset</th>
<th>Severity TBI: GCS, coma duration, PTA duration</th>
<th>Baseline functioning (at start of treatment)</th>
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<tr>
<td><strong>Neurobehavioural treatment programmes</strong></td>
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<tr>
<td>Wood et al., Unable to live independently and persisting history of aggressive behaviour. Criteria not specified. Minimum of 6 months of rehabilitation.</td>
<td>$n = 76$, Drop-out 0%</td>
<td>TBI 12, stroke 1, encephalitis</td>
<td>PTA 23.5 days</td>
<td>Incapable of independent life in the community, dependent on others for their day to day social and domestic functioning. Neurobehavioural deficits on admission: aggression, disinhibition, mood disorders, impulsiveness, poor insight. Cognitive: not described.</td>
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<tr>
<td>Residential community reintegration treatment programmes</td>
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<tr>
<td>Willer et al., 1999 (24)</td>
<td>E: Severe brain injury, multiple disabilities and behavioural disabilities, often excluded from post-acute rehabilitation and referred to chronic care hospitals; C: from the roster of a support group.</td>
<td>$n = 10252$, Drop-out 3 before treatment, 3 at FU: Total 6 (1.15%).</td>
<td>TBI 3 years</td>
<td>Coma &gt;72 h, most (18 of 23) &gt;3 weeks</td>
<td>E: Prior in acute care (1/23), inpatient rehabilitation (7/23), chronic care/psychiatric (7/23), own home family (8/23), severe behavioural disabilities (not specified), not accepted by other regional programmes, HALS Total 20.39, CIQ Total 10.94. C: Lived with family (20/23), inpatient rehabilitation (2/23) or chronic care facility (1/23). HALS Total 20.30, CIQ Total 13.13 RDRS 9.9, FIM+FAM motor score 67.5, FIM+FAM cognitive score 48.4. No description of behavioural or cognitive functioning. Almost 60% were referred from acute care facilities.</td>
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<tr>
<td>Gray &amp; Burnham, 2000 (28)</td>
<td>Severe brain injury, adult age, “slow to recover” with perceived potential to participate and benefit, but not appropriate for other community- or facility-based rehabilitation programmes</td>
<td>$n = 349$, Drop-out 0%</td>
<td>TBI 16%, SAH 9%, Anoxia 7%, PTA in 89.6% &gt;7 days</td>
<td>GCS 5.9</td>
<td>Behaviour: 33% had alcohol and drug abuse problems. 41.6% was living independently, 21% were following education and 37.5% were working. CQ Total 14.0, CES-D 20.1, ERS 2.3. Cognitive: Many slow in processing information, some had attention deficits, some participants had executive problems. Severe memory problems were infrequent.</td>
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<td>Geurtsen et al., 2008 (29)</td>
<td>Brain injury and having severe problems in social areas, emotional areas, and labour/work integration</td>
<td>$n = 24$, Drop-out 2 (8.3%)</td>
<td>TBI 18, Stroke 3, tumour GCS 5.9</td>
<td>Coma duration 15.1 days (range 3–42 days)</td>
<td>Behaviour and cognitive not described.</td>
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<td><strong>Day-treatment programmes</strong></td>
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<tr>
<td>Ruff &amp; Nieman, 1990 (19)</td>
<td>Age between 16 and 65 years, moderate to severe head injury (coma at least one hour), chronicity between 1–7 years, no premorbid history of psychiatric disorders requiring hospitalization, sufficient cognitive functioning, sufficient expressive and receptive language skills, sufficient vision, at least one functional hand, motivation and availability to participate in 8-week programme and evaluations</td>
<td>$n = 24$, Drop-out 1 (4.2%, missing data)</td>
<td>Acquired brain injury: aetiology not specified.</td>
<td>E coma 25.5 days (range 0.5–47)</td>
<td>Behaviour and cognitive not described.</td>
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</table>
Christensen, Brain injury, 16 years and older, good family support, return to employment or education should be feasible, 7 years of grade school, insight into own situation and/or motivation, partly preserved ability to communicate, ambulatory
Exclusion: progressive central nervous system illness, significant history of substance abuse, psychiatric illness requiring treatment, chronic deteriorating illness

Rattok et al., 1992
TBI with at least 1 hour coma or hypoxia with at least 12 h of coma, at least 1 year post-injury, unsuccessful prior vocational or educational rehabilitation, residence in greater New York metropolitan area during study, age between 18 and 55 years, functional English, at least partial independence in basic self-care, independence in ambulation, at least one functional hand, continence, minimal IQ of 80, motivation for rehabilitation, intact basic level of social appropriateness, manageable in non-coercive environment
No past or present significant psychiatric complications, no history of significant alcohol or drug abuse, no history of sociopathy, no major aphasic or dysarthric difficulties

Teasdale et al., 1993
Brain injury, age at least 16 years, good family support, subsequent education or employment considered realistic, at least 7 years grade school, insight into own situation, at least partial ability to communicate, ambulatory
No progressive central nervous system illness, no significant history of substance abuse, no long-term psychiatric illness requiring treatment, no chronic deteriorating illness

Malec, 2001
Brain injury, limited self-awareness, cognitive impairments, ineffecual communication and social skills, limited emotional and behavioural self-control. Independent in mobility, functional communication, sufficient memory for carry over of new information, no significant risk to selves or others
Note: only 25% referred for treatment admitted

n = 46
Drop-out 0 (0%)
M/F 28/18
Age: 30 SD 10.8 (range 16–58)

n = 59
Drop-out 0 (0%)
E1: n = 23, M/F 15/8, Age: median 26.8
E2: n = 18, M/F 16/2, Age: median 27.1
E3: n = 18, M/F 11/7, Age: median 28.5

n = 36
Drop-out 1 (2.8%)
TBI: M/F: 73%/27%
Age: 27.2 (SD 9.1).
CVA: M/F: 43%/57%
Age: 36.4 (SD 12.1)

n = 113
Drop-out during treatment 17, loss to FU 1. Total 18 (16%)
Remaining n = 96
M/F: 73%/27%
Age: 34.2
TBI 47.8%, CVA 30.4%, Hypoxia 15.2%, Rest 6.5%

Time post-onset 2.9 years (range 0.5–14.2)
Note 1: Same patients as in Christensen, Pinner et al 1992
Note 2: TBI and CVA seem to be reported in Teasdale (1993) too.

Acquired brain injury: 56 TBI and 3 Hypoxia
Time post-onset:
E1: median 32 months
E2: median 33.8 months
E3: median 40.2 months

Hemi-paresis 28%, impairments of fine motor dexterity 24%, dysarthria 13%, ataxia 9%

E3: BCI 7.2, self-esteem 13.12, self-appraisal 6.47, interpersonal empathy 20.82, social cooperation 20.50

41 cognitive tests pre and post measurement
All scores displayed but no description of meaning/explanation

TBI n = 22
CVA n = 14
Note: Same patients seem to be reported in Christensen et al., 1992

Time post-onset:
TBI: 3.1 years (SD 2.8)
CVA: 2.6 years (SD 2.2)

TBI 72%, CVA 19%, Rest 9%

Time post-onset 4.6 years

None were active in employment and more than one-third had experienced failed attempts to return to work. 31% receiving help pre-treatment. Further characteristics not specified

GCS:
Mild TBI 7%
Moderate 7%
Severe 82%

47% living independently, 84% unemployed, 6% sheltered work, 3% supported, 3% transitional and 4% independent work placement

MPAI-22 score: 546.3, determined mean 102.4 days before treatment

Behaviour and cognitive not described
Cicerone et al., 2004
ICRP: medical stable, independent self-care skills, cognitive able to participate in treatment, TBI, 18 years or older, adequate language expression and comprehension, family member or other participate in treatment plan
Exclusion: current substance abuse or psychiatric disturbance
SRP: inclusion and exclusion criteria not specified

Sarajuuri et al., 2005
E + C: Inclusion: independence daily life, only slight physical disabilities, age 16–55 years, completed compulsory education, adequate potential to achieve productivity
Exclusion: significant psychiatric history, alcohol or drug abuse, previous brain injury, another malignant disease during follow-up
Matching on: age, sex, education level, injury severity, time since injury, pre-injury employment

Hashimoto et al., 2006
E + C: Near independent in ADL, goal of returning to work or school, having no place to visit frequently except outpatient clinic

Cicerone et al., 2008
Inclusion for rehabilitation: medical stable, independent self-care, clinical judgement to benefit from comprehensive rehabilitation
Exclusion for treatment study: TBI at least 3 months post-injury, 18–62 years, adequate language expression and comprehension, require at least 4 months comprehensive treatment, clinical appropriate for both treatments, capable of attending treatment 3 days a week, be capable of giving informed consent
Exclusion: active psychiatric illness, substance abuse or pain preventing compliance to treatment

n = 56
Drop-out 0 (0%)
ICRP n = 27.
SRP n = 29.
M/F: ICRP 17/10
SRP 23/6
Age: ICRP 37.8, SRP 37.1

n = 42, drop-out 3 (7.1%).
Remaining n = 39 described
E: n = 19, M/F 16/3
Age at injury: 30.5
All TBI
42.4 months
C: n = 20
M/F 17/3
Age at injury: 29.5

n = 37
Drop-out 0 (0%)
E: n = 25, M/F 18/7
Age: 26.6 (range 19–56)
C: n = 12, M/F not specified.
Age: 28.7

n = 68
Drop-out 6 (8.8%)
ICRP n = 34
SRP – 34.
M/F: ICRP 25/9
SRP 21/13
Age: ICRP 38.7, SRP 34.5

All TBI
Time post-onset:
ICRP 33.9 months, SRP 4.8 months

All TBI
Time post-onset:
46.6 months

E: GCS 7.9
C: GCS 8.0

E: 19 of 25 severe
5 moderate;
1 not clear
Time post-onset 527.3 days
C: 10 of 12 severe TBI, rest?
Time post-onset 487.6 days

Severe TBI 59%
moderate TBI 13%
undetermined 3%

Moderate to severe TBI 89%
mild TBI 11%

ICRP: CIQ: Total 11.6, Home 3.1, Social 7.0, Productivity 1.4
Neuropsychological functioning: overall T score: 35.5. Behaviour not described
SRP: CIQ: Total 16.7, Home 3.5, Social 6.8, Productivity 3.4
Behaviour and cognitive not described

ADL: activities of daily living; BCI: Behavioral Competence Index; BI: brain injury; C: control; CES-D: Centre for Epidemiological Studies-Depression; CIQ: Community Integration Questionnaire; CVA: cerebral vascular accident; E: experimental; ERS: Employability Rating Scale; FAM: Functional Assessment Measure; FIM: Functional Independence Measure; FU: follow-up; GCS: Glasgow Coma Scale; HALS: Modified Health and Activity Limitation Survey; ICRP: Intensive Cognitive Rehabilitation Programme; IQ: intelligence quotient; MPAI: Mayo-Portland Adaptability Inventory; PIQ: Perimal IQ; PTA: post-traumatic amnesia; SAH: subarachnoid haemorrhage; SD: standard deviation; SRP: standard neurorehabilitation; TBI: traumatic brain injury; TIQ: total IQ; VIQ: verbal IQ; WAIS-R: Wechsler Adult Intelligence Scale-Revised.
Table IV. Intervention characteristics

<table>
<thead>
<tr>
<th>Author, year (Ref)</th>
<th>Intervention</th>
<th>Treatment characteristics: duration/intensity</th>
<th>Treatment team</th>
<th>In- or outpatient</th>
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<tr>
<td><strong>Neurobehavioural treatment programmes</strong></td>
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<tr>
<td>Wood et al., 1999 (30)</td>
<td>Social and neurobehavioral rehabilitation directed at recovering functional and behavioral skills for semi-independent living in the community relying heavily on therapy care assistants</td>
<td>Duration mean 14.3 (range 6–32) months</td>
<td>Relying heavily on therapy care assistants, rather than on professional therapy staff. Staff-patient ratio and treatment team not specified</td>
<td>Inpatient</td>
</tr>
<tr>
<td>Wilier et al., 1999 (24)</td>
<td>Structured social environment based on neurobehavioral model by trained and guided paraprofessionals; goal-directed rehabilitation: content not specified</td>
<td>E: treatment by professionals (physician, OT, PT, ST) and trained paraprofessionals. Duration: 8 months</td>
<td>E: staff-patient ratio not specified. Treatment team: professionals (physician, OT, PT, ST), neuropsychologist team coordinator and trained paraprofessionals C: none or OT, PT, neuropsychologist, case manager or home-maker service. Staff-patient ratio not specified</td>
<td>E: Inpatient C: Outpatient</td>
</tr>
<tr>
<td>Gray &amp; Burnham, 2000 (28)</td>
<td>Comprehensive multidisciplinary rehabilitation in a hospital setting for slow-to-recover brain injury patients</td>
<td>Duration mean 359 days</td>
<td>Staff-patient ratio not specified Treatment team: medicine, psychiatry, nursing, PT, OT, dietetics, ST, psychology, neuropsychology, social work, recreation therapy</td>
<td>Inpatient</td>
</tr>
<tr>
<td>Geurtsen et al., 2008 (29)</td>
<td>Three modules (independent living, social-emotional, work). Training in safe therapeutic environment with continuous feedback on behaviour. Training skills. Increasingly applying learned skills in daily life at home. Relatives are actively involved and supported</td>
<td>Duration 198.9 days</td>
<td>Staff-patient ratio not specified Treatment team: neuropsychology, physiatry, neuropsychiatry, OT, cognitive therapy, social work, ST, PT, nurses</td>
<td>Inpatient</td>
</tr>
<tr>
<td><strong>Residential community reintegration treatment programmes</strong></td>
<td></td>
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</tr>
<tr>
<td>Ruff &amp; Nieman, 1990 (19)</td>
<td>E: cognitive remediation: attention, visuospatial abilities, learning and memory, problem-solving C: day-treatment programme focussed on psychosocial functioning and activities of daily living</td>
<td>Duration: E and C: both 8 weeks 4 days a week</td>
<td>Staff-patient ratio and treatment team not specified</td>
<td>Outpatient</td>
</tr>
<tr>
<td>Christensen, 1992 (25)</td>
<td>Group treatment 10–15 persons: Cognitive training, special education lessons, psychotherapy, voice therapy, workshops, physical training, lectures, relatives group</td>
<td>Duration/intensity: Phase 1: 4 months group treatment, 4 days a week for 6 h per day Phase 2: monthly group meeting. Furthermore coordination of gaining employment, education and disability pensions. Intensity not specified</td>
<td>Staff-patient ratio not specified. Treatment team: neuropsychologist, clinical psychologist, special education teacher, ST, voice therapist, PT</td>
<td>Outpatient</td>
</tr>
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<td>Christensen, 1992 (25)</td>
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<td>Staff-patient ratio not specified. Treatment team: neuropsychologist, clinical psychologist, special education teacher, ST, voice therapist, PT</td>
<td>Outpatient</td>
</tr>
<tr>
<td>Rattok et al., 1992 (20)</td>
<td>All 3 treatment packages: Attention training 80 h, Community activities 60 h E1: Cognitive remediation 120 h, Small-group interpersonal exercises 100 h, Personal counselling 40 h E2: Cognitive remediation 90 h, Small-group interpersonal exercises 200 h, Personal counselling 60 h E3: Cognitive remediation 200 h, Small-group interpersonal exercises 0 h, Personal counselling 60 h</td>
<td>Duration/intensity: 400 h during 20 consecutive weeks 5 h per day 4 days per week Those judged by staff to be viable for work trials were assigned to vocational counsellor. Vocational trials ranged from 12 weeks to 6 months. Actual job search and placement was initiated by vocational counsellor. Patients were followed up indefinitely on work status and general adjustment. Some were placed immediately after remedial phase without work trials One psychologist per 2 patients</td>
<td>Staff-patient ratio not specified</td>
<td>Outpatient</td>
</tr>
</tbody>
</table>
Group treatment 10–12 patients: cognitive therapy, speech and language therapy and psychotherapy (individual and group), special education when required and physical exercise. Relatives group sessions twice a month.

Most group treatment according to model of Prigatano and Ben-Yishay and others. General goals: self-awareness, coping and compensation skills, personal organization, emotional and behavioural self-management, participation in work and leisure activities, health maintenance.

ICRP: structured and integrated individual and group treatment; cognitive remediation, increasing awareness; interpersonal communication; psychotherapy; family support; work trials and placements.

SRP: primarily physical, occupational, speech and neuropsychological therapies determined to individual needs. Some recreational, educational, or psychological counselling when needed.

ICRP: integrating interventions for cognitive deficits, emotional difficulties, interpersonal behaviours and functional skills within a therapeutic community with performance feedback and active self-evaluation. Individual (4 h) and group (11 h) therapy.

SRP: individual interdisciplinary treatment, primarily discipline-specific interventions. Physical, occupational, and speech therapies. One hour neuropsychological treatment. Some patients psychological, recreational, vocational or educational. Individual (≥ 12 h) and group (≤ 3 h) therapy.

Duration: 4-5 months group treatment 4 days a week for 6 h per day. Followed by 6 months contact and meetings with emphasis on return to work or educational environment.

Duration: ICRP 3.8 months
ICRP 4 days per week 5 h per day (typically 15 h therapy per week) + 1 day per week work trial.

Duration: SRP 3.9 months
SRP: initially 15 h per week and adjusted varying from 12 to 24 h per week. Intensity not specified.

Duration: ICRP + SRP
Duration: 16 weeks
Intensity: 15 h per week therapy = 240 h

Graduates: 189.5 days (27.07 weeks)

Drop-outs: 43.4 days (6.2 weeks)

Intensity not specified

SRP: Staff-patient ratio not specified. Treatment team: PT, OT, neuropsychological therapists, recreational therapist, vocational/educational therapist, psychological counsellor.

E: Staff-patient ratio not specified. Treatment team: PT, OT, neuropsychologists, recreational therapist, vocational/educational therapist, psychological counsellor.

C: Staff-patient ratio not specified. Treatment team: neuropsychologist, OT, OT-assistant, PT, recreational therapist, rehabilitation nurse, social worker, speech pathologist, vocational counsellor, physiatrist.

ICRP Staff-patient ratio not specified. Treatment team: not described, vocational therapist supervises work trials.

E: Inpatient C: Previous inpatient/outpatient.

Outpatient doctor, nurse, social worker, clinical psychologist, ST, vocational rehabilitation counsellor, OT, welfare facility life advisor, PT, rehabilitation gymnastic trainer.

ICRP: Staff-patient ratio not specified. Treatment team: not described, neuropsychologist.

SRP: Staff-patient ratio not specified. Treatment team: PT, OT, ST, neuropsychological therapist, recreational therapist, vocational/educational therapist, psychological counsellor.

C: no active treatment

Outpatient team: neurologist, rehabilitation nurse, social worker, 2 ST, OT, PT. Consultations by neuropsychiatrist, neuroradiologist and physiatrist.

E: Extended inpatient care, extended day care, extended outpatient care.

C: no active treatment

Outpatient team: not described, vocational therapist.

SRP: Staff-patient ratio not specified. Treatment team: PT, OT, neuropsychological therapists, recreational therapist, vocational/educational therapist, psychological counsellor.

E: Staff-patient ratio not specified. Treatment team: PT, OT, neuropsychologists, recreational therapist, vocational/educational therapist, psychological counsellor.

C: control; E: experimental; ICRP: intensive cognitive rehabilitation programme; OT: occupational therapy; PT: physical therapy; SRP: standard neurorehabilitation; ST: speech and language therapy.
Residential community reintegration programmes. Two original cohort studies have compared 56 patients with TBI who were allocated either to an experimental integrated comprehensive treatment or to a control treatment that was less intensive and less structured. There was a pre- and post-treatment measurement with a validated instrument (CIQ), but no follow-up. The experimental treatment seemed to result in a higher level of community integration, but allocation bias was a major confounding factor (21).

In the third comparative study, Sarajuuri et al. (22) offered day-treatment to 19 patients who were compared with patients with similar demographic and injury characteristics and who were seen for neuropsychological assessment only. The treatment duration was 7.5 h per day, 5 days per week for 6 weeks. After the training, the patients received neuropsychological support and coaching in work or education. There was no direct post-treatment measurement, only a follow-up measurement at 2 years. This study showed significant improvements in terms of productivity compared with the control group. Only descriptive instruments of work and education were used as outcome measures.

Hashimoto et al. (23) compared the effects of day-treatment with a control intervention in 25 and 12 patients, respectively. All patients were included from the same hospital and at the same time, but the selection procedure was not described. The treatment duration varied per group, from 4 to 16 h per week, for 3–6 months. The mean duration of treatment was 100 h. There were pre- and post-treatment measurements, but no follow-up. Furthermore, the control treatment was not specified. Despite this, the authors reported positive effects on the validated outcome measures (CIQ, Functional Independence Measure + Functional Assessment Measure (FIM/FAM)) in the intervention group compared with the control group.

Residential community reintegration programmes. As for residential treatment, in the fifth comparative study by Willer et al. (24), 23 patients were compared with a matched sample of 23 patients receiving limited home-based services or outpatient treatment. The residential treatment offered a structured social environment based on neurobehavioural principles in which goal-directed interventions were offered; however, its content was not specified. The duration of the residential treatment was 8 months, but the intensity was not specified. The control group received a variety of home-based or outpatient services of variable intensity and duration. Validated outcome measures were the Modified Health and Activity Limitation Survey (HALS) and the CIQ. The study showed greater improvement in functional abilities and community integration in the group receiving the residential treatment. At one-year follow-up, the functional gains and the level of community integration were maintained.

Neurobehavioural programmes. No comparative study was identified.

Uncontrolled longitudinal cohort studies
Day-treatment programmes. Two original cohort studies have been conducted on the effects of day-treatment programmes (25, 27). Christensen (25) followed 46 patients and showed a significant increase in working hours after treatment, which was maintained at one-year follow-up. However, only descriptive non-validated instruments were used. Teasdale et al. (26) seemed to present the 36 patients with TBI and stroke of the Christensen (25) study with the same results.

Malec (27) followed 96 patients with validated (Portland Adaptability Inventory, Mayo-Portland Adaptability Inventory) and descriptive outcome measures. This study showed positive effects after treatment on employment, diminished care utilization, and independent living. These effects were maintained at one-year follow-up.

Residential community reintegration programmes. Two cohort studies were published that focused on the effectiveness of residential treatment (28, 29) in addition to the comparative study by Willer et al. (24). Gray et al. (28) conducted a historic cohort study using a database of 349 low-functioning patients who did not classify for regular rehabilitation. They used validated instruments (FIM/FAM, Rappaport Disability Rating Scale (RDRS)) and demographic data. They showed significant functional improvements of patients compared with other types of brain injury rehabilitation programmes.

Geurtsen et al. (29) performed a prospective cohort study of 24 patients with behavioural deficits leading to social, emotional, and vocational integration problems. They had a follow-up of one year and used a combination of validated (CIQ, Centre for Epidemiological Studies-Depression, EuroQol group quality of life scale) and descriptive outcome measures. This study showed significant improvements in various domains of community integration (living situation, work) at discharge and at one-year follow-up.

Neurobehavioural programmes. One cohort study was directed at the effects of a neurobehavioural treatment programme (30). The neurobehavioural intervention aimed to restore behavioural and functional skills for semi-independent living in the community. Descriptive measures for living arrangement, employment, and care utilization were used. The study had a variable follow-up period with a minimum of one year and a mean of 2.8 years, and showed a significant treatment effect in terms of improved living arrangements, hours of care required, and employment. These effects were maintained at follow-up (30).

Patient characteristics
The characteristics of the study populations are described in detail in Table III. The inclusion criteria were sufficiently described in 6 studies (18, 20, 25–27, 29). In the other 7 studies the inclusion criteria were only described globally (19, 21–24, 28, 30). Determining what treatment was directed at which type of patient was impossible due to the limited information provided about baseline cognitive or behavioural functioning. Only 2 studies gave a more extended description of functioning and problems before treatment (29, 30). All studies together included 982 patients, of whom 72.5% had sustained a TBI. Other diagnoses were stroke/subarachnoid haemor-
rhage (15.3%), anoxia (3.6%), other brain injuries (5.4%), and non-specified brain injuries (2.9%). The comprehensive treatment programmes were directed at severe and complex brain injury patients (Glasgow Coma Score 3–8, coma duration > 6 h or post-traumatic amnesia duration > 24 h; (31)). The exact numbers of mild, moderate or severe TBI patients were specified in a limited number of studies only (18, 21, 23, 27). The mean age of the patient groups varied from 26.6 to 39.4 years. Overall, 72.3% of the included patients were male, 26.5% were female, whereas 1.2% of the cases were unspecified in terms of gender.

**Intervention characteristics**

The characteristics of the interventions are described in detail in Table IV. In 6 studies the content of the intervention was described only globally (19, 23, 24, 26, 28, 30). The neurobehavioural intervention (30) was directed at restoring behavioural and functional skills for (semi-)independent living in the community for severely behaviourally disturbed patients. The residential community reintegration programmes had all been developed for specific purposes. One programme was directed at patients who were excluded from regular rehabilitation in the chronic phase (24). Another programme was aimed at low-functioning patients (28), and a third programme was directed at the reintegration of chronic patients with social, emotional and vocational integration problems due to behaviour disorders and/or substance abuse (29). Finally, the applied day-treatment programmes were group programmes directed at cognitive training, and improving self-awareness, coping and compensation skills using neuropsychotherapy (18–23, 25–27).

The duration of the applied treatments was often not exactly specified. The neurobehavioural programme lasted 14.3 months (30). The duration of the residential community reintegration programmes was from 28.4 weeks (29) to 51.3 weeks (28). The duration of the day-treatment programmes was the shortest, and varied between 6 weeks (22) and 27.1 weeks (27). The treatment intensity was specified in only 4 studies (18–20, 29). One comparative study specified the treatment intensity only for the experimental group (21). The hours of therapy varied from 36 to 400 in day-treatment (18–21) and 254 (29) in a residential treatment programme, whereas the other studies did not report on intensity.

The members of the rehabilitation team were described in only 10 studies (18, 20–24, 25, 27–29). The neurobehavioural intervention (30) relied on therapy care assistants. It was not specified who coached and trained these assistants. The residential community reintegration programmes were all multidisciplinary (24, 28, 29). The day-treatment programmes varied from therapy by psychologists alone (20) to multidisciplinary interventions (18, 22, 23, 25, 27). Cicerone et al. (18, 21) specified the therapists only for the control treatment. Some studies (19, 26) did not specify the therapists at all. The neurobehavioural programme and residential community reintegration programmes were all inpatient programmes, but Willer et al. (24) used an outpatient group as a control. The day-treatment programmes were given on an outpatient basis, but the patients in the study by Sarajuuri et al. (22) stayed in an inpatient setting during the treatment. Only the day-treatment interventions were described (22).

**DISCUSSION**

This systematic review of the effectiveness of comprehensive rehabilitation programmes for chronic patients with severe brain injury identified 13 relevant articles that fulfilled pre-established minimal criteria for internal validity. Seven studies used comparative designs, of which only 2 were RCTs. These RCTs (18, 19) were both directed at day-treatment programmes showing positive effects on daily life functioning and community integration. The effectiveness of the day-treatment was substantiated by 4 controlled, comparative studies (20, 21–23) and 3 uncontrolled longitudinal cohort studies (25–27). The positive effects after treatment were maintained in all 4 studies with a follow-up (18, 25–27). Residential treatment also led to changes in daily life functioning and social participation, but this was shown by only one comparative study (24). The effectiveness of residential treatment was substantiated by 2 cohort studies (28, 29) showing positive effects of these treatment programmes on daily life functioning, community integration and employment. The functional gains were maintained at one-year follow-up (24, 29). Only one study (30) investigated a neurobehavioural treatment programme showing improved functioning in several life areas (living accommodation, employment, hours of care needed) that was maintained at follow-up.

The first research question concerning the effectiveness of the comprehensive programmes for treating long-term psychosocial problems in patients with severe acquired brain injury cannot be answered adequately based on the current literature. Generally, it may be stated that daily life functioning and community integration can be enhanced by comprehensive programmes, with the highest level of evidence for the effectiveness of day-treatment programmes. However, for each of the 3 programme types, more qualitatively high-level research needs to be performed. Yet, in severely behaviourally disturbed patients, RCTs are difficult to perform because a control treatment may be unethical or unacceptable to caregivers. In these cases, cohort studies using a waiting period as a control condition may be an alternative to provide more evidence on the effectiveness of comprehensive programmes.

All treatment programmes included relatively young and predominantly male brain injury patients, most of whom had severe TBI, which is in accordance with TBI population rates. In general, the inclusion criteria for the treatment programmes were only marginally described: baseline cognitive and behavioural functioning were specified in only 2 studies (29, 30), while other patient characteristics were not described at all. As a consequence, it must be concluded that the specific patient characteristics for the different comprehensive treatment programmes are not known. In order to accumulate evidence in this field, researchers must elaborate carefully on the patient characteristics in future work. With this informa-
Implications for future research

Given the present lack of high-quality studies, well-designed controlled studies (preferably RCTs) are necessary to further enhance the field of comprehensive treatment programmes for patients with severe acquired brain injury. Although performing an RCT in this area is notoriously difficult, this review shows that, at least in the field of day-treatment programmes, RCTs are possible. When treating patients with severe behavioural disorders in the chronic phase, other ways to control bias appear to be justified, such as using a waiting period before enrolment in the treatment arm. In all types of controlled studies, researchers are strongly encouraged to work according to the CONSORT Statement checklist, describing the general principles of a RCT (12–16) even when using a non-randomized design.

In the same way as for pharmacological trials, the treatment characteristics should be described in detail, including dosage, duration and means of administration (32). The same is true for patient inclusion and exclusion criteria, in order to be able reliably to compare different studies. Editors and reviewers should be very strict in requiring that all studies provide this descriptive information.

Outcomes should always be presented as absolute scores and effect sizes with parameters of central tendency and variation. Effectiveness must be measured with responsive instruments validated in patients with brain injury in the chronic phase. For instance, the CIQ that was used in 5 of the 13 studies in this review is reliable and responsive (33) and is recommended to assess community integration objectively (34). And the World Health Organization Quality Of Life Assessment Abbreviated (35) is a well-validated and responsive instrument for brain injury patients (35). The Centre for Epidemiologic Studies-Depression Scale is a valid instrument to measure mood in this population (36) and the McMaster Family Assessment Device is a reliable and valid tool to measure family functioning (37). In addition, more individually tailored instruments, such as Goal Attainment Scaling, can be used (38).

When sound evidence of the effectiveness of different comprehensive treatment programmes is available, the next steps should entail the comparison of treatment mixes and testing differences in treatment duration and intensity to determine cost-effectiveness. Lastly, better theoretical underpinning of the interventions seems essential and possible using models from neuropsychology and cognitive psychology as well as knowledge from neurobiological research on severe brain injury, for instance about the impact of diffuse axonal injury (39) on the clinical course of cognitive impairments after severe brain injury. The hypotheses based on these models and neuroscientific information can then be tested to improve the results of comprehensive rehabilitation programmes (40).

ACKNOWLEDGEMENT

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REFERENCES


APPENDIX I. Literature search in PubMed, PsychInfo and PsychLit and number of references

<table>
<thead>
<tr>
<th>Text words*</th>
<th>Number of references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain injury + comprehensive rehabilitation</td>
<td>133</td>
</tr>
<tr>
<td>Brain injury + post-acute rehabilitation</td>
<td>80</td>
</tr>
<tr>
<td>Brain injury + neurobehavioral rehabilitation</td>
<td>73</td>
</tr>
<tr>
<td>Brain injury + neurobehavioural rehabilitation</td>
<td>59</td>
</tr>
<tr>
<td>Brain injury + holistic rehabilitation</td>
<td>29</td>
</tr>
<tr>
<td>Brain injury + residential community integration</td>
<td>4</td>
</tr>
</tbody>
</table>

*Limits: human and English and 1990-2008 and adult (19–44) or middle-aged (45–64).