SEVERE BRAIN INJURY:

IMPACT ON FAMILY MEMBERS IN THE EARLY PHASES OF REHABILITATION

PhD thesis by Anne Norup
Severe brain injury: Impact on family members in the early phases of rehabilitation
Severe brain injury: Impact on family members in the early phases of rehabilitation.

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2012
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APPENDIX 1: Paper I: Emotional distress and quality of life in relatives of patients with severe brain injury: the first month after injury

APPENDIX 2: Paper II: Neuropsychological support to relatives of patients with severe traumatic brain injury in the sub-acute phase.


APPENDIX 4: Paper IV: Neuropsychological intervention in the acute phase: a controlled trial investigating the emotional wellbeing of relatives of patients with severe brain injury.

This thesis is submitted as part of the requirements for obtaining the PhD degree at the Faculty of Health and Medical Sciences, University of Copenhagen. The work funding this thesis was carried out primarily at the Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup. A part of the study was conducted in close collaboration with the Neuro Intensive Care Unit, Rigshospitalet, Copenhagen University Hospital.

I initiated and prepared this work while working as a clinical neuropsychologist at the Traumatic Brain Injury Unit 2005-2008. The PhD project started in the autumn of 2008 and was concluded medio 2012, interrupted by maternity leave.

This project was supervised by Professor Erik Lykke Mortensen, Institute of Public Health and Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark, and Lars Siert, Department of Neurorehabilitation, Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup, Denmark.

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Copenhagen 22\textsuperscript{nd} of June 2012

Anne Norup
The primary objective of this thesis was to investigate emotional distress and quality of life experienced by relatives of survivors of severe brain injury during the first year after injury. Moreover, the thesis aimed at identifying predictors of the condition of the relatives during the first year after injury. At last, the thesis investigated whether a neuropsychological intervention consisting of information and emotional support administered in the acute setting had beneficial effects on the emotional distress and quality of life in relatives. The total sample consisted of 94 patients and their relatives, admitted for intensive rehabilitation in the sub-acute phase. The relatives completed a questionnaire regarding quality of life (SF-36) and emotional distress (SCL-90-R) at four or five different assessment points during the first year after injury: in the intensive care unit, at admission to sub-acute rehabilitation, discharge from sub-acute rehabilitation, three months after discharge, and one year post-injury. During the enrolment period, preliminary cross-sectional investigations were conducted, and these findings have been published as a part of this thesis.

The thesis consists of a total of five papers. Paper I reported the preliminary cross-sectional findings of the condition of the relatives at the patients’ admission to sub-acute rehabilitation. The paper reported that the 31 participants had significantly lower quality of life and significantly more symptoms of anxiety and depression compared to a reference population. Relatives of patients with lower level of function and consciousness experienced more depression and anxiety. Paper II assessed the amount of neuropsychological support to relatives during patient’s rehabilitation in a sub-acute unit. On average, the relatives received 18 units of 15 minutes and had six sessions with a neuropsychologist during hospitalisation. A total of 38% of the relatives participated in group sessions. Relatives’ symptoms of anxiety on admission were associated with the number of sessions as well as the amount of support indicating that relatives with more symptoms of anxiety received more support during hospitalisation. Paper III investigated the condition of the relatives during the patient’s stay in a Neuro Intensive Care Unit. Of the 45 relatives, 51% and 69% reported symptoms of anxiety and depression respectively, as well as significantly impaired quality of life compared to normal reference populations. Regression analysis revealed that up to 20% of the variance in depression and anxiety scores could be explained by the CRASH 2 Mortality prediction.
Paper IV investigated the effects of acute neuropsychological intervention to relatives of patients with severe brain injury. Participants were enrolled in an intervention group consisting of 39 relatives, and in a control group comprising 47 relatives. The intervention consisted of supportive and psycho-educational sessions with a neuropsychologist in the acute care setting. An ANCOVA model, adjusted for group differences, showed a borderline significant difference between the intervention and the control group on the anxiety scale and the Mental Health scale favouring the intervention group.

Paper V investigated changes in the condition of the relatives during the first year and found that the development in anxiety and depression was described by two different trajectories. Anxiety symptoms showed a steeper decline during the first three months and a continued decrease at a slower pace during the rest of the year. Depression symptoms decreased significantly over the first six months, and the decline continued the last six months, although not significantly.

All together, this thesis confirmed our clinical experience of relatives being in an emotionally draining and distressing situation during the early phases of rehabilitation, continuing throughout the first year after injury. Moreover, we have emphasised the necessity for future research that implements and investigates the effects of a family intervention program in the early phases of rehabilitation.
DANSK RESUME

Det primære formål med ph.d. projektet var at undersøge den følelsesmæssige tilstand og livskvalitet hos pårørende til patienter med svær hjerneskade og identificere prædiktorer af de pårørendes tilstand i løbet af det første år efter skaden. Derudover undersøgte projektet om en neuropsykologisk intervention bestående af information og emotionel støtte administreret i den akutte fase havde en profiterende indvirkning på den følelsesmæssige tilstand og livskvalitet hos de pårørende.

I alt blev der inkluderet 94 patienter og pårørende i projektet, alle indlagt til intensiv rehabilitering i den sub-akutte fase. De pårørende udfyldte et spørgeskema vedrørende deres livskvalitet (SF-36) og følelsesmæssige tilstand (SCL-90-R) på fem forskellige tidspunkter i løbet af det første år efter patientens skade: på neuro intensivt terapi afsnit, ved indlæggelse til sub-akut rehabilitering, udskrivelse fra sub-akut rehabilitering, tre måneder efter udskrivelse og et år efter skadestidspunktet. Under inklusionsperioden gennemførtes en række præliminære tværsnits undersøgelser, og disse resultater er blevet publiceret som en del af denne afhandling.

Afhandlingen består af fem artikler. Artikel I omhandler de præliminære tværsnits resultater af de pårørendes følelsesmæssige tilstand ved patienternes indlæggelse til sub-akut rehabilitering. Artiklen fandt, at de 31 inkluderede pårørende havde signifikant lavere livskvalitet og signifikant flere symptomer på angst og depression i forhold til en normal population. Pårørende til patienter med lavere funktions- og bevidsthedsniveau oplevede mere angst og depression.

Artikel II undersøgte mængden af neuropsykologisk støtte til pårørende under patientens indlæggelse til sub-akut rehabilitering. De pårørende modtog gennemsnitligt 18 enheder af 15 minutter og havde 6 sessioner med en neuropsykolog under patientens indlæggelse. Pårørende, der scorede høj på angskalaen ved indlæggelsen, modtog mere støtte under patientens indlæggelse. Artikel III undersøgte de pårørendes tilstand under patientens indlæggelse på neuro intensivt terapi afsnit. Ud af de 45 pårørende, 51% og 69% rapporterede symptomer på henholdsvis angst og depression og signifikant nedsat livskvalitet. Regressionsanalyser viste, at optil 20% af variansen i depression og angst kunne forklares af patienternes CRASH 2 Mortality score.

Artikel IV undersøgte effekten af neuropsykologisk intervention til pårørende til patienter med svær hjerneskade administreret i den akutte fase på et neuro intensivt terapi afsnit. Deltagerne blev allokeret til en interventionsgruppe (n=39) og en kontrol gruppe (n=47). Interventionen bestod af støttende og psycho-educationelle sessioner med en neuropsykolog i den akutte fase. En ANCOVA
model justerede for forskelle mellem grupperne og fandt en borderline signifikant forskel mellem de to grupper på angstskalaen og psykisk velbefindende skalaen.

Artikel V undersøgte forandringer i de pårørendes tilstand i løbet af de første år og fandt, at udviklingen i angst og depression blev beskrevet af to forskellige mønstre. Angstsymptomer havde et steglere fald de første seks måneder og faldet fortsatte, blot mindre de sidste seks måneder. Depressionssymptomer faldt også signifikant over de første seks måneder, og faldet fortsatte, men ikke længere signifikant.

Afhandlingen bekræfter den kliniske erfaring om, at de pårørende befinder sig i en emotionelt belastende situation i de tidlige faser i rehabiliteringen, og at dette fortsætter det første år. Desuden understreges vigtigheden af, at kommende forskningsprojekter implementerer og undersøger effekten af et interventionsprogram til familien i de tidlige faser af rehabiliteringen.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCOVA</td>
<td>Analysis of Covariance</td>
</tr>
<tr>
<td>APACHE</td>
<td>Acute Physiology and Chronic Health Evaluation</td>
</tr>
<tr>
<td>BAI</td>
<td>Beck Anxiety Inventory</td>
</tr>
<tr>
<td>BDI</td>
<td>Beck Depression Inventory</td>
</tr>
<tr>
<td>BIFI</td>
<td>Brain Injury Family Intervention</td>
</tr>
<tr>
<td>BSI</td>
<td>Brief Symptom Inventory</td>
</tr>
<tr>
<td>CRASH2</td>
<td>Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage</td>
</tr>
<tr>
<td>DRS</td>
<td>Disability Rating Scale</td>
</tr>
<tr>
<td>EFA</td>
<td>Early Functional Abilities</td>
</tr>
<tr>
<td>FIM</td>
<td>Functional Independence Measure</td>
</tr>
<tr>
<td>GCS</td>
<td>Glasgow Coma Scale</td>
</tr>
<tr>
<td>GHQ</td>
<td>General Health Questionnaire</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IES-R</td>
<td>Impact of Events Scale-Revised</td>
</tr>
<tr>
<td>ISS</td>
<td>Injury Severity Score</td>
</tr>
<tr>
<td>MCS</td>
<td>Minimally Conscious State</td>
</tr>
<tr>
<td>MH</td>
<td>Mental Health</td>
</tr>
<tr>
<td>NICU</td>
<td>Neuro Intensive Care Unit</td>
</tr>
<tr>
<td>NTBI</td>
<td>Non Traumatic Brain Injury</td>
</tr>
<tr>
<td>PIM</td>
<td>Paediatric Index of Mortality</td>
</tr>
<tr>
<td>PTA</td>
<td>Post Traumatic Amnesia</td>
</tr>
<tr>
<td>PTS</td>
<td>Post Traumatic Stress</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>RLA</td>
<td>Rancho Los Amigos</td>
</tr>
<tr>
<td>RE</td>
<td>Role Emotional</td>
</tr>
<tr>
<td>SAPS</td>
<td>Simplified Acute Physiology Score</td>
</tr>
<tr>
<td>SCL-90-R</td>
<td>Symptom Checklist-90-Revised</td>
</tr>
<tr>
<td>SDS</td>
<td>Self-rating Depression Scale</td>
</tr>
<tr>
<td>SF</td>
<td>Social Function</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short Form 36</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>STAI</td>
<td>State-Trait Anxiety Inventory</td>
</tr>
<tr>
<td>STBI</td>
<td>Severe Traumatic Brain Injury</td>
</tr>
<tr>
<td>SWLS</td>
<td>The Satisfaction With Life Scale</td>
</tr>
<tr>
<td>TBI</td>
<td>Traumatic Brain Injury</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
</tr>
<tr>
<td>VS</td>
<td>Vegetative State</td>
</tr>
<tr>
<td>VT</td>
<td>Vitality</td>
</tr>
</tbody>
</table>
This thesis is based on the following five papers:

**I**

**II**

**III**

**IV**
Norup, A., Siert, L. & Mortensen E.L. Neuropsychological intervention in the acute phase: a controlled trial investigating the emotional wellbeing of relatives of patients with severe brain injury. *In manuscript*.

**V**
Norup, A., Petersen, J., Siert, L. & Mortensen E.L. Relatives of patients with severe brain injury: growth curve analysis of the first year after injury. *In manuscript*.

Papers I-III have been reprinted with permission from the publishers.
Acquired brain injury has been called a silent epidemic because it is the leading cause of mortality and disability among the younger age groups in the Western world\textsuperscript{1,2}, and because many of the resulting deficits are not directly visible. A brain injury can leave significant damage without visible signs, and the costs of treating, rehabilitating and reintegrating these patients in society are substantial.
A recent report by the Danish National Board of Health counted all cases of traumatic brain injury (TBI) and non-traumatic brain injury (NTBI) based on the Danish Patient Registry and according to the report, 328 patients acquired a severe TBI and 706 a severe NTBI in Denmark in 2009\textsuperscript{3}.
The costs of acquired brain injury are substantial both financially for society and emotionally for the patient and the family as a whole. Most brain injury survivors require yearlong and intensive rehabilitation imposing a significant economic burden in rehabilitation services and early retirement. Moreover, both the survivor and the surrounding family experience the emotional impact and consequences of brain injury.
The emotional impact on the family is seen very early in the process of rehabilitation. The acute crisis in the neuro intensive care unit (NICU) is replaced by another form of emotional distress and draining, when the patient starts the rehabilitation. This is experienced first hand when working with the relatives in the sub-acute phase, and this clinical experience was the beginning of this dissertation. Relatives in the beginning of the sub-acute phase express an unmet need for information as well as psychological support. The aim of this PhD thesis was to explore the emotional condition of the relatives and to investigate and evaluate effects of a neuropsychological intervention in the early phases of rehabilitation.

\textbf{1.1 Objectives}

The primary objectives of this thesis were to investigate:

1) The emotional distress and quality of life in relatives during the first year after injury.

2) Predictors of emotional distress and quality of life in relatives.
3) If an early neuropsychological intervention consisting of information and emotional support had beneficial effects on the emotional distress and quality of life in relatives of patients with severe injury.

Objective 1 and 2 was investigated in paper I, II, III and V. Objective 3 was investigated in paper IV.

1.2 Overview of the thesis
CHAPTER 1 is a general introduction to this thesis and the chapter lists the objectives of this work. CHAPTER 2 provides the background for the study and presents a literature overview investigating brain injury’s impact on the family and intervention to families. CHAPTER 3 provides the methods and materials used in the study. CHAPTER 4 describes the methods of analysis. CHAPTER 5 presents the ethical concerns addressed before conducting the study. CHAPTER 6 summarises the results of papers I to V. CHAPTER 7 interprets the results and discusses methodological considerations and limitations of the findings. CHAPTER 8 presents the essential conclusions of the study and comments on future directions on related research.
This chapter provides a literature review of the field of family research after brain injury. The chapter shortly introduces the rehabilitation process after severe brain injury in Denmark and describes the common consequences of severe brain injury.

The following sections give a thorough review of the literature on families and relatives living with the effects of brain injury. The first section of the review investigates emotional distress and quality of life in relatives during ICU/NICU and rehabilitation, the second section concerns predictors associated with emotional distress and impaired quality of life and the last section investigates studies evaluating interventions to families.

### 2.1 Rehabilitation in Denmark

In Denmark, neurorehabilitation after severe brain injury is divided into three phases covering the acute, sub-acute phase in hospital and the rehabilitation after discharge. Sub-acute rehabilitation of patients is centralised in two different centers: one covering the western part of Denmark, and one serving inhabitants in the eastern part of Denmark, Greenland and the Faroe Islands. The unit serving the eastern part of Denmark has been the primary place of enrollment of participants for this thesis. The TBI-unit admits patients with severe brain injury after the following admission criteria:

1: Adults: Glasgow Coma Scale (GCS) 3-9
   
   Children < 5 years: GCS 3 – 9
   
   Children 5 – 15 years: GCS 3 – 11

2: Patients with GCS > 9 with severe focal neurological deficits such as aphasia, hemiparesis or agitation

3: Patients with severe cognitive deficits as well as paresis or agitation

The unit opened in the year 2000 and primarily treats patients with traumatic brain injuries. Since 2005, the unit has received patients with non-traumatic injuries. The unit has treated 446 patients with
TBI, and 131 patients with NTBI\(^A\). The TBI patients had a mean age of 44.4 years (SD 17.9) and most were male (76.2%). Causes of TBI were primarily related to traffic and falling accidents (See Table 1). The NTBI patients had a mean age of 49.9 (SD 13.6) and just above half of the patients were male (55%). The primary cause of NTBI was subarachnoid hemorrhage or arterio-venous malformation. The distribution of causes of injury is shown in Table 1:

<table>
<thead>
<tr>
<th>Cause of injury</th>
<th>TBI n (%)</th>
<th>NTBI n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traffic-related</td>
<td>236 (52.9%)</td>
<td></td>
</tr>
<tr>
<td>Fall</td>
<td>146 (32.7%)</td>
<td></td>
</tr>
<tr>
<td>Violence</td>
<td>18 (4.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>46 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td></td>
<td>34 (26.0%)</td>
</tr>
<tr>
<td>SAH/AVM</td>
<td></td>
<td>48 (36.6%)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>41 (31.3%)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>8 (6.1%)</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; AVM, arterio-venous malformation.

The patients are admitted for lengthy and intensive neurorehabilitation in the sub-acute phase. The average length of stay for patients with TBI is 107.7 (SD 74.6) days, and for patients with NTBI 102.9 days (SD 70.9) days (data retrieved from local database at the TBI-Unit).

### 2.2 Severe brain injury and common consequences.

Decreased consciousness is a common feature for both TBI and NTBI in the acute and sub-acute phase. After the initial comatose period, most patients enter a vegetative state (VS) with spontaneous eye-opening and sleep-wake cycles, however still remaining unconscious and unresponsive. Long-term outcome for survivors of severe brain injury ranges from almost complete recovery of function to persistent vegetative state. The numerous different lesions with various location and severity can explain the heterogeneity of outcome after brain injury\(^d\).

The majority of patients do recover to a conscious state, but have temporary or persistent impairments of varying degrees. The deficits after severe brain injury are many and affect most areas of the survivor’s life. Loss of function is typically seen in more than one domain, and common physical impairments are paralysis, spasticity, seizures and fatigue. However, the most common deficits after severe brain injury are cognitive, behavioural and emotional changes. Cognitive problems arising after brain injury are mental slowness, memory impairment, executive dysfunction and language

\(^A\) These numbers were retrieved from the local database at the TBI-Unit and included patients admitted from 2000 till ultimo 2011.
related problems. Even more important are changes in behaviour and personality as these changes have substantial implications causing reduced social and occupational adaptability$^{5-9}$. In some patients, premorbid personality traits are emphasised and existing traits can become more rigid. Personality changes have been identified as an important predictor of distress and impaired family functioning$^{10-12}$, as changes in personality cause severe frustration in families living with acquired brain injury$^{13}$.

During recent years, researchers in different fields have acknowledged and underlined the importance of including and informing family members during the treatment and rehabilitation of not only brain injury but also in other disabling and chronic diseases$^{14}$. The families of brain injury survivors are uniquely challenged, as the injury often causes both physical and cognitive deficits. This has been confirmed by studies comparing the situations of relatives of different patient populations, and it seems that relatives of patients with brain injury are in an especially emotionally draining and distressing situation compared to relatives of patients with e.g. dementia and spinal cord injury$^{15,16}$.

In the papers providing the scientific foundation for this thesis, the term relative is referring to a close family member. The term relative was chosen, as it refers to the relationship to the patient and not to caring responsibilities of the family member. The term caregiver or carer refers to a close family member taking care of a patient with a brain injury. The term is often used in American publications, where family members often have responsibilities in providing care.

2.3 Emotional distress and quality of life in relatives

During the last four decades, researchers in the field of brain injury have been concerned with the consequences of brain injury on the family. The first studies were based on clinicians’ experience and described the impact of the brain injury on family members$^{12,13}$. In the 1980’s longitudinal studies examined the closest relative of the individual with brain injury and reported high levels of burden, distress, anxiety and depression$^{12,17-21}$. Consequently, the studies provided the scientific evidence supporting the clinical experience that brain injury does not only affect the individual acquiring the injury, but the whole family, and especially the marital relationship$^{8,9,13,22,23}$. During the 1990s, research confirmed the distress in families reported earlier and sought to explore predictors of the condition of the relatives$^{24-27}$. Recently, there has been an increased availability of interventions to
families and caregivers, raising the need for research investigating the effects of well-designed interventions.28,29.

Two search strategies were used to find published studies on emotional distress in families of patients with brain injury. The first strategy involved computerised database searches using PubMED and PsycInfo. The following keywords were used: TBI, brain injury, head trauma, head injury, family, relatives, carers, caregivers, emotional reactions, distress, support to families, family intervention, anxiety, depression. The second search strategy was footnote chasing examining references cited in previous studies.

*Studies reporting specific frequencies of distress, anxiety and depression are shown in tabular form in Table 2, as are details regarding studies concerning intervention to families, Table 3. Details regarding studies not shown in the two tables are provided in the text. Note that this literature overview only includes studies concerning adult relatives. Thus, research specifically targeting children of parents with TBI is not included in this review.*

2.3.1 In critical care

Only one study has investigated the emotional condition of relatives in a population of patients with brain injuries during critical care. Pielmaier et al.30 investigated symptoms of post-traumatic stress (PTS) in relatives the first weeks after severe traumatic brain injury, and 52% of the relatives had a clinically relevant level of PTS symptoms.

Authors in critical care medicine have reported high frequencies of depression and anxiety in large populations of relatives of patients admitted to an Intensive Care Unit (ICU). Fumis & Deheinzelin31 found frequencies of 71% and 50.3% of anxiety and depression respectively in relatives of patients with cancer admitted to an ICU. Pochard et al.32,33 have reported frequencies of 69.1-73.4% and 35.3-35.4% of anxiety and depression in family members of patients admitted to ICU. Pérez-San et al.34 also found that more than 50% of relatives of patients with different types of trauma had symptoms of depression. The mentioned studies have found high frequencies of anxiety and depression in general ICU’s. However, the populations are not comparable to those with brain injury. Fumis & Deheinzelin’s sample consisted of cancer patients admitted to treatment in an ICU. Certainly, the relatives of patients with cancer are in different situation compared to relatives experiencing the
sudden impact of a brain injury (Details about methods, results, frequencies of emotional distress are shown in Table 2).

### Table 2: Cross-sectional studies on distress, anxiety and depression in relatives

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Patient pop.</th>
<th>Post-injury</th>
<th>Distress/burden</th>
<th>Anxiety</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pérez-San (1992)</td>
<td>76</td>
<td>Head/polytrauma</td>
<td>2 days*</td>
<td>---------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Pochard (2001)</td>
<td>920</td>
<td>ICU</td>
<td>3-5 days*</td>
<td>---------------</td>
<td>HADS 69%</td>
<td>HADS 35.4%</td>
</tr>
<tr>
<td>Pochard (2005)</td>
<td>544</td>
<td>ICU</td>
<td>9 days*</td>
<td>---------------</td>
<td>HADS 73%</td>
<td>HADS 35.3%</td>
</tr>
<tr>
<td>Fumis (2009)</td>
<td>300</td>
<td>Cancer</td>
<td>3-5 days*</td>
<td>---------------</td>
<td>HADS 71%</td>
<td>HADS 50.3%</td>
</tr>
<tr>
<td>Piembaier (2011)</td>
<td>69</td>
<td>STBI</td>
<td>11 days</td>
<td>IES-R 52%</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Pérez-San (1992)</td>
<td>76</td>
<td>Head/polytrauma</td>
<td>2 days*</td>
<td>---------------</td>
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<td>--------------</td>
</tr>
<tr>
<td>Pochard (2001)</td>
<td>920</td>
<td>ICU</td>
<td>3-5 days*</td>
<td>---------------</td>
<td>HADS 69%</td>
<td>HADS 35.4%</td>
</tr>
<tr>
<td>Pochard (2005)</td>
<td>544</td>
<td>ICU</td>
<td>9 days*</td>
<td>---------------</td>
<td>HADS 73%</td>
<td>HADS 35.3%</td>
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<tr>
<td>Fumis (2009)</td>
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<td>Cancer</td>
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<td>HADS 71%</td>
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### ICU

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Patient pop.</th>
<th>Post-injury</th>
<th>Distress/burden</th>
<th>Anxiety</th>
<th>Depression</th>
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<tr>
<td>Brooks (1987)</td>
<td>134</td>
<td>TBI</td>
<td>2–7 yrs</td>
<td>Likert 89%</td>
<td>--------------</td>
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<td>60</td>
<td>TBI</td>
<td>~ 6 yrs</td>
<td>---------------</td>
<td>SCL-90 55%</td>
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<td>Kreutzer (1994)</td>
<td>62</td>
<td>TBI</td>
<td>1.5–60 mth</td>
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<td>BSI 32%</td>
<td>BSI 23%</td>
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<td>Mintz (1995)</td>
<td>21</td>
<td>TBI</td>
<td>~ 4 yrs, 7 mth</td>
<td>---------------</td>
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<td>LSAD 24%</td>
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<td>116</td>
<td>TBI</td>
<td>10 to &gt;48 mths</td>
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<td>BSI 32%</td>
<td>BSI 21%</td>
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<td>TBI</td>
<td>12-24 mth</td>
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<td>BDI 19-38%</td>
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<td>Douglas (2000)</td>
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<td>3.5-10 yrs</td>
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<td>SDS 60%</td>
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<tr>
<td>Wallace (2000)</td>
<td>50</td>
<td>BI</td>
<td>0.19-9.44 yrs</td>
<td>---------------</td>
<td>BAI 39%</td>
<td>BDI 34%</td>
</tr>
<tr>
<td>Harris (2001)</td>
<td>58</td>
<td>TBI</td>
<td>6 mth/1/2/3 yrs</td>
<td>---------------</td>
<td>SDS 23%</td>
<td></td>
</tr>
<tr>
<td>Machamer (2002)</td>
<td>180</td>
<td>TBI</td>
<td>6 mths</td>
<td>---------------</td>
<td>CES-D 14-54%</td>
<td></td>
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<tr>
<td>Ergh (2002)</td>
<td>60</td>
<td>TBI</td>
<td>0.33 – 9.96 yrs</td>
<td>BSI (GSI) 37%</td>
<td></td>
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<tr>
<td>Ponsford (2003)</td>
<td>143</td>
<td>TBI</td>
<td>2, 3 or 5 yrs</td>
<td>---------------</td>
<td>LSAD 25%</td>
<td>LSAD 22%</td>
</tr>
<tr>
<td>Rivera (2007)</td>
<td>60</td>
<td>TBI</td>
<td>36-298 mths ^</td>
<td>---------------</td>
<td>CES-D 48%</td>
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<tr>
<td>Kreutzer (2009)</td>
<td>273</td>
<td>TBI</td>
<td>1,2 or 5 yrs</td>
<td>BSI (GSI) 18%</td>
<td>BSI 18%</td>
<td>BSI 19%</td>
</tr>
<tr>
<td>Boycott (2012)</td>
<td>48</td>
<td>TBI</td>
<td>9.3 yrs</td>
<td>BSI (GSI) 18%</td>
<td>BSI 18%</td>
<td>BSI 19%</td>
</tr>
<tr>
<td>Leonardi (2012)</td>
<td>487</td>
<td>BI (VS/MCS)</td>
<td>Post acute/long-term/home</td>
<td>BDI-II 59.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calvete (2012)</td>
<td>223</td>
<td>TBI</td>
<td>&gt;1 yr after dis</td>
<td>---------------</td>
<td>CES-D 28.5%</td>
<td></td>
</tr>
</tbody>
</table>

Percentages refer to number of cases above the defined cut-off. Dis, discharge; STBI, severe TBI; Mths, months; yrs, years; VS, vegetative state; MCS, minimal conscious state; CAQ, Clinical Analysis Questionnaire; HADS, Hospital Anxiety and Depression Scale; SCL, Symptom Checklist; IES-R, Impact of Events Scale-Revised; BSI, Brief Symptom Inventory; SAI, State Anxiety Inventory; BDI, Beck Depression Inventory; LSAD, Leeds Scales of Anxiety and Depression; CES-D, Center for Epidemiologic Studies – Depression scale; CSI, Caregiver Strain Index. ^ After admission to ICU. ~ value refers to a mean of days after injury (is only given if no range were given in the paper). This study only registered the length of time that the relative had cared for the injured person.

### 2.3.2 During rehabilitation – cross-sectional studies

**Anxiety and depression:** Linn reported high frequencies of depression (73%) and anxiety (55%) almost six years after brain injury in spouses using the Symptom Checklist (SCL-90-R). The sample was recruited from self-help associations, whose members had participated in a course discussing
family issues. It is very likely that the families participating were not representative of the majority of families living with brain injury as they had already sought assistance and help. Furthermore, Linn and colleagues used a lower cut-off than the one recommended by Derogatis. Linn reported any T-scores≥ 60 as a case, where Derogatis recommend T-scores≥ 63. Kreutzer et al. used the short version of the SCL; the BSI and found much lower frequencies: 23% above caseness on depression and 32% on anxiety. When applying the caseness criteria defined by Derogatis (T-scores≥ 63 on at least two scales), only 13% met this criterion.

Mintz et al. applied both the Leeds Scales of Anxiety and Depression and Beck’s inventories regarding anxiety (BAI) and depression (BDI). The researchers found frequencies ranging from 24-52% on the depression scales and 43-48% on the anxiety scales. This study emphasised the following facts: 1. using different measures sheds light on different aspects of the distress experienced by the relatives, 2. different measures affect the findings. These important aspects of conducting research warrant attention and caution when interpreting and comparing results of different studies.

Gervasio et al. described the level of distress experienced by relatives in three different intervals after injury (10-24 months; 25-48 months; >48 months). Overall, 21% had scores above cut-off on the depression scale and 31% on the anxiety scale, and time since injury did not affect the level of distress experienced.

Wallace & Bogner found that 34% reported depression and 39% reported anxiety with a duration ranging between 0.19 to 9.44 years since injury. The restricted population limits the results as participants included were those who continued to attend follow-up assessments with a psychiatrist after discharge. Douglas & Spellacy found that 60% of carers of TBI patients suffered from depression using the Self-Rating Depression Scale (SDS). Harris et al. also used the SDS but found a much lower rate of depression (23%). Carers participated in the study at six months, one year, two years or three years following injury, and the authors did not specify the frequencies at the different assessment times. Rivera found that about half of the participants scored above cut-off on the Centre for Epidemiologic Studies—Depression Scale.

In 2009, Kreutzer and colleagues published a large-scale multi-centre investigation revealing that approximately two thirds of the relatives had no scores exceeding cut-offs on the BSI. Another large multi-centre study was conducted by an Italian group of researchers investigating relatives of patients in VS or minimally conscious state (MCS) being treated post-acute, in long-term care or at home. The study included 487 carers and found a high level of tension and apprehension compared to an Italian normative sample and 59.5% reached the severe level of depression on the BDI-II. A
sample of Spanish family caregivers was recently investigated in the chronic phase after TBI (81% >2 years after discharge, 19% 1-2 years after discharge) and results revealed that 28.5% were above cut-off on the depression scale used. A Danish study investigated families in the chronic phase after brain injury (mean 3.7 years after injury/diagnosis), where one of the parents had acquired a brain injury and included both TBI and NTBI. Spouses of the injured family member had mean T-scores on both depression (52.7±8.7) and anxiety (51.5±10.6) close to the norm average (i.e. T-score=50). The authors did not report caseness levels⁴⁷, and the study was limited by a very small sample (n=35).

Other studies have investigated the emotional distress in different types of carers. Perlesz et al.⁴⁸ differed between primary, secondary and tertiary carers based on who had most responsibility in terms of caregiving. The authors found that more primary carers experienced depression (37.7%) and anxiety (44.1%) than secondary (respectively 18.6% and 15%) and tertiary (27.3% and 31.8%). Interestingly, more tertiary carers had scores above cut-off than secondary. The authors conclude that tertiary carers may need greater assistance than previously thought.

Machamer⁴⁹ compared distress experienced by the significant others of TBI patients six months after injury. The authors divided the participants into three different groups based on their experience of being a caregiver; negative, positive aspects of caring, and an intermediate group. In the group perceiving the burden as negative, 54% were depressed. In the intermediate group, 17 % were depressed, and in the group perceiving the burden of caregiving as primarily positive, 14% were depressed. The paper also indicated that relatives experiencing caregiving as primarily negative had problems prior to the injury e.g. alcohol and substance abuse, history of arrests.

Ponsford et al.⁵⁰ reported a similar finding investigating long-term adjustment of families following TBI and found that relatives responsible for care were more likely to be depressed and anxious. Out of the sample invited to participate in the study, almost 35% did not attend, which may have introduced bias even though no differences were found between injury severity in the two groups.

Strain and quality of life: Boycott et al.⁵¹ investigated strain in a retrospective cross-sectional cohort study in the chronic phase after TBI reporting that 42% of the carers had elevated levels of strain. McPherson et al.⁵² used the Short Form-36 (SF-36) to estimate quality of life in a sample of 70 carers about 15 -18 months after injury. Carers reported lower quality of life compared to a reference population on the following subscales: role-physical, social functioning, role-emotional and mental health, however the difference was not significant.
Kreutzer and colleagues\textsuperscript{44} also employed a quality of life measure, the Satisfaction With Life Scale, in their multi-centre investigation revealing how the scores of the sample of relatives were comparable to those of a normal population. Arango-Lasprilla and coworkers\textsuperscript{53} also used the SF-36 on a sample of carers comparing the results with a healthy control group. The carers had significantly lower scores on role-emotional, vitality, social functioning, mental health, bodily pain and general health compared to a healthy control group matched on age, gender, marital status and education. Carers had been responsible for taking care of their relative for at least three months, and the follow-up interval varied. Moules and Chandler\textsuperscript{54} found that six years after injury (range: 1.6 years to 17 years) relatives reported lower quality of life than normal populations, however the variation in scores was large. Koskinen\textsuperscript{55} reported quality of life in 15 relatives of patients with severe TBI 10 years after injury and found the majority of relatives were ‘rather satisfied’. Variables related to functioning of the injured were related to the strain experienced by the relative, but not with quality of life in relatives. The authors reported that many other factors influence the quality of life ten years after injury, as almost half of the relatives reported to have suffered severe illnesses during the last five years.

The cross-sectional studies reviewed provide useful information about the relatives’ emotional wellbeing at different points in time after an acquired brain injury in the family. The studies have reported incidence estimates ranging from 18\% to 89\%. Variability may very well be caused by methodological factors. Only one study have emphasised the proportion of relatives that do actually report positive aspects of caregiving\textsuperscript{49}.

Most of the studies reviewed have assessed emotional distress in families living with the impact of brain injury with a follow-up time varying from a few weeks to many years after injury, and have then reported a mean time since injury. Many studies have employed a quantitative approach using self-report scales or questionnaires asking relatives in very diverse situations to participate. Thus, it appears to be two very different situations with dissimilarly emotional distress, depending on whether your loved one is still having treatment in hospital or whether you are caring for your husband or child within your own facilities many years after the brain injury. Caution should be employed, when comparing and interpreting the results of studies with follow-up varying from a few weeks to years. Moreover, the innate problems of cross-sectional studies are that they do not provide any information regarding changes over time, and it is difficult to determine the direction of causality. Longitudinal
studies are more elucidative, as they do provide information about changes as well as giving the possibility of determining causality.

2.3.3 During rehabilitation - longitudinal studies

Anxiety and depression: A group of researchers from London were the first to investigate the condition of the relatives with a standardised method. They reported that 39% of the 54 relatives included, were above the cut-off score for clinical depression one month after injury using the Wakefield Depression Scale\textsuperscript{20}. Levels went down to about 20-25% at six and 12 months post injury. Oddy et al\textsuperscript{8} conducted a long-term follow-up study revealing that the condition of the relatives was comparable to a reference population seven years after the injury. This group of researchers found significantly increased levels of anxiety and depression during the first year with symptoms then levelling off reaching reference populations. This study emphasised the fact that even though families experience severe distress, adaptation can occur over time.

Around the same time, the Glasgow group\textsuperscript{17,18,56,57} conducted two independent longitudinal studies reporting on anxiety, depression, stress and burden in two different samples of relatives. The first study investigated psychiatric and social adjustment at three, six and 12 months after trauma. Three months after injury, 45% and 21% scored above cut-off on respectively the anxiety and the depression scale. The percentage scoring above caseness on the depression scale remained in the twenties at six and 12 months after injury (for the specific frequencies see Table 3). About a third of the relatives scored above cut-off on the anxiety scale during the study period. The authors concluded that twice as many relatives reported psychiatric dysfunction compared to the general population. However, a major limitation of this study is that only 65% of the relatives were assessed on all three occasions\textsuperscript{58}. A significant contribution from the authors was their finding that more severe injuries were associated with more distress and anxiety in relatives. This association was not found in regards to depression. Novack et al\textsuperscript{59} assessed levels of depression and anxiety at time of admission to acute rehabilitation in hospital and found that 9% were clinically depressed and 33% of the caregivers were clinically anxious at admission. Novack et al. found that both anxiety and depression decreased during the study period (See Table 3). This study reported lower levels of both anxiety and depression compared to other studies, however these can partly be explained by the caseness criteria used. The caseness criteria used were higher (BDI>18, State Trait Anxiety Inventory (STAI)>90th percentile) than the recommended\textsuperscript{60}. If milder cases of depression (BDI>12) and anxiety (STAI>80th percentile) had been included, 51% of the sample would have been anxious and 26% depressed.
Gillen et al.\textsuperscript{61} assessed level of distress in caregivers residing with the TBI patient at two different time points (T1; range 2 to 72 months ~ mean 18.5 months, T2; six months after T1). At T1, 47% of the caregivers met the DSM-III-R diagnosis of major depression according to the Diagnostic Interview Schedule Revised. Of those, 69% had a prior episode of depression. At T2, 43% of the caregivers met the criteria, and 65% of the ones depressed at T1 remained depressed.

Marsh et al.\textsuperscript{7,62,63} investigated levels of depression and anxiety six months and one year after injury and reported frequencies of 39% and 37% on anxiety and depression, respectively, and the frequency remained relatively stable during the first year after injury.

Turner et al.\textsuperscript{64} examined 29 caregivers during the patient’s transition from hospital to home. On the depression scale, 27% reported some level of depression pre-discharge, and this number dropped to 12% one and three month post injury. Turner et al. adds that 18% of the general adult population reports symptoms of depression. At the anxiety scale, 13% reported some degree at pre-discharge only somewhat higher than in the general population (11%), and the frequency dropped to below reported number in the general population. Compared to the other longitudinal studies, Turner’s sample does report low anxiety scores. The authors do not offer any explanation for this result, and the authors are reporting on a very small sample.

Turner and Novack have conducted the only two studies investigating the relatives’ condition around the patients’ discharge, even though relatives often report that transitions in the rehabilitation process are specially straining.
Distress and burden: The second longitudinal study done by the Glasgow group investigated subjective burden on a seven point Likert scale\textsuperscript{19,57}. The term subjective burden was defined as the amount of psychological strain on relatives that is attributable to changes in the person with the brain injury\textsuperscript{19}. The subjective burden assessed at three months was 69\%, and this frequency gradually increased to a level of 89\% seven years after injury\textsuperscript{19,57}. Brooks later commented that the social and psychological adjustment of the relatives deteriorates over the years\textsuperscript{65} contrasting Oddy’s findings, where the relatives seemed to adjust to the situation. Brooks attributed this to difference between samples, as Oddy’s population had less severe injuries. The Glasgow group has made an early and significant contribution to the field of family research after brain injury, however criticism has been

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Patient pop.</th>
<th>Post- injury</th>
<th>Distress/burden</th>
<th>Anxiety</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oddy (1978)</td>
<td>46</td>
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<td>1 mth</td>
<td>--------</td>
<td>--------</td>
<td>WDS 39%</td>
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<tr>
<td></td>
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<td>SBI</td>
<td>6 mth</td>
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<td>--------</td>
<td>WDS 20%</td>
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<tr>
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<td>34</td>
<td>SBI</td>
<td>12 mth</td>
<td>--------</td>
<td>--------</td>
<td>WDS 24%</td>
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<td>WDS 20%</td>
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<tr>
<td>Livingston (1985)</td>
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<td>3 mth</td>
<td>GHQ 40%</td>
<td>LSAD 34%</td>
<td>LSAD 20%</td>
</tr>
<tr>
<td></td>
<td>32</td>
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<td>GHQ 37%</td>
<td>LSAD 37%</td>
<td>LSAD 23%</td>
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<tr>
<td></td>
<td>35</td>
<td>SBI</td>
<td>12 mth</td>
<td>GHQ 28%</td>
<td>LSAD 37%</td>
<td>LSAD 26%</td>
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<td>McKinlay (1981)</td>
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<td>--------</td>
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<td>5 yrs</td>
<td>Likert 89%</td>
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<td>--------</td>
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<tr>
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<td>SBI</td>
<td>12 mths</td>
<td>Likert 57%</td>
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<td>6 mths</td>
<td>Likert 73%</td>
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<td>--------</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>SBI</td>
<td>12 mths</td>
<td>Likert 75%</td>
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<td>Novack (1991)</td>
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<td>TBI</td>
<td>Adm (~46 days)</td>
<td>STAI 33%</td>
<td>BDI 4%</td>
<td>BDI 4%</td>
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<tr>
<td></td>
<td>45</td>
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<td>Dis (~86 days)</td>
<td>STAI 7%</td>
<td>BDI 4%</td>
<td>BDI 4%</td>
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<td>BDI 0%</td>
<td>BDI 0%</td>
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<tr>
<td>Marsh (1998)</td>
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<td>6 mths</td>
<td>STAI 39%</td>
<td>BDI 37%</td>
<td></td>
</tr>
<tr>
<td>Marsh (2002)</td>
<td>52</td>
<td>STBI</td>
<td>12 mths</td>
<td>STAI 35%</td>
<td>BDI 31%</td>
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</tr>
<tr>
<td>Turner (2010)</td>
<td>29</td>
<td>TBI</td>
<td>Pre-dis (~149 days)</td>
<td>DASS 27%</td>
<td>DASS 12%</td>
<td>DASS 12%</td>
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<td></td>
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<td>1 mths post dis (~179 days)</td>
<td>DASS 3%</td>
<td></td>
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<td></td>
<td>3 mths post dis (~239 days)</td>
<td>DASS 6%</td>
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</tr>
</tbody>
</table>

Percentages refer to number of cases above the defined cut-off. Adm, admission; dis, discharge; mths, months; yrs, years; MSTBI, moderate to severe TBI; MSBI, moderate to severe brain injury; SBI, severe brain injury. WDS, Wakefield Depression Scale; GHQ, General Health Questionnaire; STAI, State Trait Anxiety Inventory; BDI, Beck Depression Inventory; LSAD, Leeds Scales of Anxiety and Depression; DASS, Depression Anxiety Stress Scale; DSM-III-R, Diagnostic and Statistical Manual. ~ value refers to a mean of days after injury (is only given if no range were given in the paper). Abbreviations of the different outcome measures used can be seen in the beginning of the thesis.
raised about different issues (e.g. Perlesz et al., 1999\textsuperscript{58}). First of all, only 39 relatives remained from the original sample throughout the investigation, which limits the generalisability of the results. Another criticism of the Glasgow group has been their use of a 7-point scale to report experienced burden. The researchers collapsed the categories medium (3-4) and high burden (5-7) to report the frequency of experienced burden. Relatives, who rated their burden ‘3’ was included in the group reporting medium to high burden. This way of reporting data is questionable as the number ‘3’ is actually below the halfway mark on a 7-point scale. If the categories had been collapsed differently (e.g. medium burden and low burden categories together or dichotomised the scale), then the numbers reported would have been completely different.

Hall et al.\textsuperscript{24} interviewed caregivers at admission to rehabilitation and by phone at six, 12 and 24 months and administered among other things the Perceived Stress Scale. The authors did not report the specific frequencies at the different time points, but reported no changes during the first year and a significant decrease during the last year, even though the relatives reported that the amount of stressful experience increased during the same period. The authors commented that the decrease during the second year may be a reflection of family members learning to cope and not necessary less distress.

Turner et al.\textsuperscript{64} also reported on stress and strain in the study presented above. Levels of stress symptoms decreased to 27\% at three months follow-up compared to 20\% in the general population. Of the caregivers, 69\% reported abnormal levels of strain at pre-discharge, and this number decreased to 41\% at one month follow-up and increased at 3 months follow-up to 52\%\textsuperscript{64}.

Despite different methodology, the longitudinal findings regarding anxiety, depression and distress are more or less comparable during the first year after injury. There is evidence that symptoms of anxiety and depression decrease during the first year after injury despite the different measures used. Distress seems to decrease during the first year\textsuperscript{18,64}, and the level at seven years follow up is comparable to the general population\textsuperscript{8}. The picture is different when investigating results regarding subjective burden, as this seems to increase during the first year and up to seven years after injury\textsuperscript{66}. However, there are several methodological issues concerning these findings.
2.4 Predictors of the emotional condition of the relatives

After underlining the increased frequencies of emotional distress in relatives of patients with brain injury, researchers have sought to identify predictors associated with higher levels of anxiety and depression and impaired quality of life. Identified predictors related to both the patient and the relative are presented in this section of the thesis.

The relative’s gender: Pielmaier et al.\textsuperscript{30} found that women had significantly higher levels of symptom severity on the IES-R in the acute setting. Turner et al.\textsuperscript{64} found that female caregivers experienced greater strain than males at three months follow-up after discharge, and Linn et al.\textsuperscript{35} found that female spouses had higher levels of anxiety and depression six years after injury. In contrast, Gervasio et al.\textsuperscript{39} found that male caregivers displayed more distress. Perlesz et al.\textsuperscript{48} reported that male relatives reported their distress in term of anger and fatigue, whereas female might report their distress in terms of anxiety and depression. This study was conducted almost 20 months after injury. Harris et al.\textsuperscript{42} did not find any association between the carer’s gender and experienced depression, and this negative finding was replicated by Boycott et al.\textsuperscript{51} in relation to strain. Different results have been found in terms of the effect of gender. Due to the unequal distribution of gender in the samples, difficulties and uncertainties remain when investigating the issue.

Relationship to the patient: Mauss-Clum & Ryan\textsuperscript{67} conducted one of the first studies describing a support group and reported that a larger frequency of wives experienced depression compared to mothers. Other studies have confirmed this finding\textsuperscript{39,48}. Kreutzer and colleagues\textsuperscript{25} found that spouses were significantly more likely to report elevated depression scores compared to parents as well as a trend toward spouses reporting greater family dysfunction. Nevertheless, the study found no difference in terms of perceived stress. This is in contrast to Leathem et al.\textsuperscript{68}, who used the Hassles and Uplifts Scale to assess experienced hassles in daily life in a group of parents and a group of partners (assessment ranging from four months to 8 years). Both groups experienced mild stress, and partners indicated a greater degree of role change and a slightly higher degree of stress. McPherson et al.\textsuperscript{52} found that spouses reported lower quality of life than parents on all the subscales of the SF-36, and significantly lower on bodily pain, vitality and role-emotional 15-18 months after injury.
The opposite effect was reported by Turner who found that immediate family members (parents and children of the patient) experienced more anxiety than spouses and partners at one month follow-up after discharge from hospital. However, this was reported on a very small sample.

Pielmaier found no group differences for type of relative (spouses vs. other) in the acute phase, and neither did Oddy et al. comparing spouses and parents’ emotional condition, but this may be due to lack of statistical power, as only 14 spouses were included. Knight et al. reported on subjective burden, distress and depression in 52 caregivers of TBI patients on average six years after injury and did not find any difference between parents and spouses. Neither did Gillen et al. in relation to depression. Ergh et al. investigated social support as a predictor of distress and life satisfaction and found no differences when comparing spouses with parents (range: 0.33 – 9.96 years after injury). Kreutzer and colleagues found no difference between spouses, parents and non-family caregivers on any dimension of the BSI or in relation to quality of life.

The results of the studies are mixed, and it is not possible to make any certain conclusions about the role of relationship in predicting distress.

Cohabitation: Harris et al. did not find any association between the cohabitation status of the carer and the survivor and the carer’s depression scores. Boycott and coworkers also reported no association between cohabitation status and strain reported by carers.

No other studies have been identified investigating effects of cohabitation, and many studies have limited participants to residing relatives.

Relatives’ premorbid history: Gillen et al. found that the best predictor of depression among caregivers was premorbid history of depression. Sander et al. investigated 191 caregivers on average 36 days after injury (IQR: 21-47 days) and reported that a large proportion of caregivers indicated symptoms of emotional distress and unhealthy family functioning before injury, which may make them more vulnerable to the stress and burden associated with the injury and the coping process more difficult. These two studies underlined the necessary focus on the family’s level of function before the injury.

Relatives’ coping satisfaction and style: Sander et al. investigated 69 caregivers divided into three different groups depending on time since injury (0-6mths/6-18 mths/ >18 mths) and found that coping style was associated with caregivers’ psychological health assessed by General Health Questionnaire.
(GHQ). An increase in emotion-focused coping raised level of psychological distress. Knight et al.\(^6^9\) found that the most predictive factor of depression was coping satisfaction on average six years after injury. Gregório and colleagues\(^7^3\) investigated coping styles within the family in the chronic phase after brain injury (median=3.5 years). The study included TBI patients as well as patients with cerebrovascular accidents. Caregivers who used a passive coping style (e.g. isolating oneself from others, worrying about the past, taking refuge in fantasies) experienced lower quality of life and family function as well as a higher strain than relatives using an active coping style (e.g. tackling a problem at once, seeing problems as a challenge, remaining calm in difficult situations). Chronister et al.\(^7^4\) and Calvete & de Arroyabe\(^7^5\) found that coping responses such as acceptance, cognitive restructuring and distraction are related to positive psychological adjustment and lower levels of distress.

Not surprisingly, coping style did seem to affect the condition of the relatives, and emotional-focused coping increased stress and burden, and problem-focused coping lowered levels of distress.

**Social support:** Ergh et al.\(^7^6\) found that caregivers without adequate support experienced increased distress with time elapsed since injury (mean: 4.8 years since injury). Douglas and Spellacy\(^4^1\) found that levels of social support accounted for 45% of the variability in carers’ depression scores, and Calvete and de Arroyabe\(^7^5\) found that both emotional and instrumental support were negatively associated with depression in a large group of caregivers in the chronic phase of TBI. Harris et al.\(^4^2\) found that social support moderated the psychological distress experienced by the caregivers. Riley et al.\(^7^7\) investigated 44 carers who had lived with the TBI patient for at least six months after injury and found a negative correlation between number of persons that the caregiver could call for support and scores on both a depression and stress scale indicating a similar association as mentioned above. Sander et al.\(^2^7\) found that relatives’ satisfaction with social support was significantly related to psychological distress. Chronister et al.\(^7^4\) assessed quality of life with the World Health Organisation Quality of Life and found that social support and family needs are important to caregiver’s quality of life and appraisal of stress.

It is well accepted that social support moderates distress, and this was confirmed in this area as well. Only one study did not find social support to moderate burden and depression scores\(^6^9\).
Stressful life events: Harris et al.\(^{42}\) did not find any association between concurrent stressful life events and depression experienced by carers. Hall et al.\(^{24}\) found that the level of stressful life events increased slightly at two years follow-up even though perceived stress declined. As these two studies are the only ones identified investigating impact of concurrent life events, it is difficult to determine a possible impact. However, so far the effect of other life events on the condition of the relative has not been found, as it has in reference populations\(^{78}\). This might be due to measures not being sensitive enough, or because the relatives already are in severe distress, so stressful life events do not affect them any further.

Caregiving responsibility: Perlesz et al.\(^{48}\) found that more primary carers experienced depression and anxiety than secondary and tertiary carers. Interestingly, more tertiary carers had scores above cut-off than secondary. The authors conclude that tertiary carers may need greater assistance than previously thought\(^{48}\). Machamer et al.\(^{49}\) reported that relatives experiencing caregiving as primarily negative had higher scores depression scores, and Ponsford et al.\(^{50}\) found that anxiety and depression were more likely to be present in those directly responsible for the care of their injured family member. These three studies underline the different aspects of caregiving, which should be considered when investigating the condition of the relatives.

The patient’s age: The studies from the critical care medicine conducted in the NICUs have found the age of the patient to be associated with the distress that relatives experience\(^{32,33}\). In the field of brain injury, studies have not identified a similar association between age and the condition of the relatives\(^{35,42,69,79}\). Turner et al.’s\(^{64}\) study is the only to identify that patient’s age was associated with caregiver’s level of stress at three months follow-up. However, at pre-discharge, one and three months post discharge no associations between patient’s age and anxiety, depression and strain were found. A major limitation of the study was sample size, and the many analyses conducted on the small sample size. No evidence is provided for an age effect on relatives’ wellbeing in the field of brain injury.

Severity of injury: Livinston et al.\(^{18}\) found that more severe injuries were related to greater psychological distress and anxiety in relatives assessed on the General Health Questionnaire (GHQ), but this difference was not apparent on the depression scale. Most studies have not been able to validate the hypothesis generated by clinical experience that the most severe injuries causes the greatest distress in relatives\(^ {16,19,26,30,35,39,50,51,61,69,76}\). The few studies that have actually some influence
of the severity of injury have reported other characteristics such as social isolation, behavioural problems etc. as being more important. Another factor affecting these findings is how severity of injury was measured in the studies. In many studies the GCS has been used, and this has been discussed, because this score is affected by sedation, time of assessment etc. In other studies, severity of injury has been assessed with duration of post-traumatic amnesia (PTA), which is known to be a more reliable indicator of injury severity, even though it is most often assessed retrospectively and with different measures. Uncertainties in terms of measuring injury severity influence the findings regarding severity of injury and distress experienced by relatives.

**Patient’s level of function and consciousness:** Katz et al. did not find any association between disability level and experienced burden more than one year after injury, and neither did Douglas & Spellacy also in the chronic phase of TBI. In contrast, the same authors and Turner et al. did find that total score on the Rappaport Disability Rating Scale (DRS) was a significant predictor of depression in carers. Kreutzer and colleagues found that caregiver stress were inversely related to the survivor’s functional status on different indices amongst others the DRS. In contrast, Novack et al. did not find a correlation between the patient’s functional status as measured by DRS and the caregiver’s symptoms of anxiety or depression. Sander et al. also used DRS and failed to find any association to relatives’ scores on the GHQ.

Turner et al. did not find any associations between the patient’s score on the Functional Independence Measure (FIM) at discharge and the condition of the relatives at any of the three assessment points. This study did find that relatives of patients with a lower GCS, had higher scores on the stress scale administered. Along the same line, Pielmaier et al. found that GCS on the scene of the accident and on hospital admission were inversely related to the relatives’ scores on the IES-R. Livingston et al. investigated life satisfaction using the SWLS in a sample of 336 family members caring for individuals with TBI one and two years after injury. A logistic regression model showed that family members caring for individuals having a substance abuse at follow-up and with lower levels of function at discharge were more likely to report low levels of life satisfaction.

Based on the mentioned studies, it is difficult to make conclusions regarding level of function and consciousness.

**Neurobehavioral disturbances:** Ergh et al. found that neurobehavioral disturbances were the strongest predictor of psychological distress in caregivers. Ponsford et al. found that cognitive,
behavioural and emotional changes were the strongest predictor of anxiety and depression in relatives, and Groom et al.\textsuperscript{85} examined 153 family members (1 mths to 40 years after injury) and found that neurobehavioral disturbances were related to family dysfunction and to experienced caregiver distress. Other studies with long-term follow-up have reported similar results\textsuperscript{7,19,69,80,86,87}.

Wells et al.\textsuperscript{88} used the Satisfaction with Life Scale to assess quality of life in 72 survivors and family members (1 to 40 years since injury) and reported that TBI survivors’ lack of showing empathy was the most diminishing factor to the quality of life experienced by the relative. Wells also reported that memory disturbances in the injured patient was a poor predictor of condition of caregivers. Similarly, Jackson et al.\textsuperscript{15} found that all problem behaviours, e.g. excessive activity, aggressive problems passive/low mood, except cognitive problems predicted poor well being in caregivers to some extent (time since injury ranged from 3 months to 44 years).

Prigatano et al.\textsuperscript{89} investigated a sample consisting of patients with TBI, dementia and memory complaints. The TBI patients were examined at mean of 10.5 months after injury. Prigatano and co-workers found a significant correlation between the patient’s awareness and the distress experienced by the relative. The higher level of distress, the less aware of difficulties, the relatives judged the person with TBI to be.

There seems to be a certain level of agreement regarding the effects of certain neurobehavioral deficits affecting the condition of the relatives.

\textit{Time since injury:} Gillen et al.\textsuperscript{61} and Harris et al.\textsuperscript{42} both found that time since injury was not related to frequency of depression. Groom et al.\textsuperscript{85} found that time since injury was inversely related to distress experienced by caregivers, suggesting that relatives experienced less distress over time. Kreutzer et al.\textsuperscript{25} found that time since injury was unrelated to caregiver distress and positively related to family functioning. This suggests that families adjust to the consequences of the injury over time, but caregivers do not - or that they still experience distress despite a well functioning family. Kreutzer and colleagues\textsuperscript{44} confirmed their earlier finding in a larger study recently, where frequencies of distress where similar at one, two and five years.

This effect of time on distress is unclear, but the majority of studies were unable to find evidence supporting a relationship between time and experienced distress. Families may adjust to changes and responsibilities associated with caregiving over time. However, caregiving may also accumulate emotional distress over time. As discussed, the effects of time are not clear and inconsistent results have been presented. However, its possible that distress may increase in some family members and
decrease in others. However, the variable needs to be considered when investigating the emotional condition of caregivers.

In summary, evidence seems to support the effects of premorbid history, coping style, social support, care responsibility and certain neurobehavioral deficits on the condition of the relatives. Uncertainties remain about the effect of the relatives’ gender, relationship to the patient and the patient’s functional level. The reviewed studies found no evidence supporting cohabitation, stressful life events, patient’s age, severity of injury and time since injury.

2.5 Intervention to the family

As described throughout the previous sections, relatives of brain injury survivors experience high frequencies of distress during the different phases of rehabilitation. The studies conducted in relation to reported needs almost unanimously found that most important needs are those related to information, and most unmet needs are those related to emotional support. Consequently, this highlights the importance of access to both psycho-educational and emotional intervention for the family. Moreover, the importance of family intervention have been emphasised by studies showing how the family influences the patient’s recovery. The investment in the wellbeing of the family is valuable not only for the family and the patient, but also for society.

Most intervention studies have focused on the situation of the family during and after rehabilitation and not in the early phases of hospitalisation, even though this time is known to be critical and families face a great amount of anxiety and distress.

Few studies have been conducted in the area, and only five randomised controlled trials studies (RCT) have been identified. The studies conducted have primarily investigated the efficacy of intervention in three areas: information, education and psychological support (details regarding the studies are shown in Table 4).

**Information:** Morris et al. investigated the effect of an information booklet on anxiety in two different groups receiving the booklet at different times. The participants were assessed before receiving the booklet and 3-4 weeks after. The booklet contained information about head injury and different levels of severity, cognitive impairments, emotional and behavioural changes and included a section concerning “how to look after yourself”. The authors expected that especially the early group would benefit from the provided information, but the authors failed to report any significant
improvements in psychological distress and anxiety in the two groups. However a trend towards alleviation of anxiety was found in the early group. The finding is far from conclusive, as the study is limited by a small sample size and the lack of a control group.
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention/measure</th>
<th>Design</th>
<th>Time of assessment</th>
<th>Significant findings</th>
</tr>
</thead>
</table>
I2: >12 mth post injury  
Follow-up: 3-4 weeks after intervention | No significant findings                                                               |
|                  | I1 (n=11): booklet  
I2 (n=15): booklet  
Allocated to groups depending on time since injury (2-9 mths vs.>12 mths) |                                 |                                                        |                                                                                      |
| Sanguinette (1987)| 2 videotapes addressing cognitive and physiological problems at discharge/rating on cognitive extrapolation test | RCT                             | Inclusion: at discharge from hospital.  
Follow-up: after intervention | I-group were more informed about consequences of brain injury                         |
| Albert (2002)    | Caregiver education at discharge, designated social worker/ Likert scale assessing burden, satisfaction & mastery | Quasi-experimental               | Inclusion: at discharge  
Follow-up: 1, 2-4, 5-7 or 8-13 mths after discharge | Significantly lower burden, better quality of life                                       |
| Carnevale (2002) | Behaviour management (8x2 hours) and education (4x2 hours) administered by psychologist and behaviour technician/QRS & MBI | RCT                             | Inclusion: 11: 7.8 yrs since injury  
I2: 10 yrs since injury  
C: 8.5 yrs since injury  
Follow-up: 1, 5 and 14 wks after intervention | No significant findings                                                                |
| Sinnakaruppan (2005)| 8 sessions of didactic presentation with a neuropsychologist: written material, role play, discussion etc. addressing memory, emotional, executive problems/HADS, GHQ, RSE &COPE | Pilot study (RCT)                | Inclusion: 1: 2-97 mths  
C: 7-84 mths  
Follow-up: 3 mths after intervention | I-group showed significantly improvement compared to controls in terms of severe depression (GHQ). |
Follow-up: 4, 8 & 12 mths. | Significant decrease in depression, health complaints and in dysfunctional problem-solving. No effects on wellbeing, burden or constructive problem-solving styles |
(>7.1 mths after injury).  
Follow-up: 18 mth after the last training | High overall satisfaction: gained knowledge was applicable to everyday problems       |
<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Support Group</th>
<th>Duration</th>
<th>Follow-up</th>
<th>Inclusion</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singer (1994)</td>
<td>2 types of support groups (9 sessions of 2 hours): a stress management group and an information and support group</td>
<td>9 sessions</td>
<td>3 months</td>
<td>3-66 months</td>
<td>2 months</td>
<td>Increased anxiety and depression compared to 12.</td>
</tr>
<tr>
<td>Acyn (1995)</td>
<td>Quasi-experimental (12 modules)</td>
<td>9 sessions</td>
<td>6 months</td>
<td>12: (n=12); Information and support group</td>
<td>12: (n=12)</td>
<td>No significant change in terms of coping ability, self-esteem, or life satisfaction</td>
</tr>
<tr>
<td>Perlez (1998)</td>
<td>Quasi-experimental (8 modules)</td>
<td>12 modules</td>
<td>2 months</td>
<td>12: (n=12); Both groups</td>
<td>2 months</td>
<td>No significant change in family cohesion, significant decrease in psychological distress (GHQ), and subjective burden and strain.</td>
</tr>
<tr>
<td>Brown (1999)</td>
<td>Support group (9-10x1.5-2 hours): on-site vs. telephone groups led by social work or psychology professionals</td>
<td>9-10x1.5-2 hours</td>
<td>6 months</td>
<td>2.6 yrs since injury</td>
<td>6 months</td>
<td>Similar improvements for both groups: significant improvement in POMS and a trend toward improvement in FAD and CBI.</td>
</tr>
<tr>
<td>Liamaki (2003)</td>
<td>Support group (6 sessions)</td>
<td>6 sessions</td>
<td>1 month</td>
<td>10.5 months</td>
<td>1 month</td>
<td>No significant changes</td>
</tr>
<tr>
<td>Kreutzer (2009/2010)</td>
<td>Ten week program (BIFI) with interactive format addressing issues as communication, problem solving, and goal setting</td>
<td>10 weeks</td>
<td>3 months</td>
<td>1.2-185 months</td>
<td>3 months</td>
<td>Increase in met family needs and perceived access to services. No impact on psychological distress, family functioning, and satisfaction.</td>
</tr>
<tr>
<td>Backhouse (2010)</td>
<td>CBT (16 x 2 hours): 16 x 2 hours including supportive psychotherapy, psycho-education, stress management, problem-solving skills, and coping</td>
<td>CBT (n=20)</td>
<td>3 months</td>
<td>6 months</td>
<td>3 months</td>
<td>I-group improved Perceived Self-Efficacy compared to controls. No difference on BSI.</td>
</tr>
</tbody>
</table>

**Psychological/Supportive**

1. I refers to intervention/experimental group, C refers to control group. Mths, months; yrs, years; wks, weeks; HADS, Hospital Anxiety and Depression Scale; GHQ, General Health Questionnaire; QRS, Questionnaire on Resources and Stress; MBI, Maslach Burnout Inventory; COPE, TheCOPE Scale; RSE, The Rosenberg Self-Esteem Scale; CES-D, Center for Epidemiologic Studies Depression Scale; BSI, Brief Symptom Inventory; PCI, Personal Coping Inventory; FAD, Family Assessment Device; CBI, Caregiver Burden Inventory; BICQ, Brain Injury Coping Skills Questionnaire. Way of Coping Questionnaire; FNS, Family Needs Scale; BSI, Brief Symptom Inventory; PCI, Personal Coping Inventory; PCI, Personal Coping Inventory. 
2. The range refers to the number of months that the participants had care for the TBI survivors. Time since injury was not provided in the study. 
3. Parent of children with ABI.
Educational and psychological intervention: The earliest intervention study identified was done by Sanguinetti and Catanzaro\textsuperscript{102}. The authors conducted a RCT of educational videotapes. The tapes were administered at discharge and addressed cognitive dysfunctions and physiological problems. The intervention group received two videos; one regarding cognitive dysfunctions and one addressing physiological problems. The control group only received the video regarding physiological problems. After watching the videos, the groups completed a cognitive extrapolation test, where they were asked about cognitive dysfunction, and how to react to a particular situation. The findings suggested that the intervention group were more informed about brain–injury induced behaviour, which made the relatives more prepared to help the survivor compensate for dysfunctions. The study did not investigate the effect of this ‘more prepared’ strategy on emotional distress.

Albert et al.\textsuperscript{103} assessed the effects of a social work liaison program on caregiver outcomes. The intervention had three components: education at discharge, designation of a social worker to support each family caregiver up to time of discharge and maintenance of the social work liaison after discharge. A structured questionnaire developed by the authors assessed a variety of outcomes related to both the patient and the caregiver. Effects were assessed by comparing findings to a historical cohort from the same hospital, and the findings suggested lower burden and better quality of life in the intervention group. A major limitation of this study is the lack of standardised outcome measures making generalisations of the findings difficult.

Carnevale et al.\textsuperscript{104} investigated the effect of two different interventions; an educational consisting of behaviour management, and a behavioural intervention conducted in the natural setting. Despite the amount of intervention (Table 4), the RCT reported no significant findings at either five or 14 weeks follow-up. The authors concluded that the outcome measures used might not have been sensitive to detect change, which was perceived as clinically meaningful. Moreover, the authors suggested that changing the experienced burden and distress of caregivers was not possible during the reasonable short study period. The main limitations of this study were the small sample size and the insensitive measures.

Sinnakaruppan et al.\textsuperscript{105} conducted a pilot study investigating effects of a didactic presentation with exercises, advice, role play and group discussions. The sessions addressed memory problems, emotional problems, and executive problems and were performed by a neuropsychologist. Both groups showed positive changes on the GHQ. The intervention group showed significant positive
change in terms of severe depression compared to controls. The authors suggested that follow-up should be longer, as symptoms of depression and anxiety might require longer time to change.

Rivera et al.\textsuperscript{106} investigated the effect of 12 monthly sessions over a year in problem solving in the sample reported on earlier\textsuperscript{43}. The sessions were not standardised and four were conducted in-home and the rest over the phone. In the intervention group, the sessions had a positive impact on psychological distress, depression and dysfunctional problem-solving styles compared to a control group only receiving written educational material. The relatively small sample size resulted in a modest level of power for the analyses, which warrants for replication in a larger sample.

Sander et al.\textsuperscript{107} employed a web-based videoconferencing approach to training caregivers in rural areas. The program combined education and interactive problem-solving to compensate for problems relating to the brain injury. The study was conducted as a feasibility study, and the results showed that the participants’ overall satisfaction was high. They perceived gaining knowledge that was applicable to everyday problems. The authors did not investigate if this had any effect on the distress experienced.

\textit{Psychological and supportive intervention:} Singer et al.\textsuperscript{108} investigated the effect of two types of support groups: a stress management group and an information and support group. The participants were parents of children with ABI, and no control group were included. Both groups experienced reduced anxiety and depression, and only the group receiving stress management had significantly reduced symptoms of depression compared to the information group. Because of the lack of a control group, it is not possible to assess whether the effects were due to the intervention or due to time (because of the limited number of RCT’s, this study is included in the review even though the study only included parents of children with TBI).

Acorn\textsuperscript{109} investigated effects of a group programme consisting of both education and psychological support. The intervention consisted of ten modules, each module started with a presentation by the facilitator followed by sharing experiences of the participants and the provision of emotional support. The study revealed no significant change in coping ability, self-esteem or life satisfaction in the participants. The only significant difference noted was increased use of supportive coping techniques after attending the program.

Perlesz & O’Loughlan\textsuperscript{110} examined the effect of family therapy on changes in stress and burden among spouses of patients with TBI. Significant increase in family cohesion, significant decrease in
family conflict, psychological distress (GHQ), subjective burden and strain were found. However, follow-up data cited increasing levels of anger and marital dysfunction approaching baseline levels. Brown et al.\textsuperscript{111} compared an on-site intervention versus telephone intervention. The groups themselves chose the topics debated. The study reported a significant improvement in psychological distress for both groups, but no decrease in experienced family burden or function. The authors conclude that support groups conducted over the phone can be an alternative to on-site meetings in rehabilitation facilities covering large distances.

Liamaki & Bach\textsuperscript{112} investigated effects of a support group on a very small sample of relatives. The support group was conducted with two goals; providing education about brain injury and an opportunity for the participants to talk and share ideas. During the study period, two participants dropped out, and the authors conducted the analyses on only four participants, which did not provide enough power to detect changes.

Kreutzer and co-workers have developed the Brain Injury Family Intervention (BIFI); a structured intervention program, which includes educational, skill building and psychological support components\textsuperscript{113}. The outpatient program consists of five two-hour intervention sessions, and the intervention is conducted by doctoral level psychologists trained by the first author. The benefits of the BIFI program have been reported in two different publications. First, a preliminary investigation on 53 caregivers and TBI survivors indicated a greater number of met needs and perception of fewer obstacles to receiving services, but the program had no effect on standardised measures of psychological distress (BSI), family function (FAD) and satisfaction with life (SWLS)\textsuperscript{114}.

One year later the authors published new results on the program, this time on a larger sample (n=76 survivors and caregivers, however still including the first sample). Outcomes measures reported were a Learning Survey, a Session Report Form and Program Satisfaction Survey. The outcome measures were designed to evaluate the different aspects of the program on Likert type scales. Patients and caregivers rated sessions ‘helpfulness’ high, as they did in terms of meeting their goals. The authors conclude that BIFI is perceived as helpful and that the treatment methods may facilitate the achievement of goals. The authors did not report results on any of the standardised outcome measures used in the most recent publication\textsuperscript{115}.

Marks et al.\textsuperscript{116} adopted the BIFI program and tried to implement this in the acute and post-acute phases of hospitalisation. Ten neurosurgical nurses have used and evaluated the program and agreed that a structured program would lead to more positive interaction between staff and families. However, effects of the program on the distress of the relatives have not yet been investigated.
Backhaus and colleagues\textsuperscript{117} completed a RCT investigating effects of a Brain Injury Coping Skills Group for both the survivor and caregiver. Participants were included from both outpatient and inpatient rehabilitation, and the majority of the participants had sustained their brain injury during the last year. The program had positive effects on perceived self-efficacy, but not on psychological distress.

Most authors do conclude that the carers benefit from the different programmes, even though the results of the reviewed studies are not convincing. Only two\textsuperscript{106,108} of five RCT’s conducted\textsuperscript{102,104,106,108,117} found significant effects of the administered interventions on anxiety, depression and health complaints. Rivera also found effects on dysfunctional problem-solving, and Backhaus found an intervention effect on Perceived Self-efficacy, but not on experienced distress. The third RCT found an effect on knowledge about brain injury and cognitive problem\textsuperscript{102}, and the forth reported no significant findings\textsuperscript{104}.

The rest of the conducted studies had a pretest-posttest quasi-experimental design revealing mixed results. Acorn\textsuperscript{109}, Liamaki & Bach\textsuperscript{118} and Morris\textsuperscript{101} reported no significant findings of their administered interventions (e.g. support groups and an information booklet). Kreutzer et al.\textsuperscript{114,115} and Albert et al.\textsuperscript{103} reported a significant decrease on subjective outcome measures primarily on Likert type scales. Kreutzer et al.\textsuperscript{114,115} also used standardised measures, but failed to report improvements on any of these. Perlesz et al.\textsuperscript{110} and Brown et al.\textsuperscript{111} were actually the only two of the quasi-experimental studies, which were able to report significant improvements on standardised scales. Improvements were found in relation to family cohesion and conflict as well as psychological distress. Nevertheless, it is difficult to assess effects of these quasi-experimental studies, as no control group (in one case a historical control group) have been included. It is not possible to assess with definite, whether the reported effects were due to the interventions or just time.

Moreover, many of the findings have been reported on subjective measures, sometimes constructed by the authors themselves. There is no consensus on important outcome measures or which methodology that is most appropriate. In most studies, samples were small and in some cases biased as they were recruited from diverse support groups, which are not representative for the whole population. Most authors do not comment on the situation and condition of the patient, which is maybe one of the most important factors, when evaluating the status of the caregivers. Many authors fail to report when in the different phases of rehabilitation the intervention occurs and to
what extent the patient has received rehabilitation services. This is a major concern, as relatives do have different needs in the different phases of rehabilitation and because the condition of the relatives is intertwined with the patients.
In this chapter the methods and materials will be described.

3.1. Design
Different research designs were employed in the different papers. Paper I - III were conducted as cross-sectional studies investigating the condition of the relatives at different time points during rehabilitation: in a NICU and at admission to sub-acute rehabilitation. Paper IV was conducted as a controlled trial assessing effects of an acute neuropsychological intervention. The study described in Paper V employed a longitudinal design, where the participants were followed from admission to sub-acute rehabilitation till one year after injury.

3.2 Procedure
The cohort of patients was primarily recruited from the Traumatic Brain Injury Unit, Department of Neurorehabilitation, Glostrup Hospital (see the admission criteria in section 2.1). The participants were included as soon as possible after admission. The relatives were contacted by one of the neuropsychologists working in the unit, who in detail described the study and provided written information about the study. If the relatives gave consent to participate, they were included. The sample described in papers III and IV were recruited at the acute phase, at the NICU, Rigshospitalet. A physician from the NICU contacted the author of this thesis, when an eligible patient with a relative meeting the inclusion criteria, was admitted. The physicians monitored the condition of the patient the first 48 hours, and if the patient survived and met the admission criteria for the TBI-unit (see section 2.1), indicating a need for further rehabilitation, the author or a colleague contacted the relatives and arranged a meeting in the NICU. At this meeting the relatives received oral and written information about the study and the relatives gave consent to participate. All relatives approached in the NICU agreed to participate, and one relative declined to participate at admission to the TBI-unit.

If the relative did not speak Danish, had a psychiatric diagnosis or a progressive brain disease, both relative and patient were excluded from the study. If the patient died during the study period, the relative was excluded.
The relatives completed questionnaires about their emotional condition at four or five different time points (depending on time of enrolment) during the first year after the patient’s injury (See Figure 1 below). If the relative had not returned the questionnaire within a week after admission, the relatives were contacted by the neuropsychologist as a reminder. If the relative did not return one of the questionnaires administered after discharge, they received a letter with a reminder. If the relatives still failed to return the questionnaire, a phone call was made as a reminder.

3.3 Data collection
The study is based on one sample of relatives followed from time of injury to one year after injury. The sample completed questionnaires at the following time points:

**T1:** At the NICU, Rigshospitalet (n=46)
**T2:** At admission to sub-acute rehabilitation, TBI Unit, Glostrup Hospital (n=85)
**T3:** At discharge from the TBI Unit (n=70)
**T4:** Three months after discharge (n=59)
**T5:** One year after injury (n=58)

The five different papers have investigated sub-samples at the different assessment points (see Figure 1). Paper I-II assessed two different samples included at T2. Paper II only included patients and relatives fulfilling the requirements to participate in the present study as well as an ongoing study\(^B\) at our unit. Paper III investigated the condition of a sample of relatives in the acute phase at T1. Paper IV investigated the effect of an acute neuropsychological intervention comparing an intervention and a control group at admission to sub-acute rehabilitation (T1-T2). Paper V assessed the different trajectories of depression and anxiety in a sample of relatives during the first year after the patient’s injury (T2-T5)\(^C\).

\(^B\) The ongoing study was done in collaboration with Moss Rehabilitation Research Institute, Philadelphia. This study had extensive exclusion criteria and these are specified in paper II (see appendix 2).

\(^C\) For practical reasons the different time points are labelled T1 to T4 in paper V, which corresponds to T2 to T5 in this dissertation.
3.4 The sample

The complete sample consisted of 94 patients and 94 relatives. The sample of relatives were primarily females (74.5%) and the majority of the relatives were working at the time of injury (81.9%). About half of the relatives (59.6%) were living with the patient, when he or she was injured. Most of the relatives were spouses (34.0%) or parents (42.6%), and the remainders were siblings (3.2%), children (13.8%) or boy-or girlfriends (4.3%). In two cases (2.1%) the relatives included were aunts of the patients, as they were the closest relatives.

Of the patients, 68 (72.3%) had sustained a traumatic injury and 26 (27.7%) a non-traumatic brain injury. The patients were admitted to rehabilitation about three weeks after injury (Median= 18; IQR=13-25) (See Table 5 for sample characteristics). Of the total sample, four patients died during stay in the NICU, and five patients died during stay in the TBI-unit.
Table 5: Sample characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency/Median</th>
<th>Mean ± SD</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n=94)</td>
<td>70.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (n=94)</td>
<td>29.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INJURY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic (n=94)</td>
<td>72.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-traumatic (n=94)</td>
<td>27.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AGE</strong></td>
<td>39</td>
<td>38.78 ± 20.20</td>
<td>20-58</td>
</tr>
<tr>
<td>ISS (n=64)^</td>
<td>29</td>
<td>31.75 ± 9.61</td>
<td>25-38</td>
</tr>
<tr>
<td>GCS adm. (n=81)</td>
<td>11</td>
<td>10.81 ± 3.12</td>
<td>8-14</td>
</tr>
<tr>
<td>EFA adm (n=81)</td>
<td>38</td>
<td>43.33 ± 18.18</td>
<td>29-53</td>
</tr>
<tr>
<td>FIM adm (n=83)</td>
<td>18</td>
<td>23.24 ± 12.93</td>
<td>18-20</td>
</tr>
<tr>
<td>RLA adm (n=61)^</td>
<td>4</td>
<td>3.87 ± 1.53</td>
<td>2-5</td>
</tr>
<tr>
<td>Adm. rehab, days after injury (n=88)</td>
<td>18</td>
<td>21.46 ± 14.45</td>
<td>13-25</td>
</tr>
<tr>
<td>LOS, days (n=83)</td>
<td>112</td>
<td>119.01 ± 65.38</td>
<td>69-153</td>
</tr>
<tr>
<td><strong>RELATIVE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (n=94)</td>
<td>Female</td>
<td>74.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>25.5%</td>
<td></td>
</tr>
<tr>
<td>Relationship (n=94)</td>
<td>Spouse</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parent</td>
<td>42.6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>13.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Siblings</td>
<td>3.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boy-/girlfriends</td>
<td>4.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>2.1%</td>
<td></td>
</tr>
<tr>
<td>Occupational status (n=94)</td>
<td>Full time work</td>
<td>81.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pension</td>
<td>18.1%</td>
<td></td>
</tr>
<tr>
<td>Cohabitant status (n=94)</td>
<td>Cohabiting</td>
<td>59.6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not-cohabiting</td>
<td>40.4%</td>
<td></td>
</tr>
<tr>
<td>Social support (n=40)^</td>
<td>Very satisfied</td>
<td>77.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fairly satisfied</td>
<td>22.5%</td>
<td></td>
</tr>
<tr>
<td>Life events (n=41)^</td>
<td>Last year</td>
<td>1</td>
<td>1 ± 1.21</td>
</tr>
<tr>
<td></td>
<td>Entire life</td>
<td>2</td>
<td>1.93 ± 1.59</td>
</tr>
</tbody>
</table>

ISS, Injury Severity Score; GCS, Glasgow Coma Score; EFA, Early Functional Abilities; RLA, Rancho Los Amigos Scale; LOS, Length of Stay; ^ Only applicable for patients with TBI; *The measures regarding social support and life events were administered after the data collection had begun, so the whole sample did not complete these questions.

3.5 Neuropsychological intervention

Paper IV investigated the effect of an acute neuropsychological intervention to relatives of patients with severe brain injury administered in an NICU in Copenhagen, and paper II assessed the amount of neuropsychological support administered as a standard part of the treatment during the patient’s stay in the TBI Unit in the sub-acute phase.

3.5.1 Acute neuropsychological intervention

*Method:* The intervention group received neuropsychological support during acute care conducted by neuropsychologists trained in dealing with psychological trauma and having years of experience in the field of brain injury rehabilitation. The sessions were not manualised as the emotional
condition and consequently the needs of relatives differed considerably. In each session, the neuropsychologist decided on the most beneficial structure according to the needs of the relatives balancing between psychological support and psycho-education. This method was chosen after conducting a few pilot sessions facing the very different situations and needs of the families.

**Purpose and expected benefits:** The purpose of the intervention was twofold and consequently a flexible mixture of both emotional support and psycho-education. The sessions were targeted on the family’s immediate situation with a close family member severely injured in hospital. The first purpose of the intervention was to provide psychological support to the family in terms of dealing with the distressing situation of having a critically injured family member. The primary objective for the neuropsychologist was to listen and to instill hope in the families by identifying progress in the patient’s condition and personal strengths in the relatives. This was expected to help families regain hope in the future and indirectly causing emotional relief. The second purpose of the intervention was psycho-educational, thus providing information about treatment in the acute setting and consequences of brain injury. Giving needed information was expected to improve understanding of the patient’s condition and reduce anxiety and more general symptoms of distress. The relatives were only given information they requested, and in each session the neuropsychologist carefully evaluated how much information the relatives were capable of receiving without causing further distress.

**Content and topics:** The specific topics of the sessions depended on the relatives’ specific needs. Every session began with the neuropsychologist asking the family how they experienced the accident, if they witnessed it or were involved. In cases where the relatives had not been present, they were asked to share how they received the message about the accident. The relatives often requested immediate psychological support to help them deal with their own emotional reactions and needs during the first critical phases of the patient’s stay in the acute setting. Topics often addressed in the supportive part of the sessions were how to handle each day with a close family member in hospital, feelings of isolation, guilt and emotional distress. The second part of the sessions was psycho-educational, and the relatives could ask questions regarding treatment in the acute setting, the first period of unconsciousness, post-traumatic amnesia, consequences of brain injury and recovery from brain injury.
3.5.2 Sub-acute neuropsychological intervention

The intervention, described in Paper II, provided in the sub-acute phase was part of the standard treatment procedure during the hospitalisation of the patient. All relatives of patients admitted to intensive rehabilitation in the TBI Unit were offered two types of neuropsychological intervention provided by the neuropsychologists working in the unit with years of experience in the field of brain injury rehabilitation.

*Individual sessions:* The neuropsychologist in the patient’s team contacted the relatives, when the patient was admitted and prompted the first session. This appointment was scheduled as soon as possible after the patient’s admission to the unit, and the neuropsychologist invited the closest family to participate in the first session. This appointment was primarily aimed at giving the relatives information about severe TBI and its possible consequences. The first session was often the beginning of a more supportive psychological process with the relatives. In some cases, the process continued through the patient’s hospitalisation, but this varied greatly. Generally, more than one family member was present, but if necessary one-on-one sessions were offered. The sessions with the neuropsychologist were psycho-educational as well as supportive. Their content depended on the relatives and their specific needs. Usually, the relatives expressed a need for information about TBI, possible consequences, recovery from TBI, including the first period of unconsciousness, post-traumatic amnesia and the following remaining deficits. Furthermore, the relatives often needed support to help them deal with their own emotional reactions and needs during the patient’s recovery. Topics often addressed in the supportive part of the sessions were: role shifting in the family, mixed feelings about the person with the brain injury, how to handle each day with a close family member in hospital, feelings of isolation, guilt and emotional distress. The intervention was individualized according to the relatives’ needs and is a flexible mixture of both psycho-education and emotional support.

*Support group:* The relatives were also offered the opportunity to participate in a support group led by a neuropsychologist, where the relatives could debate topics of their own choice. The neuropsychologist moderated the group, but otherwise the group was not structured. The group session started with an introduction, where the relatives were asked to tell the group what had happened to their family member and their own reactions. However, if a relative merely wanted to listen at their first visit, this was also accepted. The objective of the group was primarily supportive.
and only educational in the sense that relatives learned about the different types of brain injury, their consequences and recovery in interaction with the neuropsychologist and the other relatives, when listening to other relatives.

The acute neuropsychological intervention was thought to be an early supplement to the standard procedure for intervention to relatives in the sub-acute setting. Early on, the relatives included in the acute setting would receive the requested support, and this was presumed to make the transition from acute hospital to the sub-acute unit easier and indirectly causing emotional relief. Both the acute and sub-acute intervention had psycho-educational and supportive components as described above. The major differences between the two interventions were the duration and the content. The acute intervention was in most cases limited to only one session, since the patient was then transferred to the sub-acute TBI-unit. For this reason, it was important to finish each session properly, making sure that the relatives had no further questions or queries. The acute intervention primarily focused on emotional handling of the acute situation with a loved one admitted to critical care and aspects related to the immediate situation, whereas the sub-acute intervention also focused on the future and concerns related to this.

### 3.6 Measures

#### 3.6.1 Assessment of relatives

The following measures were administered:

**Quality of life**: Each relative was asked to complete the Short Form 36 (SF-36), a measure of self-reported health-related quality of life. The questionnaire comprises 36 items addressing eight dimensions of health. Scores in each domain of the SF-36 range from 0-100 with higher scores indicating better health. Only four scales were used in the present study: Role Emotional (RE), Social Function (SF), Mental Health (MH) and Vitality (VT). Low scores on the RE-scale means problems with work or other daily activities as a result of emotional problems, and high scores indicate no problems in this area. Low scores on the SF-scale indicate extreme and frequent interference with normal social activities due to physical and emotional problems, and high scores indicate no problems. On the MH-scale, low scores indicate feelings of nervousness and depression, and high scores mean that the respondent feels happy, peaceful and calm. On the VT-scale, low scores refer to feeling tired and worn out, and high scores mean feeling full of pep and energy. The scores of the relatives were evaluated in terms of the Danish norms provided by Bjørner et al,
and this normative study showed high Cronbach’s alpha coefficients on all the subscales used in this study ranging from 0.75 to 0.85\textsuperscript{119}.

We chose to use the sub-scales related to the mental components of quality of life. It was considered too time consuming for the relatives to complete all eight sub-scales along with the other measures administered. This was especially the case at time of enrolment, where relatives often were very distressed and easily could feel overwhelmed by the length of the questionnaire.

The relatives were also asked to rate their own perception of quality of life on a visual analogue scale (VAS) with a range from 0 to 10, 0 indicating “very dissatisfied” and 10 indicating “very satisfied”.

**Anxiety and depression:** The relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of SCL-90-R; a self-report checklist designed to reflect the symptom pattern and level of distress\textsuperscript{36}. Each item is scored on a scale of 0 (‘not at all’) to 4 (‘extremely’) indicating the degree of distress for that particular item. The respondents are asked to rate each item according to their condition during the past seven days. Raw-scores were converted into T-scores, and the responses were evaluated in terms of the gender-specific norms for a Danish sample provided by Olsen et al.\textsuperscript{78}. This Danish population study revealed high alpha coefficients on all the SCL subscales, and in particular for the depression and anxiety scales used in this study ($\alpha=0.91$ and $\alpha=0.86$ respectively)\textsuperscript{78}. Because of the concerns about the length of the questionnaire, only the anxiety and depression scale were administered. These two scales were chosen, as they seemed to represent the most frequently reported symptoms in relatives of brain injury survivors.

The outcome measures, SF-36, VAS and SCL-90-R, were administered at four (T2-T5) or five (T1-T2) time points depending on time of enrolment.

**Social support:** Questions regarding the relatives’ social support included a question about how often they had contact with different people (parents, children, other family, colleagues after work, neighbors, childhood friends, other friends, professional caregivers), and how satisfied the relative was with this contact. The relatives also reported, how many people they were able to share very personal matters with. The questions were modified versions of the questions used in the Copenhagen City Heart Study\textsuperscript{120}.
**Life events:** Questions about traumatic life events over the past year and over the entire life span included five work related questions (unemployment, not being promoted, conflicts with colleagues, superiors or subordinates) and seven questions related to events in the family (children severely ill, severe educational problems for children, severe conflicts with grown-up children, severe problems in marriage, own severe illness, severe illness or death among relatives, severe economical problems). These questions were also modified from the Copenhagen City Heart Study\textsuperscript{120}, and we counted the total amount of traumatic events in the past year and over the entire life. Questions regarding social support and life events were administered at baseline and at one year follow-up.

3.6.2 **Assessment of patients**

As a standard procedure at admission and discharge, relevant data was collected regarding the patient’s condition: severity of injury, level of consciousness and function.

**Severity of injury:** The severity of injury was assessed by two well-known and validated scales: The GCS\textsuperscript{121}, and the Injury Severity Score (ISS)\textsuperscript{122}. GCS is scored from 3 to 15. Patients with scores less than nine are considered to be in coma, and patients with scores of 15 are able to follow commands, have spontaneous eye opening and are fully oriented. According to criteria for injury severity, GCS scores of eight or less are classified as severe injuries.

The treating physician also estimated the ISS, which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0 to 75. Each injury is assigned an Abbreviated Injury Scale score and is allocated to one of six body regions (head, face, chest, abdomen, extremities (including pelvis) and skin). Only the highest AIS score in each region of the body is used. The scores of the three most severely injured regions are added together to produce the ISS. The ISS was only assessed for patients with a traumatic brain injury.

The treating physician assessed GCS and the ISS at admission to the TBI-Unit.

**Level of consciousness:** Rancho Los Amigos (RLA) score\textsuperscript{123,124} was assessed by a neuropsychologist at admission to sub-acute rehabilitation. This score ranges from level one, which describes a comatose condition with no observable response, to level eight, which is a condition with
purposeful and appropriate responses. The scale was designed for use on patients with a traumatic brain injury. This score was assessed by the neuropsychologist in the patient’s team at both admission and discharge.

*Functional level:* The patient’s functional level at admission was assessed with the Early Functional Abilities (EFA) and the Functional Independence Measure (FIM). The EFA is an assessment tool for patients with severe cerebral impairments in the early neurological rehabilitation stage, which describes clinically observable changes in a patient’s early functional abilities. The EFA Scale contains 20 items and assesses early basic abilities related to four functional areas: vegetative, face and oral, sensory-motor and sensory cognitive functions. Each item is rated on a five-point scale from “not obviously observable” to “no essential functional limitation”. The total score is the sum of the item scores ranging from 20 to a maximum of 100. High scores indicate better functional ability. The FIM is an 18-item rating scale assessing activities of daily living (ADL): self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a seven-point scale from “total assistance” to “complete independence”. A total FIM score ranges from 18 to 126 with higher scores indicating greater independence. The FIM Scale has been shown to be valid and reliable for measuring functional outcome after TBI. The interdisciplinary team of nurses, physio- and occupational therapists obtained both FIM and EFA scores at admission and discharge.

The following measures were assessed on patients included in the NICU: *Clinical condition at the NICU:* Simplified Acute Physiology Score II (SAPS II) and Acute Physiology And Chronic Health Evaluation II (APACHE II) were designed to measure the severity of disease for patients above age 15. Both scores are obtained 24 hours after admission to the ICU. SAPS II includes parameters such as age, GCS, blood pressure, heart rate, body temperature, urine output amongst others. The measurement results in an integer point score between 0 and 163 and a predicted mortality between 0% and 100%. We only used the predicted mortality in this study. The APACHE point score is calculated from information about previous health status, age and 12 routine physiological measurements (such as blood pressure, body temperature, heart rate etc.)
during the first 24 hours after admission. The calculation results in an APACHE II score and an estimated risk of hospital death. We used the predicted death rate in percent as with the SAPS II. The Pediatric Index of Mortality (PIM)\textsuperscript{129} was used instead of SAPS and APACHE in the pediatric cases. The PIM is calculated from information collected when a child is admitted to ICU. The PIM describes how ill the child is when intensive care is started and is based on the observations of blood pressure, pupil reaction, mechanical ventilation etc. A predicted death rate is calculated in percentage.

CRASH 2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage)\textsuperscript{130} score was only used for TBI patients. This prognostic model is an aid to estimate mortality at 14 days and death and severe disability at six months in patients with traumatic brain injury (TBI). The predictions are based on the average outcome in adult patients with Glasgow Coma Score (GCS) of 14 or less, within 8 hours of injury and calculated on the patient’s age, GCS, pupil reaction, presence of major extra cranial injury and a CT scan description. The authors calculated this score retrospectively based on the relevant information collected from the patient’s file. We used both the mortality rate at 14 days as well as the disability rate at six month. Both numbers are given in percentages.

The SAPS II, APACHE II and PIM scores were estimated as a part of the standard procedure at admission to the NICU. These scores as well as the CRASH 2 can be calculated online on the relevant websites, and the scores used in this study were the mortality prediction in percent.

_Treatment in the NICU:_ We registered number of surgeries during NICU stay, days under sedation, length of time and number of times treated on mechanical ventilation. Furthermore, three dichotomous variables were registered: if the patient had a craniotomy or craniectomy performed, if the patient had intraventricular monitoring or intraventricular drainage inserted. Furthermore, the number of conferences with attending physician (only formal meetings documented in the patient’s chart) was registered as well as commuting time for the relative to the hospital. This information was retrieved from the patients’ files.
The analyses conducted in these studies were both descriptive and analytic. Descriptive statistics were used as percentages and means with standard deviations when normally distributed. For data with a non-normal distribution, medians and interquartile range were presented. One sample t-tests were used when comparing scores of the sample to the Danish reference populations. When comparing different groups, independent t-tests were used. Correlation analyses were performed using Spearman’s rho for non-parametric data and Pearson’s correlation for parametric data. Cohen’s $d$ was calculated as an effect size measure.

In paper I, comparisons between groups were performed using one sample and independent samples t-tests. Correlations were investigated using rank correlation, Spearman’s rho.

In paper II, descriptive statistics were used; results are presented as percentages and means with standard deviation and range. Parametric statistics were used, and comparisons between groups were performed using one sample and independent samples t-tests. Associations were investigated using Pearson’s correlation analysis for parametric data.

In paper III, descriptive statistics (means, standard deviations and minimum-maximum range for quantitative variables) were used to describe demographics. Group comparisons were made using one sample and independent samples t-tests. For every outcome variable, Pearson’s correlation analyses were completed identifying significantly associated variables. Multiple linear regression analyses were carried out to investigate associations between the predictor variables and the individual outcome measures.

In paper IV, descriptive statistics were used; results are presented as percentages and means with standard deviation and range. Categorical and ordinal data were analysed using chi-square and Mann-Whitney tests. Changes in the relatives’ condition between T1 and T2 were analysed with paired samples t-tests and the condition of the intervention and control group were compared using independent samples t-tests. ANCOVA was used to adjust for the relatives’ gender and for the
observed differences in means on variables with significantly different distributions in the two groups. We calculated Cohen’s $d$ to estimate effect size.

In paper V, a latent growth curve-modelling framework was used. We modeled a growth curve for each of the two outcome measures; anxiety and depression. The outcome measures were assessed at four different times, and these time points were the indicators of the growth model. The models accounted for the means, variances and covariances of the four repeated measures. Two growth factors were specified, an intercept and a slope factor; the two factors were assumed to correlate. The loadings for the intercept factor were all fixed at 1.0 indicating that this factor had a fixed and equal influence on the given outcome measure. The loadings for the slope factor (the growth trend) were fixed at the known values of the time measures. We constructed a baseline model to describe the development in outcome measures over time. Secondly, we tested the model with different covariates related to the patient and the relative.

All data were analysed using two-tailed testing and $p = 0.05$ as a threshold for statistical significance. Standard statistical analyses were conducted in SPSS versions 17.0 to 19.0, and growth curve models were employed using Mplus version 5.1.
The Committees on Biomedical Research Ethics of the Capital Region of Denmark (journal number H-KF-311150) approved the study, and the Danish Data Protection Agency (journal number 2007-41-0583) gave consent for data registration.

The relatives were informed about the study when included. They received written as well as oral information regarding the study, the aims of the study and the requirements if enrolled. If the relative agreed in participation immediately, they gave oral consent to participate to a neuropsychologist, which is acceptable by Danish law. If the relatives wanted to consider participation further before accepting, they were given 24 hours notice.

It was emphasised that the relatives could withdraw their participation at any time without having to give a specific reason.

When planning the study described in paper IV, we wanted to include both groups in the NICU. Nevertheless after conducting a few pilot sessions at the NICU, we decided to include the control group at T2. It was not considered appropriate to ask relatives at the critical time of enrolment in the NICU to participate in the study and not offer them any psychological support in the acute phase. This was simply not deemed morally and ethically acceptable. Moreover, when approaching the relatives and presenting yourself as a neuropsychologist, questions immediately arose, and it was considered unethical not to try and answer these and thereby already providing some kind of intervention.

Possible downsides of providing an early neuropsychological intervention were also considered. In some cases, sessions with a neuropsychologist may result in more distress as the relatives may have gained insight in the prognosis and future consequences of brain injury. However, the sessions primarily focused on the immediate situation in the NICU, and consequently it is unlikely that the intervention generated worries about the future in many relatives. The benefits of the early intervention were considered larger than any possible disadvantages.
CHAPTER 6

RESULTS

This section of the dissertation will briefly present the findings of papers I-V.

In preparation for this thesis, supplementary analyses were conducted investigating the condition of the relatives one year after injury.

Table 6 presents the essential results of the five papers in tabular form.

<table>
<thead>
<tr>
<th>PAPERS</th>
<th>Research question</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>To investigate emotional distress and quality of life in a sample of Danish relatives with severe brain injury at admission to sub-acute rehabilitation</td>
<td>Cross-sectional investigation</td>
<td>The sample had significantly lower scores on all quality of life scales and significantly more symptoms of anxiety and depression than reference population</td>
</tr>
<tr>
<td>II</td>
<td>To investigate amount of neuropsychological support administered to relatives of patients with severe TBI admitted to intensive sub-acute rehabilitation and possible associations between the relatives condition and the amount of support</td>
<td>Cross-sectional investigation</td>
<td>Relatives received about 18 units of 15 minutes of support during patient’s hospitalisation. Relatives with more symptoms of anxiety at admission received more support.</td>
</tr>
<tr>
<td>III</td>
<td>To investigate emotional well-being of relatives of patients with severe brain injury in the acute setting as well as risk factors associated with high anxiety and depression scores and impaired quality of life</td>
<td>Cross-sectional investigation</td>
<td>Of the sample, 51% and 69 % reported anxiety and depression respectively, as well as significantly impaired quality of life. Regression analyses revealed that up to 20% of the variance in depression scores could be explained by the CRASH 2 mortality prediction.</td>
</tr>
<tr>
<td>IV</td>
<td>To investigate if a group of relatives receiving neuropsychological intervention in the acute setting experienced a decrease in symptoms of anxiety and depression and an increase in quality of life, and if the group receiving the intervention had significantly fewer symptoms of anxiety and depression and better quality of life compared to a control group</td>
<td>Controlled Trial</td>
<td>The intervention group had a significant decrease in anxiety scores from the acute to the sub-acute setting. In the sub-acute setting, an ANCOVA model showed a borderline significant difference between the intervention and the control group on the anxiety scale.</td>
</tr>
<tr>
<td>V</td>
<td>To investigate changes in the emotional condition of relatives of patients with severe brain injury the first year after injury</td>
<td>Longitudinal design employing a latent variable growth curve analysis</td>
<td>The development in anxiety and depression was described by two different trajectories; Anxiety symptoms showed a steeper decline during the first three months and a continued decrease at a slower pace during the rest of the year. Depression symptoms decreased significantly over the first six months, and the decline continued the last six month although not significantly.</td>
</tr>
</tbody>
</table>
6.1 Emotional distress and quality of life in relatives during the first year after injury

6.1.1 Anxiety and depression

Paper I, II and III examined the condition of the relatives at different times during the patient’s rehabilitation, and all three papers found high prevalence of anxiety and depression, significantly increased compared to reference populations. Paper III examined the condition of 45 relatives during the patient’s stay in the Neuro Intensive Care Unit ~ 14 days after injury, and found that 53% had scores above cut-off (T-score ≥ 63) on the anxiety scale. Of the relatives, 69% had scores above cut-off on the depression scale, and 47% had scores above cut-off on both scales indicating clinical caseness as described by Derogatis (Derogatis defined caseness as having a T-score equal or above 63 on two sub-scales). Paper II assessed the emotional wellbeing of 26 relatives ~ 24 days after the patient’s injury at admission to sub-acute rehabilitation and found that 65% and 58% had scores above cut-off on the anxiety and depression scale, respectively. Of the relatives, 54% met the criteria for clinical caseness. Paper I also investigated the condition of 31 relatives when the patient was admitted to sub-acute rehabilitation ~ 36 days after injury. In this sample, 61% scored above cut-off on both the depression as well as the anxiety scale, and 55% met the criteria for clinical caseness. Frequencies of anxiety ranged from 53-65% and 58-69% on the depression scale, and the frequency reaching caseness ranged from 47-55%.

Paper V found an improvement in both anxiety and depression during the 12 months study period and identified the most significant improvement during the first six months. Our analysis revealed different trajectories for anxiety and depression. Anxiety had a significant decrease during the first three months, and a less steep decrease during the last nine months. The decrease found in depression was significant during the first six months, and the decline continued, but was not significantly different from zero the last six months. Symptoms of depression remained for a longer period than anxiety. It seemed that symptoms of anxiety were a more immediate reaction, which also made a more rapid recovery.

6.1.2 Quality of life

Papers I-III also found that the three samples had significantly lower quality of life than reference populations on the four scales administered (see mean, SD, range in the tables in the corresponding papers in the appendix).
6.1.3 Supplementary results
Supplementary analyses were conducted on the total sample as a part of the preparation for this thesis. The number of relatives scoring above cut-off on the anxiety and depression scale at the five different time points were investigated, and plots were constructed showing the unadjusted estimated mean scores on the VAS and the SF-36 for the whole sample during the first year after injury.

Anxiety and depression: As shown in figure 2, the number of cases above cut-off decreased with time. One year after injury, 22.4% of the relatives had scores above cut-off on the depression scale, and 26.3% had scores above on the anxiety scale.

![Figure 2: Frequency above cut-off on the anxiety and depression scale during the first year after injury](image)

Of the relatives, 16.9% was reaching caseness one year after injury, which is actually below what has been reported in the reference population, where 18% scored above cut-off. Even so, when calculating the mean T-scores one year after injury, we found a mean of 53.48 (SD 10.99) on the
anxiety scale and 55.31 (SD 9.95) on the depression scale. In both cases, mean scores were significantly different from reference population.

Quality of life: We plotted the unadjusted estimated mean VAS scores and SF-36 scores for the whole sample during the first year after injury.

Figure 3: Mean scores on the VAS scale indicating self-reported quality of life.

As shown in Figure 3, the mean VAS increases during the first year. However, it seems that relatives report a slight decrease after the patient’s discharge from hospital. However, the change only ranges from around 6.2 to 7.3, roughly just one point on the VAS scale during the 12 months. On the four different sub-scales, SF-36, the relatives experience an increase in quality of life on all four scales. The increase stabilises after six months on the RE-, VT- and MH-scale, and remains at the same level the last six months (Figure 4). The development in SF-scores is slightly different as the increase continues after six months with an average of 10 points.
The mean scores on the five time points on all four scales were all significantly different from scores of a reference population\textsuperscript{119}.

### 6.2 Predictors of emotional distress and quality of life

Papers I-III investigated associations between assumed predictors of the condition of the relatives and outcome. The predictor variables were related to the patient, the relative or in one case the setting (paper III) and the variables were chosen based on former findings in the literature and clinical experience.

**The relative’s gender:** Paper III found a trend towards male relatives having higher anxiety scores (p=0.052, d=0.85). None of the other papers found a difference related to gender.

**Relationship to the patient:** Paper I found a borderline significant difference between the levels of depression of spouses and parents (t=2.035, p=0.06, d=0.89) since spouses had more symptoms of depression than parents. Paper IV found that spouses had higher levels of depression (p<0.001) and anxiety (p=0.001) and reported lower quality of life at MH- (p=0.002) and VT-scale (p=0.007) than
other relatives. Papers III and V did not find any difference related to the relationship to the patient, and paper II did not investigate this matter.

Cohabitation: Paper III found significantly lower scores on the Social Function scale for relatives, who did not live with the patient (p=0.041) compared to relatives living with the patient at time of injury. A stepwise regression analysis showed that this variable explained 9.6% of the variance in Social Function scores. Paper I did not find any difference in depression, anxiety and quality of life scores related to whether or not the relative was living with the patient at time of injury, and Papers II, IV and V did not investigate this matter.

Social support and stressful life events: Paper V found that relatives reporting to have more personal contacts experienced a steeper decrease in depression during the first six months (p=0.010). Additionally, Paper V found that relatives having experienced more serious life events the last year, had higher initial anxiety scores (p=0.002). Interestingly, these relatives had a more rapid decline in anxiety scores (p<0.000).

The patient’s age: Paper IV reported that the age of the patient was associated with anxiety and depression indicating that relatives of older patients experienced less anxiety (p<0.001) and depression (p<0.001). Relatives of older patients experienced better quality of life having higher scores on the VAS (p=0.001), RE- (p=0.001), MH- (p<0.001) and the VT-scale (p<0.001) indicating better quality of life. Paper V found a trend towards relatives of older patients experiencing less anxiety initially (p=0.052). Paper I-III did not find any association between the patient’s age and the quality of life and anxiety and depression experienced by the relative.

Patient’s level of function and consciousness: Paper I found an association between the patient’s EFA-score at admission to sub-acute rehabilitation and the depression experienced by the relative (r=-0.44, p=0.02) indicating that relatives of patients with low EFA score experienced more depression.

Paper III found a correlation between the anxiety experienced by the relative and the patient’s GCS score on the day the relative completed the questionnaire (r=-0.31, p<0.05), however in regression analysis GCS did not contribute significantly to the variance in anxiety scores. Paper I and II did not
find any associations between GCS initially or at admission and the emotional condition of the relatives, and Paper IV did not investigate this matter.

Paper I identified associations between the patient’s RLA score at admission and the relatives’ depression scores ($t_r=-0.45, p=0.04$) and anxiety scores ($t_r=-0.45, p=0.04$) indicating that relatives of patients on lower levels of consciousness experienced more depression and anxiety. Paper V also reported this association; relatives of patients with a lower level of consciousness (RLA) reported more anxiety ($p=0.066$) and depression ($p=0.019$). However, this effect seemed to disappear with time.

**Treatment in the NICU:** Paper III found that stepwise regression analysis revealed that the variable craniectomy/craniotomy explained 12.2% of the variance in the relatives’ mental health scores. Relatives of patients who had this procedure performed had lower mental health scores.

Paper III found that CRASH 2 Mortality prediction explained 20.7% of the variance in the anxiety scores of the relatives and 16.5% of the variance in depression scores. In both cases, higher mortality predictions were associated with higher anxiety and depression scores in the relatives.

### 6.3 Neuropsychological intervention

#### 6.3.1 In the acute phase

Paper IV investigated the effects of a short neuropsychological intervention in the acute setting using a controlled design. The majority of the relatives (67.4%) received one session, and the duration of the sessions was one to one and a half hours depending on the relatives. Of the relatives, 17.4% had two sessions, 13.0% had three sessions and one relative had four sessions (2.2%). An independent samples t-test showed no difference in the relatives’ emotional wellbeing on T2 depending on whether or not the relative received more than one session of intervention. The content of the intervention was described in section 3.5.1.

The results showed that the intervention group experienced a significant decrease in symptoms of anxiety from T1 to T2 ($t=2.70, p=0.010, d=0.30$), and also scored lower on depression at T2 compared to T1, although not significantly lower ($t=1.77, p=0.085, d=0.29$). The intervention group became significantly worse from T1 to T2 ($t=2.12, p=0.043, d=0.40$) on the RE scale, but a trends towards improvement was found on the VT-scale ($t=-2.02, p=0.051, d=0.18$).

An ANCOVA model was used to adjust for gender and variables showing significantly different distribution in the intervention and the control group. The model adjusted for the relative’s gender,
the relative’s relationship to the patient (spouse vs. other), the patient’s age, ISS and the number of
days after injury that the relatives completed the questionnaire. The control group obtained higher
anxiety (p=0.066, d=0.59) and depression scores (p=0.338, d=0.31) than relatives in the
intervention group at T2, but the difference was not significant. With regards to quality of life, the
control group showed non-significantly lower adjusted VAS scores (p=0.354, d=0.30) and this was
also the case on the MH-scale (p=0.070, d=0.61). Scores on the anxiety and Mental Health scale
were borderline significant.

6.3.2 In the sub-acute phase
Paper II investigated the amount of neuropsychological support administered to relatives in the sub-
acute rehabilitation unit. The support was administered as a standard part of the rehabilitation
during the patient’s hospitalisation and included both individual sessions and group sessions.
Most of the individual support consisted of scheduled meetings with the neuropsychologist in the
interdisciplinary team treating the patient, and all relatives except one participated in at least one
session with the neuropsychologist. The largest amount of individual neuropsychological support
was registered during the first month of hospitalisation, where relatives received about nine units of
15 minutes on average, and the relatives met with the neuropsychologist two to three times. During
the entire period of hospitalisation, relatives had about six meetings with the neuropsychologist, and
on average the relatives received a total of 18 units corresponding to about 4.5 hours of
neuropsychological support during hospitalisation. The relatives had regular contact with the
neuropsychologists throughout hospitalisation, but the sessions shortened. Of the relatives included,
38% participated in the group sessions during hospitalisation.
We also examined whether the amount of support was related to the condition of the patient or the
relative at admission. Relatives’ symptoms of anxiety at admission were associated with the number
of sessions (r=0.50, p=0.009) as well as the amount of support (r=0.45, p=0.020) indicating that
relatives with more symptoms of anxiety received more support during the hospitalisation.
Relatives participating in the support group had higher scores on the anxiety scale at admission than
relatives not participating, almost reaching significance (t=–2.02, p=0.055). This tendency was not
replicated on the depression scale or any of the quality of life measures.
6.4 Brief summary of the results

As hypothesised, the relatives had high scores on anxiety and depression and decreased quality of life during the early phases of rehabilitation. The frequency of relatives experiencing levels above cut-off decreased to about a fifth of the total sample one year after injury. Growth curve analysis showed that symptoms of anxiety wore off faster than depression.

One year after injury, the number of relatives above caseness (T-scores ≥ 63 on both scales) was close to the numbers found in a normal Danish population, even so the mean T-scores were significantly different from the reference population. This was also the case on the four SF-36 scales administered.

A trend was found towards spouses and relatives of younger patients experiencing more anxiety and depression and lower quality of life. Moreover, relatives with better social network recovered faster from symptoms of depression. Relatives, who had experienced more serious life events during the last year, had higher anxiety scores, but also recovered faster. Moreover, lower level of function and consciousness and higher mortality prediction in the acute setting were indicators of increased emotional distress in relatives.

When investigating the effect of an acute neuropsychological intervention the results were mixed, but no significant effect of the intervention was revealed. However, many methodological issues may have biased these results. In the sub-acute phase, we found that relatives having high scores on the anxiety scale when the patient was admitted, received more neuropsychological support during hospitalisation.
This section is divided according to the aims of the thesis, and consequently, the five papers are not discussed separately.

7.1 Emotional distress and quality of life in relatives during the first year after injury

7.1.1 Anxiety and depression

The results of the papers in this thesis leave no doubt upon the fact that relatives are in severe emotional distress the first twelve months after the patient’s injury.

High frequencies of anxiety (51%) and depression (69%) have been reported during the patient’s stay in NICU comparable to those reported by researchers from critical care medicine. Only one other study in the field of brain injury has investigated the condition of relatives of patients with severe brain injury during intensive care\textsuperscript{30}, and this study found that more than half of the relatives reported a clinical relevant level of PTS symptoms. Because of the different outcome measures used, it is not possible to compare the findings of the two studies directly. But in both the Pielmaier et al. (2011) and in our study, more than half of the sample reported symptoms above the relevant cut-off on standardised scales.

At admission to sub-acute rehabilitation, the relatives also reported high frequencies of anxiety (61-65%) and depression (58-61%). In comparison, Oddy and colleagues reported that 39% of the relatives were above the cut-off score for clinical depression one month after injury\textsuperscript{20}. This frequency is lower compared to our results, however the patients in Oddy et al.’s sample had less severe injuries than the patients in our sample. Novack et al.\textsuperscript{59} found lower levels of depression and anxiety at time of admission to rehabilitation (~ 46 days post-injury); 9% were clinically depressed, and 33% of the caregivers were clinically anxious at admission. The levels of emotional distress reported in this study were low compared to Oddy et al.’s and our results in Paper I and III. However, as mentioned in the literature review, the caseness criteria used were higher than the recommended\textsuperscript{60}. If milder cases of depression and anxiety had been included, 51% of the sample would have been anxious and 26% depressed. Thus, the level of anxiety would then be comparable to our sample, but the level of depression would still be considered low compared to the level reported in Oddy et al.’s sample. Novack et al.’s investigation took place 46 days after injury, while
the study in Paper I was conducted 36 days earlier and paper II 24 days post injury. Novack et al. investigated relatives of patients with severe TBI defined as a period of post-traumatic amnesia or coma greater than 1 week. In our study, the severity of injury was assessed by ISS and GCS, which also indicated that our sample had severe brain injury. The mean age of the patients in the Novack et al.’s sample was 24 years, which is somewhat lower than in our samples (Paper I: 41 years old, and paper II; 33 years old). These differences between time of assessment and sample characteristics may also have influenced the results.

**Trajectories of anxiety and depression**: Paper V found an improvement in both anxiety and depression in the 12 months study period and identified the most substantial improvement during the first six months. Our analysis revealed different trajectories for anxiety and depression. Anxiety had a significant decrease during the first three months, and a less steep decrease during the last nine months. The decrease found in depression was significant during the first six months, and the decline continued, but was not significantly different from zero the last six months. Symptoms of depression remained for a longer period than anxiety. It seemed that symptoms of anxiety were a more immediate reaction, which also recovered faster. Other authors have found that symptoms of anxiety wear off faster than depression in a sample of caregivers (e.g. Turner et al., 2010). This finding is not surprising, as anxiety normally is a reaction to an external event. Depression is not necessary specifically related to a stressful life event, but is a more general condition. Anxiety is an emotional reaction with physical components, which occurs after an experience of danger or threat. To experience anxiety in relation to a real threat is normal, as long as the reaction is proportional with the experienced danger. The anxiety that relatives experience is most likely associated with the uncertainty about the patient’s condition in the early phases of rehabilitation. When the condition of the patient is stabilised, the uncertainty passes, but worries about the future emerges, as deficits after brain injury appears, and the symptoms of depression are maintained. Depression is normally associated with isolation and reduced social function, and the SCL depression sub-scale contains a representative sample of symptoms for a clinical depression.

**Supplementary analyses**: The frequency of both anxiety and depression leveled off during the study period and only about a fifth of the sample reported scores above cut-off one year after injury. This frequency is quite comparable to other studies conducted in the field. Oddy et al. found that 25% were above cut-off on the depression scale one year after injury, and Livingston et al. findings
were similar; 37% on anxiety, and 26% on the depression scale. A more recent study done by Marsh and colleagues\(^7\) found that 35% scored above cut-off on the STAI one year after injury, and 31% were above on the cut-off on the BDI.

Of the relatives 16.9% reached caseness one year after injury, which is actually below what has been reported in the reference population, where 18% scored above cut-off\(^7\). The difference between the normal population and our sample is small, but even though still surprising. As discussed in the methodological discussion below, it might be that the relatives completing the study are actually emotionally resilient compared to those dropping out. This might be the reason for the low frequency one year after injury.

Previous research and our current have used the cut-off defined by Derogatis (e.g. T-score on the GSI equal to or above 63 or a T-score equal to or above 63 on at least two subscales). This definition has been used on both the SCL as well as the BSI and has proven useful in different contexts. The term and definition of caseness was originally developed in order to be able to screen for psychiatric ‘cases’ in normal populations, and it operationalises when the score of one subject goes from being in the normal range to ‘abnormal’. This certainly has its benefits, as it is possible to compare large groups of patients and normal populations or as in this case compare frequencies above cut-off during a period of time. However, the caseness criteria have not been validated across groups. Moreover, it is important to recognise that relatives scoring high on both the anxiety and depression scale in the study are not a psychiatric case and warrant psychiatric intervention. Caseness simply indicates experiencing emotional distress at specific assessment point, and this emotional distress is related to the items on the anxiety and depression scale. This issue is emphasised in our results, where the mean T-scores in our samples were significantly different from the reference population one year after injury even though the number of cases had decreased to a level comparable to the reference population.

During the early phases of rehabilitation, high frequencies of emotional distress have been reported regardless of methodological diversities such as different times of assessment, different scales and patient populations. The frequency above cut-off dropped during the first year and reached a level comparable to reference population.

7.1.2 Quality of life

A quality of life measure was included, as studies have showed that quality of life can be high in caregivers even though high levels of distress are experienced\(^8\). The caregivers may still be
satisfied with their life for many reasons e.g. because their family member survived the brain injury, feeling competent in the caregiver role, positive life experiences etc. This might explain the relatively minor change in the mean VAS scores in our sample over time despite the relatives at the same time reported high levels of anxiety and depression. The changes in quality of life are more visible on the SF-36, which measures different components of quality of life.

Table 6: Quality of life assessed in different samples and with different follow-up intervals.

<table>
<thead>
<tr>
<th>SF-36</th>
<th>Paper III ~14 days (n=45)</th>
<th>Paper II ~24 days (n=26)</th>
<th>Paper I ~31 days (n=31)</th>
<th>Suppl. results ~1 year (n=57)</th>
<th>Arango-Lasprilla ~varying (n=90)</th>
<th>McPherson ~17.6 mths (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MH-scale</td>
<td>Mean±SD 33.3±18.5</td>
<td>Mean±SD 38.4±19.2</td>
<td>Mean±SD 30.4±15.0</td>
<td>Mean±SD 70.74±18.75</td>
<td>Mean (95% CI) 49.93 (46.35-53.52)</td>
<td>Mean±SD 68.80±21.00</td>
</tr>
<tr>
<td>VT-scale</td>
<td>Mean±SD 28.6±19.2</td>
<td>Mean±SD 33.0±18.1</td>
<td>Mean±SD 31.3±18.1</td>
<td>Mean±SD 55.79±23.05</td>
<td>Mean (95% CI) 43.56 (40.32-46.80)</td>
<td>Mean±SD 57.79±23.69</td>
</tr>
<tr>
<td>RE-scale</td>
<td>Mean±SD 29.2±30.9</td>
<td>Mean±SD 15.9±25.0</td>
<td>Mean±SD 26.7±33.2</td>
<td>Mean±SD 63.74±40.55</td>
<td>Mean (95% CI) 40.93 (32.61-49.25)</td>
<td>Mean±SD 71.01±38.74</td>
</tr>
<tr>
<td>SF-scale</td>
<td>Mean±SD 54.3±29.7</td>
<td>Mean±SD 55.8±30.1</td>
<td>Mean±SD 54.0±24.0</td>
<td>Mean±SD 81.36±24.19</td>
<td>Mean (95% CI) 63.69 (59.35-68.03)</td>
<td>Mean±SD 81.75±25.31</td>
</tr>
</tbody>
</table>

SF-36, Short Form 36; MH, Mental Health; VT, Vitality; RE, Role Emotional; SF, Social Function.

The mean scores in paper I-III were lower than means reported by Arango-Lasprilla and McPherson, who investigated samples with longer follow-up. Findings of the supplementary analyses on the SF-36 one year after injury are more or less comparable to McPherson’s findings. The authors reported similar results, however investigating with follow-up varying from 15 to 18 months. The results of the Mexican sample reported by Arango-Lasprilla and colleagues are somewhat lower. The participants described by Arango-Lasprilla and colleagues had cared for the patient at least three months, and the time since injury varied. At the time of assessment, all patients were in their own home, and the carers reported to be taking care of their relative for 60 hours per week on average. The rehabilitation system in Mexico is not as comprehensive as in Denmark, which more than likely influences the quality of life of the carers. Arango and colleagues reported that the Mexican carers in many cases were solely responsible for the care of their loved one, as resources for caregivers in Mexico hardly exist. This may explain the low scores obtained.

7.2 Predictors of emotional distress and quality of life in relatives

The papers in this thesis have investigated different predictors of the emotional condition of the relatives.

Gender of the relative: Paper III found a trend towards male relatives reporting higher anxiety scores; however this may be due to a very small sample of male relatives (22%), as female gender
were associated with higher anxiety and depression scores in the Danish reference population\textsuperscript{78}. Nevertheless, our finding is in concordance with Gervasio et al.\textsuperscript{39}, who reported that male caregivers experienced more distress. This finding was also reported on a small sample of male relatives (23\%). Moreover, Gervasio reported on a sample investigated from 10-48 months post injury, which is very different to our finding in the NICU.

Pielmaier\textsuperscript{30} also investigated relatives in the acute setting and found that women had higher levels of symptoms on the IES-R. This is comparable with other studies with longer follow-up\textsuperscript{35,64}. It is more than likely that the distress experience affects the different genders dissimilarly, and Perlesz\textsuperscript{48} reported that the different genders might report their strain differently; with males experiencing fatigue and anger, and females anxiety and depression.

**Relationship to the patient:** Our results are somewhat mixed, when investigating the association between the relationship to the patient and the level of distress experienced. Papers I and IV found that spouses had higher depression and anxiety scores as well as lower quality of life compared to the rest of the relatives, but papers III and V did not find this association. Studies with longer follow-up have several times reported that spouses were more distressed\textsuperscript{39,48} and depressed\textsuperscript{26,67} than other relatives. Turner et al.\textsuperscript{64} found that parents and children reported more anxiety than spouses one month after discharge, but Pielmaier et al.\textsuperscript{30}, Oddy et al.\textsuperscript{20} and Kreutzer et al.\textsuperscript{44} did not find any differences. So uncertainties do remain about this issue.

**Cohabitation:** In paper III, we found that relatives not living with the patient had lower scores on the SF-scale, and paper I did not find any effect of cohabitation. Only two other studies have reported on cohabitation status of the relative in relation to distress: and they found no significant associations between the cohabitation status and the carer’s depression scores\textsuperscript{42,51}. So far, no evidence has indicated that cohabiting relatives are at more risk of distress than other relatives.

**Social support and life events:** We found that more personal contact e.g. better social support influenced the decrease in depression scores. Relatives with better social network recovered faster from the symptoms of depression. This finding was expected as other researchers have reported that psychological distress was influenced by social support\textsuperscript{41,42,76,77}.
Paper V found that relatives having experienced more serious life events the last year, had higher initial anxiety scores. Interestingly, these relatives had a more rapid decline in anxiety scores. The association between SCL scores and life events was expected, as life events have been identified to be a strong predictor of scores on the SCL\textsuperscript{78}. Only two other studies in the field of brain injury have investigated life events, and neither of these found any association between events and depression experienced by carers\textsuperscript{24,42}.

*Patient's age:* Our cross sectional studies did not find the age of the patient to be important, as our longitudinal studies did. Both paper IV and V found the age of the patient to be related to anxiety, and paper IV also found this association in relation to depression, VAS-scores, RE-, MH-, and VT-scores. Paper IV investigated this association early in the rehabilitation process, and paper V did only identify this association on the earlier assessments. When investigating the brain injury literature, only Turner et al.\textsuperscript{64} have reported a similar effect. Most studies have failed to find any association between patient’s age and the condition of the relative\textsuperscript{35,42,69,79}. In contrast, this effect has been found in critical care, where the age span often is smaller compared to TBI populations. This might partly explain the difference, as well as the fact that the studies conducted in the brain injury literature have been exploring the later phases of rehabilitation. Moreover, this matter is rather difficult to investigate, as it may very well interact with the relatives’ relationship to the patient.

*Patient's level of function and consciousness:* Paper I was the only one finding an association between patient’s functional status (assessed by EFA) and the depression experienced by the relatives at admission. Similar associations between patient’s DRS score and depression has been reported after discharge\textsuperscript{64} as well in chronic phases after TBI\textsuperscript{41,44}. Livingston also found an association between the patient’s functional level and relatives’ life satisfaction. Despite this evidence, uncertainties remain about the influence of patient’s functional level as many studies have not been able to find similar associations between functional level and the relatives’ experienced distress\textsuperscript{27,59,79}. Paper I and V both reported an association between patient’s level of consciousness and anxiety and depression reported in the relatives. Paper I found this association at admission, and paper V had a longitudinal design and found that this effect disappeared over time. Pielmaier et al.\textsuperscript{30} also reported a similar effect of level of consciousness (assessed by GCS) on the
PTS symptoms experienced by relatives in the acute setting, as did Turner et al. in relation to experienced stress.

It seems likely that the effects of the patient’s level of consciousness is large in the beginning of hospitalisation and wear off partly because the majority of patients recover to consciousness and deficits relating to the brain injury emerge and other factors become more important.

Patient’s clinical condition in the NICU: Paper III reported that variables related to the patient’s clinical status (e.g. CRASH mortality prediction and craniotomy/cranieotomy) were related to mental health scores, anxiety and depression scores. No other studies have been identified using the CRASH2 as a predictor of the condition of the relatives.

Earlier studies, consisting of regular ICU patients, have reported associations between SAPS II, APACHE II and the condition of the relatives, but paper III did not replicate this result. SAPS II and APACHE II reflect deviations from normal physiologic parameters and the presence of chronic illnesses. Trauma patients generally score low on these parameters, because they are healthy before entering NICU and much younger than ICU patients. Therefore, SAPS II and APACHE II are not as useful in predicting outcome (death) in trauma patients as in regular ICU patients. This might explain why we failed to replicate the findings of critical care researchers.

7.3 Neuropsychological intervention

Paper III reported that relatives on average received 18 units of 15 minutes ~ six session with a neuropsychologist during patients’ hospitalisation. Moreover, relatives’ symptom of anxiety was associated with amount of support and number of sessions indicating that relatives with high anxiety scores received more intervention during the patient’s hospitalisation. No associations were found between support and relatives’ reported quality of life and depression scores at admission.

When investigating the different items on the depression and anxiety scales, it is evident that the anxiety scale reflects symptoms such as nervousness, tenseness, and fear as well as physiological reactions, whereas the depression scale reflects symptoms of clinical depression, such as less interest for life, lack of energy and motivation, and hopelessness. Symptoms of anxiety might be more visible to staff working in the unit and therefore staff might be more insistent on providing the necessary support. Relatives with symptoms of anxiety might also be more support-seeking than relatives with high levels of depression as the behaviour associated with depression is more introverted as experiencing a lack of energy and feeling blue. Relatives scoring
high on these items might not be able to seek the necessary support. It is important that staff is trained to identify the symptoms of depression and provide the needed support.

Paper IV reported a trend towards less anxiety and better mental health scores in the intervention group receiving acute neuropsychological support, but it is clear that any effects of the intervention were small. Other factors appeared to be more important since the age of the patient and the relatives’ relationship to the patient overrode any effects of the intervention. This result was unexpected and in contrast to what most relatives had expressed, since the majority did spontaneously express satisfaction with the information and support received during the sessions. However, it is likely that the intervention should have been provided even earlier than it was administered. Many relatives pointed out that their need for psychological support as well as information had been more critical earlier during the patient’s stay in acute care. Moreover, in most cases the intervention was limited to only one session, and this may not be enough to produce detectable effects. When planning the study, the amount of intervention was intended to be larger, than what was actually administered. However, the time for providing the intervention was limited, as the patient had to be stabilised and fulfill the admission criteria, before relatives were approached. If the relatives agreed to participate, the relatives had to receive the intervention before the patient was transferred to the sub-acute unit. In most cases, this window of time was limited to just a few days, which often limited the amount of intervention possible to administer.

The intervention was designed in an attempt to meet needs for support and information that relatives expressed, when patients were admitted to rehabilitation in the sub-acute phase. There was no standardised support for relatives in the acute phase, when the study was planned and designed, and no other studies have provided and evaluated effects of early neuropsychological intervention in the acute phase. Only a few controlled studies have been conducted (section 2.5), and these have primarily investigated effects of psycho-educational intervention in outpatient programs. So far, few studies have provided convincing results of psychological and supportive intervention to families following brain injury, and designing studies providing evidence of effects of the different family interventions have proven to be difficult. Studies have been conducted over relatively short study periods, and a longer follow up might very well be needed to document improvement in symptoms of anxiety, depression and distress. Moreover, studies implementing a problem-solving strategy or cognitive training in the primary caregiver and family, might provide
immediate results in the patient, but the effect on distress in the relatives might require a longer follow-up period. This should be considered when designing future studies.

The necessity of choosing the right outcome measure has been emphasised by both the results of paper IV, and the literature review regarding family intervention (section 2.5). Clinical significant improvements have been reported, but unfortunately not on the different outcome measures employed. An example of this issue is the studies conducted by Kreutzer and colleagues, who showed benefits of their program on subjective measures, but were unable to find any improvements on standardised measures regarding distress. This underlines the importance of careful considerations, when choosing outcome measures in future studies.

7.4 Methodological limitations and considerations

Cross-sectional data: Paper I-III reported cross-sectional data, which have inherited limitations. Changes over time are not captured in cross-sectional studies, and it is difficult to determine the direction of causality. Analyses relying on cross-sectional data do not facilitate causal inferences. For example, paper II found that relatives with high anxiety scores received more intervention during rehabilitation. With a cross-sectional design, it was not possible to determine whether the larger amount of support was because relatives with high anxiety scores actively did seek support or because the symptoms of anxiety were visible to staff, which then provided the needed support. Factors such as distress, burden, and resources in the relative do vary over time and are influenced by personality characteristics as well as factors in the environment. It is difficult to entangle the exact causes for and consequences of the emotional distress in the relatives, and the direction of associations is difficult to establish.

Sample size: Papers I-III have small samples, which yield low statistical power and suggest caution with respect to generalising the results. However, this is primarily a concern when interpreting unexpected negative findings that may be a result of insufficient statistical power. The literature review elucidated small sample sizes as a common problem in the TBI literature. Most prior studies have had a single study design and used small convenience samples. This might very well be due to the limited number of cases of severe brain injury as well as the willingness of relatives to participate when being in a distressing situation. However, in the latter this was not a problem as all relatives approached in the NICU accepted participation in the study. The issue of small sample sizes emphasises the necessity for designing collaborative research studies across
country borders as has been done in recent studies in the US using data from the Traumatic Brain Injury Model System.

In the longitudinal study in paper V, a relatively large proportion of the participants failed to complete the questionnaire at the last assessments. It was not possible to determine the cause for this attrition. However, analyses did show that relatives dropping out were not experiencing more anxiety and depression at baseline. Instead, analyses showed that relatives not completing the last assessment were relatives of patients with lower level of function and consciousness. It is likely that these relatives were more ‘tied’ up with practical issues, and therefore did not complete the questionnaire.

**Measures:** All outcome measures were reported as self-report questionnaires, which may cause response bias, as correlations may be due to a certain type of response by the particular respondent. Personality traits might affect the response on the distress measures, and this causes a response bias, as the response does not reflect the situation of a caregiver, but rather the effects of the personality trait. For example, associations have been found between high scores on the Neuroticism scale from the Revised NEO Personality Inventory and patients with moderate to severe depression\textsuperscript{133}.

The measures assessing the condition of the patients in the TBI and Neuro Intensive Care Unit were not chosen for this particular study. The scales used were part of a standardised procedure at the two different units. Scales used to describe progress in TBI and NTBI are broad categorisations of function (e.g. RLA), as no single scale is able to capture the variability in type and severity of impairment in the many different functions affected by TBI. In general, many different outcome measures both standardised and non-standardised have been employed in the literature, which makes it difficult to draw conclusions from the different findings.

**Inclusion:** Because of the limited number of patients with severe TBI and NTBI in Denmark, we chose to include relatives of both groups in this study. It can be argued that the relatives of TBI and NTBI patients have different experiences, which could affect their emotional distress and quality of life dissimilarly. In paper I, we investigated for difference in the condition of relatives related to the aetiology of brain injury and found no significant difference. Nevertheless, the inclusion of mixed aetiologies might be a problem in Paper V, when describing the trajectories of caregiver distress over time. The recovery trajectories for persons with TBI can differ from that of other types of
acquired brain injury. However due to the sample size, it was not possible to analyse the different trajectories in the two groups of relatives of TBI and NTBI patients. However, supplementary analyses were conducted comparing the mean scores of the two groups, and no significant differences were found on any of the four time points.

Another query regarding our inclusion criteria was the inclusion of relatives of both children and elderly. It is likely that the experiences of the relatives are different depending on the patient’s age. Our longitudinal studies do suggest this, whereas our cross-sectional studies and the reviewed studies did not report this finding. However, the variable should be considered when analysing results.

A possible bias in the process of inclusion is the possible enrolment of certain types of relatives. When more than one family member was present at time of enrolment, one relative often volunteered to participate. Because of the critical time of enrolment, it was not deemed justifiable to ask specific family members to participate. This choice may have resulted in bias, as we might have included more resilient and emotionally strong relatives.

**Other relevant factors:** Other factors not examined in this thesis are likely to influence the condition of the relatives as well as effects of interventions. Personality characteristics as well as coping style are important factors when dealing with distressing life events, and these aspects have not been assessed in this thesis. A sub-sample has completed measures regarding coping style, personality changes in the patient and a comprehensive personality measure. However, this data has not been analysed yet and will be presented in future work.

**Controlled trials in a clinical setting:** Doing controlled trials in a clinical setting can provide both challenges and obstacles, because research in an active ever changing clinical unit cannot be as restricted and controlled as when conducted in laboratory settings. This was definitely acknowledged, when doing the controlled trial described in paper IV, as a number of issues appeared during the data analyses. For some unexplainable reason, the control and the intervention group differed on a number of key variables. Because of the limited number of participants, it was not possible to equalise the groups by selecting comparable cases in each group. This emphasised the need for carefully selecting a design yielding high quality evidence, but more importantly, at the same time being applicable to the given clinical setting. Doing an RCT will give results of high
quality, if the setting can be controlled accordingly. Otherwise other research designs might be preferred.
In this chapter, the main conclusions are summarised, clinical perspectives and implications are outlined, and finally future directions are proposed.

8.1 Conclusions
This thesis has investigated and discussed the emotional condition of relatives of patients with severe brain injury, predictors of experienced distress and the effect of an early neuropsychological intervention. High frequencies of anxiety and depression and decreased quality of life have been found at different time points in the process of rehabilitation. There are several potential sources of distress for relatives of survivors of brain injury, and this thesis have emphasised the importance of different stressors at different times in the process of rehabilitation. In the early phases, stressors related to the patient’s condition (age, level of function and consciousness) seem to be important, and these associations seem to disappear with time. Previous research have found that other stressors like emotional, behavioural and personality changes in the patient are important in the later phases of rehabilitation. A trend toward less anxiety and better mental health scores were found in the group of relatives receiving an acute neuropsychological intervention, however methodological issues weakened this result.

8.2 Clinical perspectives and implications
The lack of research describing the early impact of brain injury on family members as well as investigations on effects of especially early intervention is obvious. Future studies should focus on the early phases of rehabilitation, as this matter is important for the triangle in rehabilitation: patients, relatives and professionals. The patient indirectly benefits of the support provided to the relatives, as the mental state of the relative is important to the patient during the process of rehabilitation as well as in the future. The symptoms of distress experienced by relatives may have important long-term consequences for the family and the patient with respect to employment and quality of life. Early detection of symptoms of anxiety and necessary support may very well prevent the more long-term symptoms of depression at least to some extent.
At last, symptoms of distress can influence the collaboration between staff working in rehabilitation and the family, which may result in a very stressful work-environment for professionals and rehabilitation environment for the family.

Common reactions have been investigated, but no predictable patterns exist as every family and survivor is different and unique. It is important for health care professionals and organisations to have support systems that can adequately meet the needs of the families. Support systems should be based on clinical experience while still lacking evidence supported interventions in the early phases of rehabilitation. Health organisations and rehabilitation services should have a structured approach towards supporting the family during and after the patient’s rehabilitation. The support system can feature professionals working rehabilitation setting or by providing the relatives with links to other organisations, public or voluntary.

Continuity is important in the process of rehabilitation. Effective strategies linking the different services in the different phases of rehabilitation will very likely relief carers of strain and distress to some extent, as the relatives themselves often serve as the continuity during transitional periods. A continuous family-focused approach in rehabilitation may be more effective for both patient and the family.

8.3 Future directions

Future studies should include the whole family and not just the primary relative or caregiver. The whole family is affected by the brain injury, thus the whole family should be included in intervention programs. When investigating early intervention, characteristics such as content, timing and number of sessions should be described in detail. Moreover, it is important to chose a sensitive outcome measure, and it might be recommended including both subjective rating scales as well as standardised measures of distress. A long follow-up interval might be needed in order to register possible changes in distress over time adequately.

Researchers should also investigate both positive and negative aspects of caregiving, as some studies have indicated that relatives do experience acquiring new competences, when caring for their family member. Future studies should implement assessments of positive emotions towards the responsibilities of caregiving and living with a survivor of brain injury.
REFERENCES


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Emotional distress and quality of life in relatives of patients with severe brain injury: The first month after injury.

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Emotional distress and quality of life in relatives of patients with severe brain injury: The first month after injury

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Abstract

Primary objective: To investigate emotional distress and quality of life in a sample of Danish relatives of patients with severe brain injury at admission to intensive rehabilitation in the sub-acute phase.

Research design: Clinical convenience sample.

Methods and procedures: Participants included 31 primary relatives of patients with severe brain injury. The participants were recruited at admission to Traumatic Brain Injury Unit, Copenhagen University Hospital, Glostrup. All relatives completed the depression and anxiety scales from SCL-90-R (Symptom Checklist) and the Role Emotional, Social Function, Mental Health and Vitality scale of the SF-36/36 days after injury. Data concerning severity of injury, the patients’ level of consciousness and function was also collected.

Main outcome and results: The participants had significantly lower scores on all quality of life scales \(p < 0.01\) and significantly more symptoms of anxiety \(p < 0.01\) and depression \(p < 0.01\) than normal reference populations. Correlations were found between the patients’ condition and the level of anxiety and depression in relatives.

Conclusions: The majority of relatives had severely impaired quality of life and symptoms of anxiety and depression at the time of admission. Future research should focus on developing and evaluating interventions in the acute phase.

Keywords: Relatives, severe brain injury, anxiety, depression, quality of life, emotional distress

Introduction

Severe brain injuries of traumatic (TBI) or non-traumatic (NTBI) aetiology are among the major causes of death and long-term morbidity among younger age groups in the Western world [1, 2].

In 2002, 1693 incidences of contusions, diffuse shearing lesions and traumatic intracranial haemorrhage were registered in Denmark [3] and 1048 cases of non-traumatic brain injury caused by subarachnoid haemorrhage, resuscitation after cardiac arrest, electrical shock, near drowning or suffocation were reported [4]. During recent decades, attention has focused on the rehabilitation of this group of patients and today a large number of patients with severe brain injuries achieve a better level of function than previously [5]. There has been an ongoing development of guidelines for intensive centralized rehabilitation of these patients [6, 7] since the first research in the area and the need for intensive rehabilitation has been documented several times [5].

During the past 30 years, several studies have documented emotional strain and distress in family members persisting years after injury [8–11]. Studies have also shown that the relatives and their emotional condition and ability to cope with the situation are important factors in successful rehabilitation.
rehabilitation [12–15]. Despite the documented need for family support, no evidence-based guidelines for interventions providing psychological support to relatives have been developed.

The present study

In Denmark, treatment and rehabilitation of patients with severe brain injury consists of three phases: (1) the acute phase with neurosurgical and intensive treatment; (2) the sub-acute phase with intensive hospital rehabilitation; and (3) the rehabilitation phase after discharge with further rehabilitation provided by the patient’s home municipality.

When receiving patients in the sub-acute phase, the relatives express a great need for information as well as psychological support. However, in Denmark there is no standardized procedure for psychological support to relatives in the acute phase.

This present study aimed at investigating quality of life and emotional distress of relatives of patients admitted to sub-acute rehabilitation. To the authors’ knowledge no recent study has investigated the mental state of relatives as early after the patient suffered the brain injury as the present one.

It was hypothesized that the majority of the relatives would report high levels of emotional distress as well as decreased quality of life. Furthermore it was expected that patient characteristics (i.e. severity of injury, level of consciousness, level of function and age) as well as characteristics of the relatives (i.e. gender, age, relationship to the patient) might be associated with their reported emotional distress and quality of life.

Methods

Participants

The participants in the study were relatives of patients with severe brain injury. A relative was defined as a child, parent, spouse/cohabitant, sibling or boy-/girlfriend (not cohabitant). Relatives, who did not speak Danish, had a psychiatric diagnosis or a progressive brain disease (e.g. dementia) was excluded from the study.

All patients had severe brain injury and were admitted to intensive neurorehabilitation. The unit admits patients with TBI or NTBI that fulfil the following prioritized criteria of admission:

1. Adults: a Glasgow Coma Score (GCS) from 3–9; Children under the age of 5: a GCS from 3–9; Children aged 5–15: a GCS from 3–11.
2. Patients with a GCS above 9 with severe focal neurological deficits such as aphasia, hemiparesis or agitation.
3. Patients with severe cognitive deficits as well as paresis or agitation.

The unit admits patients when they have completed neurosurgery (if applicable) and are respiratorically stable. The unit primarily treats adult patients with TBI but the unit also holds some beds for adults with NTBI and for children with TBI or NTBI.

Assessment of relatives

Consent to participate in the study was obtained by a neuropsychologist at admission to the unit. Relatives were asked to complete four Short Form 36 (SF-36) scales regarding quality of life and the SCL-90-R (Symptom Checklist) depression and anxiety scales. In addition, demographic information was collected.

Quality of life. Each relative was asked to complete SF-36, a measure of self-reported health-related quality of life. The questionnaire comprises 36 items addressing eight dimensions of health. For the purpose of this present study, only four scales were used: RE–Role Emotional (performance of role as affected by emotional factors), SF–Social Function, MH–Mental Health and VT–Vitality. Scores in each domain of the SF-36 range from 0–100, with higher scores indicating better health. The scores of the relatives were evaluated in terms of gender and age-specific Danish norms provided by Bjørner et al. [16].

Anxiety and depression. At admission to the unit, the relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of SCL-90-R; a self-report checklist designed to reflect the symptom patterns and level of distress [17]. Each item is scored on a scale of 0 (‘not at all’) to 4 (‘extremely’) indicating the degree of distress for that particular item. The respondents are asked to answer each item according to their condition during the past 7 days. The responses were evaluated in terms of the age- and gender-specific norms for a Danish sample provided by Olsen et al. [18].

Assessment of patients

As a standard procedure during admission, relevant data were collected regarding the patient’s condition: severity of injury, level of consciousness and function. Demographic data were also collected.

Severity of injury. The severity of injury was assessed by two well-known and validated scales: The Glasgow Coma Score [19] and the Injury
Severity Score (ISS) [20]. GCS consists of values from 3–15. Patients with scores less than 9 are considered to be in coma and patients with scores of 15 are able to follow commands, are fully oriented and have spontaneous eye opening. According to criteria for injury severity, GCS scores of 8 or less are classified as severe injuries.

The treating physician obtained the initial GCS from the acute hospital and at admission to the Traumatic Brain Injury Unit. The treating physician also estimated the Injury Severity Score (ISS), which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0–75. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (head, face, chest, abdomen, extremities (including pelvis), external). Only the highest AIS score in each region of the body is used. The scores of the three most severely injured regions are added together to produce the ISS.

Level of consciousness. Rancho Los Amigos (RLA) score [21, 22] was assessed by a neuropsychologist at admission to the unit. This score ranges from level one, which describes a comatose condition with no observable response, to level eight, which is a condition with purposeful and appropriate responses.

Functional level. The patient’s functional level at admission was assessed with the Early Functional Abilities (EFA) and the Functional Independence Measure (FIM).

The EFA [23] describes a patient’s early functional abilities and is normally used in the beginning of the rehabilitation process. The scale consists of four functional areas with a total of 20 items, which are rated on a 5-point scale from ‘not present’ to ‘completely present’. The total score is the sum of the different item scores ranging from 20 to a maximum of 100. High scores indicate better functional ability.

The FIM [24] consists of 18 items rated on a 7-point scale from ‘total assistance’ to ‘complete independence’ describing activities of daily living. The scale reflects areas of cognitive and motor dysfunction commonly associated with neurological disorders. Total scores range from 18–126, with higher scores reflecting greater functional independence.

Both FIM and EFA scores were obtained by physio- and occupational therapists when the patient was admitted.

Data analysis
Descriptive statistics were used; results are presented as percentages and as means with standard deviation and range. Comparisons between groups were performed using one sample and independent samples t-tests. Correlations were investigated using rank correlation (Spearman’s rho). The statistical software used was SPSS version 17.0.

Results
Description of sample
Thirty-one patients and 31 relatives were included in the study and all relatives completed the questionnaire.

Patients. The majority of the patients were male (68%) and 22 (71%) of the patients had sustained a TBI. The nine cases of NTBI were caused by cardiac arrest (n = 3), spontaneous intracranial haemorrhage (n = 2), subarachnoid haemorrhage (n = 1), meningioma (n = 1), meningitis (n = 1) and brain stem stroke (n = 1). The mean age was 41.19 years (SD = 18.75; range = 1–82). Eighty-one per cent of the patients were employed at time of injury (see Table I for demographic data).

The patients’ initial GCS was 5.41 and the GCS at admission to rehabilitation was 10.79. This indicates that the sample consisted of patients with severe injuries. At admission the patients’ FIM score

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n = 31)</th>
<th>Relatives (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>41.19</td>
<td>49.13</td>
</tr>
<tr>
<td>SD</td>
<td>18.75</td>
<td>13.50</td>
</tr>
<tr>
<td>Range</td>
<td>1–82</td>
<td>28–73</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (68%)</td>
<td>8 (26%)</td>
</tr>
<tr>
<td>Female</td>
<td>10 (32%)</td>
<td>23 (74%)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time work</td>
<td>25 (81%)</td>
<td>27 (87%)</td>
</tr>
<tr>
<td>Unemployed/pension</td>
<td>6 (19%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Cohabitants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17 (55%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (45%)</td>
<td></td>
</tr>
<tr>
<td>Relationship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse/cohabitant</td>
<td>13 (42%)</td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td>10 (33%)</td>
<td></td>
</tr>
<tr>
<td>Sibling</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td>5 (16%)</td>
<td></td>
</tr>
<tr>
<td>Boy-/girlfriend</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>1 (3%)</td>
<td></td>
</tr>
</tbody>
</table>
was 24.19 and the EFA score was 43.63. The 22 patients with TBI were assessed on the ISS and RLA scale at time of admission. The TBI group had a mean RLA score of 3.91 and a mean ISS score of 29.05 (see Table II for standard deviations and range).

The sample was admitted to sub-acute rehabilitation 25.41 days (SD = 20.95; range = 8–103) after injury and the average length of stay was 114.77 days (SD = 55.28; range = 33–234). The relatives completed and returned the questionnaire as soon as possible, 36.00 days (SD = 22.84; range = 9–114) after injury.

Relatives. The group of relatives consisted primarily of females (74%) and the mean age was 49.13 years (SD = 13.50; range = 28–73). The majority were spouses (42%) or parents (33%) and the remaining relatives were adult children (16%), siblings (3%) or not cohabiting boy- or girlfriend (3%). In one case (3%) the relative participating was an aunt. She was the primary relative, as the patient was an orphan. Of the relatives, 55% were living with the patient at time of injury and 87% of the relatives were working or studying full time when the patient was injured (see Table I).

Quality of life

Mean scores on each quality of life sub-scale are presented in Table III and this table also compares the results to the Danish norms [16].

The mean in this sample on the scale RE, Role Emotional, was 26.67 (SD = 32.22; range = 0–100), which was significantly lower than the mean reported in the Danish population. On the sub-scale SF, Social Function, a mean of 54.03 (SD = 24.02; range = 12.50–100) was found in the sample, which was significantly different from the Danish norms.

Table III. Quality of life: Descriptive statistics and difference (D) to Danish norms.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>D</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE</td>
<td>26.67</td>
<td>0–100</td>
<td>59.66</td>
<td>−9.838**</td>
<td>0.000</td>
</tr>
<tr>
<td>SF</td>
<td>54.03</td>
<td>12.50–100</td>
<td>37.92</td>
<td>−8.789**</td>
<td>0.000</td>
</tr>
<tr>
<td>VT</td>
<td>31.29</td>
<td>0–75</td>
<td>38.55</td>
<td>−11.846**</td>
<td>0.000</td>
</tr>
<tr>
<td>MH</td>
<td>30.43</td>
<td>3.33–73.33</td>
<td>51.34</td>
<td>−19.157**</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Emotional distress

Depression. Table IV shows a mean on the depression sub-scale of 1.59 (SD = 0.73; range = 0.23–3.08), which was significantly different from the general population [25]. Raw scores were converted into gender-adjusted T-scores, and a mean T-score of 62.58 (SD = 7.03; range = 46–75) was found. This was significantly different from the norm population and 61% (19/31) of the sample scored above suggested cut-off (T-score > 63) [26].

Table IV. Emotional distress: Descriptive statistics and difference (D) to Danish norms.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Raw-score (SD)</th>
<th>T-score (SD)</th>
<th>Range</th>
<th>D</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>1.59 (±0.73)</td>
<td>0.23–3.08</td>
<td>1.00</td>
<td>7.622**</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.22 (±0.87)</td>
<td>0.00–4.00</td>
<td>0.78</td>
<td>5.008**</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>62.58 (±7.03)</td>
<td>46–75</td>
<td>12.58</td>
<td>9.968**</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>61.97 (±10.31)</td>
<td>37–80</td>
<td>11.97</td>
<td>6.461**</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

**p < 0.01.
population [25]. As above, raw scores were converted into T-scores and the mean T-score was 61.97 (SD = 10.31; range = 37–80). This level was significantly different from the levels reported in the general population and 61% (19/31) of the sample scored above suggested cut-off (T-score > 63) (see Table IV).

Derogatis [26] defined caseness criteria as a GSI raw score corresponding to a T-score of 63 or above or raw scores corresponding to a T-score of 63 on at least two sub-scales. In this sample 55% (17/31) of the relatives met the last criterion.

Correlations with the patient’s condition and age
Results of all correlation analyses can be seen in Table V.

Quality of life. No correlations were found between the relatives’ scores on the four sub-scales of SF-36 and the variables related to the patient’s condition. The patient’s age did not have any relation to the quality of life experienced by the relative.

Depression. No significant correlation was observed between initial GCS, GCS at admission, ISS, FIM and the relatives’ depression score. However, a significant correlation was found between the patient’s EFA score at admission and the relatives’ depression score ($r_s = -0.44$, $p = 0.02$). This indicated that the higher EFA score at admission, the fewer symptoms of depression reported by the relative. The correlation between RLA score and the relative’s depression score reached significance ($r_s = -0.45$, $p = 0.04$) indicating the lower level of consciousness of the patient, the more symptoms of depression. No significant relationship was observed between the patient’s age and the relative’s level of anxiety.

Anxiety. No significant correlation was observed between level of anxiety at admission and initial GCS, GCS at admission, ISS, FIM or EFA. A significant correlation was found between RLA at admission and the relative’s symptoms of anxiety ($r_s = -0.45$, $p = 0.04$) indicating that relatives of a patient with a low level of consciousness experienced more symptoms of anxiety. No relationship was seen between patient’s age and the relative’s level of anxiety.

Gender, age and relationship to the patient
Gender. No differences were found in levels of depression, anxiety or quality of life when testing for gender differences.

Age. No significant correlations were found between the relative’s age and their level of depression, anxiety or quality of life.

Relationship. No significant differences were found between the levels of depression and anxiety of spouses and parents. However, the difference between the two groups almost reached significance in terms of depression ($t = 2.035$, $p = 0.06$) since spouses had more symptoms of depression than parents. There was no significant difference between the two groups when comparing their quality of life.

Cohabitation. The depression and anxiety scores of the relatives were not significantly related to whether or not the relative was living with the patient at time of injury. Similarly there was no significant difference between the quality of life of relatives living with the patient and of relatives not living with the patient.

Table V. Correlation analyses: Association between the patient’s condition and their relative’s emotional wellbeing.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>GCS acute</th>
<th>GCS adm.</th>
<th>ISS</th>
<th>FIM</th>
<th>EFA</th>
<th>RLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role emotional</td>
<td>0.186</td>
<td>-0.055</td>
<td>0.088</td>
<td>0.210</td>
<td>-0.038</td>
<td>0.179</td>
<td>0.079</td>
</tr>
<tr>
<td>Social Function</td>
<td>0.144</td>
<td>0.360</td>
<td>0.216</td>
<td>-0.053</td>
<td>0.025</td>
<td>0.143</td>
<td>0.206</td>
</tr>
<tr>
<td>Vitality</td>
<td>0.073</td>
<td>-0.014</td>
<td>-0.011</td>
<td>-0.104</td>
<td>0.196</td>
<td>0.128</td>
<td>0.007</td>
</tr>
<tr>
<td>Mental health</td>
<td>0.172</td>
<td>-0.045</td>
<td>0.033</td>
<td>-0.133</td>
<td>-0.025</td>
<td>0.036</td>
<td>0.064</td>
</tr>
<tr>
<td>Emotional distress</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>-0.100</td>
<td>-0.118</td>
<td>-0.351</td>
<td>-0.043</td>
<td>-0.349</td>
<td>-0.440*</td>
<td>-0.452*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-0.275</td>
<td>-0.142</td>
<td>-0.280</td>
<td>0.023</td>
<td>-0.125</td>
<td>-0.199</td>
<td>-0.447*</td>
</tr>
</tbody>
</table>

*p < 0.05 (2-tailed).
Discussion

The results of this study demonstrate that the majority of relatives had symptoms of depression and anxiety as well as decreased quality of life. This study also identified an association between the patient’s condition (assessed by EFA) and the level of depression in relatives and an association between level of consciousness and reported anxiety and depression. In addition, a trend was found towards more symptoms of depression in spouses than in parents.

Increased emotional distress has been reported regardless of methodological diversity such as different time intervals after the patient acquired the brain injury, different measurements and cut-off points. Despite the amount of studies conducted on relatives’ emotional distress, only a few authors [27, 28] have investigated symptoms of anxiety and depression after the patient’s injury as early as in this study. In spite of the obvious limitations when comparing results of studies with methodological difference, these results do support the few previous studies showing increased levels of both depression and anxiety.

Oddy et al. [29] reported that 39% of the relatives were above the cut-off score for clinical depression 1 month after injury using the Wakefield Depression Scale. In comparison, more than half of the relatives scored above the cut-off in this sample. However, the patients in Oddy et al.’s sample had less severe injuries than the patients in this sample.

Oddy et al. [29] did not investigate the possible association between the patient’s condition and the relatives’ level of depression 1 month after injury. This is important because severity of injury might affect the emotional distress experienced as a correlation was found between the patient’s EFA score and the relative’s depression score as well as between the patient’s RLA score and the relative’s anxiety and depression score.

This suggests that early after the injury there is an association between the relative’s wellbeing and the patient’s physical condition. This finding is in contrast to studies with longer follow-up where the primary predictors of caregiver distress were personality and emotional changes in the brain damaged patient and not physical deficits [30, 31].

A more recent study by Novack et al. [27] assessed levels of depression and anxiety using Beck’s Depression Inventory and The State-Trait Anxiety Inventory at time of admission to rehabilitation (46 days post-injury) and found that 9% were clinically depressed and 33% of the caregivers were clinically anxious at admission. The levels of emotional distress reported in this study were low compared to Oddy et al.’s [29] and this sample. However, the caseness criteria used were higher (BDI > 18, STAI > 90th percentile) than the recommended [32]. If milder cases of depression (BDI > 12) and anxiety (STAI > 80th percentile) had been included, 51% of the sample would have been anxious and 26% depressed. Thus, the level of anxiety would then be comparable to this sample, but the level of depression would still be considered low compared to the level reported in Oddy et al.’s sample despite the use of different measurements.

Novack et al. [27] did not find a correlation between the patient’s functional status as measured by Rappaport Disability Rating Scale [33] and the caregiver’s symptoms of anxiety or depression, while such an association was observed in the present study.

Novack et al.’s [27] investigation took place 46 days after injury, while this study was conducted 10 days earlier. Novack et al. investigated relatives of patients with severe TBI defined as a period of post-traumatic amnesia or coma greater than 1 week. In this study, the severity of injury was assessed by ISS and GCS also indicating a sample with severe brain injury. The mean age of the patients in the Novack et al. sample was 24.3 years, which is somewhat lower than in this sample. These differences between timing of assessment of the relative and between sample characteristics may also have influenced the results.

The results did not show a higher level of anxiety than depression as Novack et al. [27] found, as could have been expected because of the early assessment. Normally anxiety is associated with an acute reaction and depression with a more general condition. However, when examining the different items on the SCL scales, the anxiety scale reflects symptoms as nervousness, tenseness, fear as well as physiological reactions, where the depression scale reflects symptoms of clinical depression such as less interest for life, lack of energy and motivation and hopelessness.

Several individual items on the depression scale had a mean score above 2.0 in this sample. This was the case for ‘worrying too much about things’, ‘feeling blue’, ‘feeling low in energy or slowed down’ and ‘crying easily’. Only one item, ‘feeling fearful’, on the anxiety scale had a mean score close to 2.0. All of these symptoms are consistent with the relatives’ reactions in the beginning of the sub-acute phase. This might explain the equality of the depression and anxiety levels observed in this sample.

Several studies have shown a significant difference between the emotional distress of respectively parents and spouses of patients with brain injury [34–42]. This study found a trend towards more symptoms of depression in spouses than in parents,
Even though this difference was not significant. Oddy et al. [28] did not find a significant difference while Novack et al. [27] did not investigate this. It seems likely that this difference is easier to detect in studies with longer follow-up where the relatives are in a more stable situation and not in an acute crisis.

No studies have investigated quality of life in relatives this early after injury. However, a decline in quality of life the first year after injury has been reported [43–45].

When investigating the emotional state of relatives this early after injury it must be taken into account that the relatives are in an acute crisis compared to assessment longer after injury. The relatives have not had time to adapt to the new life situation. It was therefore expected that the relatives' level of anxiety, depression and quality of life were severely affected. However, it is still important to investigate this matter as knowledge about the relatives' condition in this early phase is primarily based on clinical experience. The results of this study support clinical experience of relatives being in a difficult and emotionally draining situation. The relatives do express not only a need for information, but also a need for psychological support in the acute phase.

It may be argued that the relatives will not be able to profit from intervention this early as their ability to cooperate, listen and reflect is affected in the acute setting. However, the effect of acute intervention has not been investigated and therefore such conclusions remain yet to be drawn.

Methodological considerations

A major limitation of this study is the small sample size, which suggests caution with respect to generalizing the results. This is primarily a concern when interpreting unexpected negative findings that may be a consequence of insufficient statistical power. For example, the comparison between spouses and parents did not reach the statistical threshold for significance and one was expecting a gender difference on the depression scale indicating higher scores in women than men [25]. These findings may reflect both the small sample size and skewed distributions of male and female relatives. The small sample size was also the reason that it was decided not to conduct a regression analysis to identify independent predictors of the mental state of the relatives.

A second possible limitation is the inclusion of both TBI and NTBI patients. It can be argued that the relatives of TBI and NTBI have different experiences, which could affect their emotional distress dissimilarly. However, in this study no significant difference was found between levels of depression, anxiety and quality of life in relation to aetiology of brain injury.

A third query is the inclusion of relatives to both children and elderly patients. It is likely that the experiences of the relatives are very different depending on the patients' age, although the results do not support this hypothesis.

Directions for future research

The present study emphasizes the need for randomized controlled studies investigating the effect of psychological intervention at critical phases in the patient's rehabilitation process. Future studies will need to be designed using clearly defined and well-documented family interventions and matched controls.

The authors are currently conducting a randomized controlled intervention study investigating the effect of psychological intervention to relatives at different times in the patient's rehabilitation process.

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Neuropsychological support to relatives of patients with severe traumatic brain injury in the sub-acute phase.

Neuropsychological support to relatives of patients with severe traumatic brain injury in the sub-acute phase

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Many studies have reported emotional distress in relatives of patients with brain injury, but few studies have investigated neuropsychological interventions for relatives. The present study assessed the amount of neuropsychological support as well as the actual number of sessions with a neuropsychologist during rehabilitation in a sub-acute unit. The study also examined whether the amount of support was related to the condition of the patient or the relative at admission. The sample consisted of 26 patients and their closest relative, and measures included demographic variables as well as characteristics related to the patient: Glasgow Coma Scale, Injury Severity Score, Early Functional Abilities, Functional Independence Measure, Rancho Los Amigos; and to the relative: symptoms of anxiety and depression (SCL-90-R), quality of life (SF-36) and amount and number of sessions of neuropsychological support. On average, the relatives received about 18 units of 15 minutes and had six...
sessions with a neuropsychologist during hospitalisation. A total of 38% participated in group sessions. Relatives’ symptoms of anxiety at admission were associated with the number of sessions as well as the amount of support, indicating that relatives with more symptoms of anxiety received more support during the hospitalisation.

**Keywords:** Traumatic brain injury; Relatives; Neuropsychological support; Depression; Anxiety; Quality of life.

**INTRODUCTION**

Since the 1970s, several studies have documented that emotional strain and distress in families persist years after traumatic brain injury (TBI) (Brooks, Campsie, Symington, Beattie, & McKinlay, 1986; Oddy, 1985; Panting & Merry, 1972; Thomsen, 1974). Studies have shown that relatives’ emotional condition and ability to cope with the situation are important factors in successful rehabilitation (Anderson, Parmenter, & Mok, 2002; Douglas & Spellacy, 1996; Rivara et al., 1996; Rivera, Elliott, Berry, Grant, & Oswald, 2007). Despite the documented need for family support, only a few intervention studies have been performed (Boschen, Gargaro, Gan, Gerber, & Brandys, 2007; Carnevale, Anselmi, Busichio, & Millis, 2002; Sanguinetti & Catanzaro, 1987; Singer, Glang, & Nixon, 1994; Sinnakaruppan, Downey, & Morrison, 2005), and no evidence-based guidelines for interventions providing psychological support have been developed. The relationship between the well-being of the relatives of patients with a severe TBI and the neuropsychological support provided during inpatient rehabilitation have hardly been investigated in spite of the importance for families facing brain injury and the healthcare system (Anderson et al., 2002; Sander et al., 2002).

The present study

Neuropsychological support has a high priority at the Traumatic Brain Injury Unit, Department of Neurorehabilitation, Copenhagen University Hospital, Glostrup, and all relatives are asked to participate in sessions with a neuropsychologist as a routine part of inpatient neurorehabilitation.

We wanted to investigate the actual amount of support given and possible associations between the patient’s condition and the relative’s emotional well-being. The study aimed at examining:

1. The amount of neuropsychological support administered to relatives of patients with severe TBI admitted to intensive sub-acute neurorehabilitation.
2. The number of sessions with a neuropsychologist administered to relatives of patients with severe TBI admitted to intensive sub-acute neurorehabilitation.
3. Possible associations between the relatives’ emotional well-being, defined as quality of life and symptoms of depression and anxiety at admission, and the neuropsychological support administered.
4. Possible associations between the patient’s condition at admission and the amount of neuropsychological support administered.

METHODS

Participants

The study sample consisted of relatives of patients with severe TBI admitted to intensive sub-acute rehabilitation at the Traumatic Brain Injury Unit, Department of Neurorehabilitation, Copenhagen University Hospital, Glostrup.

A relative was defined as a child, parent, spouse, boy- or girlfriend or sibling. Relatives, who did not speak Danish, and relatives with a psychiatric diagnosis or a progressive brain disease were excluded from the study. The family decided which relative should complete the questionnaire, if more than one relative was present.

Relatives of patients fulfilling the following criteria were included:

- Diagnosis of TBI.
- Aged 16 years or older.
- Glasgow Coma Scale (GCS) score during the first 24 hours after injury \( \leq 8 \).
- Inhabitants in the Eastern part of Denmark.

Patients were excluded if they met any of the following criteria:

- Violence-related cause of TBI (with the exception of war-related violence).
- Serious conditions causing mental disability prior to the TBI, such as developmental handicap (Down’s syndrome), residual disability after previous TBI, confirmed dementia, or serious chronic mental illness (schizophrenia, psychosis or well-confirmed bipolar disorder).
- Severe abuse of drugs or alcohol.

We included the 71 patients with severe TBI admitted to the unit between October 2007 and October 2009. Of these eligible patients 24 had a GCS above 8 during the first 24 hours after injury and six patients were not
inhabitants in the Eastern part of Denmark. Three patients had a violence-related cause of TBI while seven patients had a serious mental disability prior to the TBI or severe abuse of drugs or alcohol. Among the relatives of the remaining 31 patients, five declined to participate and, thus, the present study sample comprises 26 relatives of 26 patients with severe TBI.

**Intervention**

As a standard part of neurorehabilitation in the unit, relatives are offered two types of neuropsychological intervention.

*Individual sessions.* The first session with a neuropsychologist is prompted by the neuropsychologist, who contacts the relatives, when the patient is admitted. This appointment is scheduled as soon as possible after the patient’s admission to the unit, and the neuropsychologist invites the closest family to participate in the first session. This appointment is primarily aimed at giving relatives information about severe TBI and its possible consequences. The first session is often the beginning of a more supportive psychological process with the relatives. In some cases, the process continues through the patient’s hospitalisation, but this varies greatly. Generally more than one family member is present, but if necessary one-on-one sessions are offered.

The sessions with the neuropsychologist are psycho-educational as well as supportive. Their content depends on the relatives and their specific needs. Usually the relatives express a need for information about TBI, its possible consequences, recovery from TBI, including the first period of unconsciousness, post-traumatic amnesia and the following remaining deficits. Furthermore, the relatives often need support to help them deal with their own emotional reactions and needs during the patient’s recovery. Topics often addressed in the supportive part of the sessions are: role shifting in the family, mixed feelings about the person with the brain injury, how to handle each day with a close family member in hospital, and feelings of isolation, guilt and emotional distress. The intervention is individualised according to the relatives’ needs and is a flexible mixture of both psycho-education and emotional support.

The neuropsychological support is provided by trained neuropsychologists with years of experience in the field of brain injury rehabilitation.

*Support group.* The relatives are offered the opportunity to participate in a support group led by a neuropsychologist, where the relatives can debate topics of their own choice. The neuropsychologist moderates the group, but otherwise the group is not structured. The group starts with an introduction, where the relatives are asked to tell the group what has happened to their
family member. However, if a relative merely wants to listen at their first visit, this is also acceptable. The objective of the group is primarily supportive and only educational in the sense that relatives learn about the different types of brain injury, their consequences and recovery, when listening to other relatives.

Both the support group and the individual sessions take place in the ward.

Measures

**Demographics.** Data concerning both the patient and the relative’s gender, age and employment status were collected at admission.

**Emotional well-being.** The emotional well-being of the relatives was investigated at admission and assessed with measures of depression, anxiety and quality of life. The relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of the Symptom Checklist (SCL), a self-report checklist designed to reflect symptom patterns and levels of distress (Derogatis, 1994). Each item is scored on a scale of 0 (“not at all”) to 4 (“extremely”) indicating the degree of distress for that particular item. The respondents are asked to answer each item according to their condition over the previous seven days. The responses were evaluated using the gender-specific norms for a Danish population sample provided by Olsen, Mortensen, and Beck (2006). The Danish population study revealed high alpha coefficients on all the SCL subscales, and in particular for the two scales used in this study, depression and anxiety: .91 and .86, respectively (Olsen et al., 2006).

Each relative was also asked to complete the SF-36, a measure of self-reported health-related quality of life. The questionnaire comprises 36 items addressing eight dimensions of health. For the purpose of the present study, only four scales were used: RE – Role Emotional (performance of role as affected by emotional factors), SF – Social Function, MH – Mental Health, and VT – Vitality. Scores in each domain of the SF-36 range from 0 to 100 with higher scores indicating better health. The scores of the relatives were compared to the Danish norms provided by Bjørner, Damsgård, Watt, and Bech (1997). This normative study showed high Cronbach’s alpha coefficients on all the subscales used in this study ranging from .75 to .85 (Bjørner et al., 1997).

The relatives were also asked to rate their own perception of quality of life on a visual analogue scale (VAS) from 0 to 10, where 0 is “very dissatisfied” and 10 is “very satisfied”.

**The patient’s condition.** As a standard procedure during hospitalisation, relevant data were collected regarding the patient’s condition. Severity of
injury was assessed using GCS (Teasdale & Jennett, 1974) and Injury Severity Score (ISS; Baker, O’Neill, Haddon, & Long, 1974). The GCS consists of values from 3 to 15. Patients with scores less than nine are considered to be in a coma, and patients with scores of 15 are able to follow commands, are fully oriented, and have spontaneous eye opening. According to criteria for injury severity, patients with GCS scores of eight or less are classified as having severe brain injuries. GCS scores were rated by the treating physician at admission, and records of initial GCS scores were obtained from the acute hospital.

The treating physician calculated the ISS, which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0 to 75. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions: head, face, chest, abdomen, extremities (including pelvis), and external (skin). Only the highest AIS score in each region of the body is used. The scores of the three most severely injured regions are added together to produce the ISS score. Only physicians familiar with the English language used the ISS, as the scale has never formally been translated into Danish.

At admission, the patient’s level of consciousness was assessed by the treating neuropsychologist using the Rancho Los Amigos (RLA) Scale (Hagen, Malkmus, & Durham, 1972). Scores on this scale range from Level 1, which describes a comatose condition with no observable response, to Level 8, which is a condition with purposeful and appropriate responses.

The scale measuring Early Functional Abilities (EFA; Heck, Schmidt, & Steiger-Bachler, 2000) is an assessment tool for patients with severe cerebral impairments in the early neurological rehabilitation stage, which describes clinically observable changes of a patient’s early functional abilities. The EFA Scale contains 20 items and assesses early basic abilities related to four functional areas: vegetative, face and oral, sensory-motor and sensory-cognitive functions. Each item is rated on a five-point scale from “not obviously observable” to “no essential functional limitation”. The total score is the sum of the item scores ranging from 20 to a maximum of 100. High scores indicate better functional ability.

The Functional Independence Measure (FIM; Keith, Granger, Hamilton, & Sherwin, 1987) is an 18-item rating scale assessing activities of daily living (ADL): self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a seven-point scale from “total assistance” to “complete independence”. A total FIM score ranges from 18 to 126 with higher scores indicating greater independence. The FIM Scale has been shown to be valid and reliable for measuring functional outcome after TBI (Corrigan, Smith-Knapp, & Granger, 1997).
The nurses, physio- and occupational therapists working in the unit are trained users of both the EFA and the FIM and, to ensure uniform assessments, raters are repeatedly trained in administration and scoring.

**Neuropsychological support.** We registered the amount of neuropsychological support administered to relatives of patients admitted to the unit. Both individual sessions as well as participation in group sessions were registered during the patient’s hospitalisation. Amount of time was registered in units of 15 minutes, and coding of a unit required a minimum of 7.5 minutes of treatment. Scheduled contacts with the relative, unplanned or informal contacts, and phone contacts regarding treatment, were registered, while time for planning treatment was not. We also registered the actual number of sessions with the neuropsychologist, regardless of duration (informal short meeting in the hallway or a longer planned session), as we wanted to investigate both the duration of the session and the regularity of contact. We registered the amount of units and the number of sessions administered during each month of the patient’s hospitalisation as well as the distribution of sessions during the hospitalisation.

**Procedure**

The study was approved by the Committees on Biomedical Research Ethics of the Capital Region of Denmark (journal number H-KF-311150) as well as by the Danish Data Protection Agency (journal number 2007-41-0583). Consent to participate was obtained by a neuropsychologist at admission to the sub-acute neurorehabilitation unit.

**Data analysis**

Descriptive statistics were used; results are presented as percentages and means with standard deviation and range. Parametric statistics were used, and comparisons between groups were performed using one sample and independent samples t-tests. Associations were investigated using Pearson’s correlation analysis for parametric data. All data were analysed using two-tailed testing and \( p = .05 \) as a threshold for statistical significance. The statistical software used was SPSS version 17.0.

**RESULTS**

**Description of sample**

All 26 relatives completed the questionnaire regarding emotional well-being at the time of admission.
The majority of the patient sample was male (81%), and the mean age was 33 years ($SD = 18$; range = 16–76). Of the 26 patients, 85% were working or studying full time at time of injury. The sample of relatives consisted primarily of females (77%), and most were parents (69%) or spouses (23%). Further demographic characteristics can be seen in Table 1.

On average, the patients were admitted to the unit 18 days ($SD = 10$; range = 7–53) after the injury, and the relatives completed the questionnaire 24 days ($SD = 12$; range = 9–69) after the injury. One patient died during the stay in the sub-acute rehabilitation unit. The mean length of stay in the unit was 106 days ($SD = 61$; range = 21–238). Characteristics related to the patients’ condition can be seen in Table 2.

**Neuropsychological support**

*Individual support.* Most of the individual support consisted of scheduled meetings with the neuropsychologist in the team treating the patient, and all relatives except one participated in at least one session with the neuropsychologist. The largest amount of individual neuropsychological support was registered during the first month of hospitalisation, where relatives received about nine units of 15 minutes on average, and the relatives met with the neuropsychologist two to three times during this time. During the entire period of hospitalisation, relatives had about six meetings with the neuropsychologist,

### Table 1

A summary of demographic characteristic for the participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients ($n = 26$)</th>
<th>Relatives ($n = 26$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean: 33</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>$SD$: 18</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Range: 16–76</td>
<td>27–78</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 21 (81%)</td>
<td>6 (23%)</td>
</tr>
<tr>
<td></td>
<td>Female: 5 (19%)</td>
<td>20 (77%)</td>
</tr>
<tr>
<td>Employment status</td>
<td>Full-time work: 22 (85%)</td>
<td>22 (85%)</td>
</tr>
<tr>
<td></td>
<td>Unemployed/pension: 4 (15%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Cohabitants</td>
<td>Yes: 17 (65%)</td>
<td>6 (23%)</td>
</tr>
<tr>
<td></td>
<td>No: 9 (35%)</td>
<td>18 (69%)</td>
</tr>
<tr>
<td>Relationship</td>
<td>Spouse/cohabitant: 6 (23%)</td>
<td>18 (69%)</td>
</tr>
<tr>
<td></td>
<td>Parents: 1 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td></td>
<td>Children: 1 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td></td>
<td>Others: 1 (4%)</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>
Table 3 includes descriptive statistics regarding the amounts of individual and group support in units registered during the first four months of hospitalisation as well as the actual number of sessions with a neuropsychologist. The total amount during the whole admission can be seen in the last column. The number of sessions, the amount of units and the distribution of support during the first four months of hospitalisation can be seen in Figure 1. The figure shows how the duration of the sessions was longer during the first month of hospitalisation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury Severity Score</td>
<td>33.5 (8.9)</td>
<td>25–59</td>
</tr>
<tr>
<td>Glasgow Coma Scale: initial</td>
<td>4.7 (2.0)</td>
<td>3–8</td>
</tr>
<tr>
<td>Glasgow Coma Scale: at admission</td>
<td>10.7 (3.5)</td>
<td>4–15</td>
</tr>
<tr>
<td>Rancho Los Amigos</td>
<td>3.9 (1.5)</td>
<td>2–7</td>
</tr>
<tr>
<td>Functional Independence Measure</td>
<td>21.9 (10.7)</td>
<td>13–61</td>
</tr>
<tr>
<td>Early Functional Abilities</td>
<td>41.7 (19.1)</td>
<td>23–90</td>
</tr>
</tbody>
</table>

Support group. Ten of the relatives (38%) participated in the group sessions during hospitalisation. The participating relatives had higher scores on the anxiety scale at admission than relatives not participating, almost reaching significance ($t = -2.017, p = .055$). This tendency was not replicated on the depression scale or any of the quality of life measures.

Table 3

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Individual sessions in units (1 unit = 15 minutes)</th>
<th>Group sessions in units (1 unit = 15 minutes)</th>
<th>Number of sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Range</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Month of hospitalisation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First ($n = 26$)</td>
<td>9.3 (4.5)</td>
<td>0–19</td>
<td>1.2 (2.4)</td>
</tr>
<tr>
<td>Second ($n = 25$)</td>
<td>3.4 (3.9)</td>
<td>0–15</td>
<td>1.4 (2.6)</td>
</tr>
<tr>
<td>Third ($n = 19$)</td>
<td>2.8 (3.1)</td>
<td>0–9</td>
<td>1.3 (3.2)</td>
</tr>
<tr>
<td>Fourth ($n = 16$)</td>
<td>2.7 (5.1)</td>
<td>0–19</td>
<td>0.8 (2.5)</td>
</tr>
<tr>
<td>Total during whole admission *</td>
<td>17.8 (12.4)</td>
<td>0–46</td>
<td>3.9 (6.1)</td>
</tr>
</tbody>
</table>

*The column reflects the total amount given during hospitalisation (including months 1–8).
Emotional well-being of the relatives

Depression. The raw scores were converted to t-scores, and the relatives had a mean score of 63.0 (SD = 7.6; range = 41–78) on the depression scale. This was significantly different (p < .0001) from the Danish reference population (Olsen et al., 2006), and 58% scored above the suggested cut-off (t-score ≥ 63.0).

Anxiety. A mean t-score of 63.5 (SD = 8.8; range = 36–80) was obtained on the anxiety scale. This was significantly different (p < .0001) from the Danish reference population (Olsen et al., 2006), and 65% scored above the suggested cut-off (t-score ≥ 63.0). Derogatis (1994) defined case-ness criteria as a Global Severity Index score corresponding to a t-score of 63 or above or raw scores corresponding to a t-score of 63 on at least two subscales. In our sample, 54% (14/26) of the relatives met the last criterion.

Quality of life. The relatives had a mean of 33.0 (SD = 18.1; range = 0–75) on the Vitality subscale; and a mean of 15.9 (SD = 25.0; range = 0–67) on the Role Emotional scale. The mean score on the Mental Health scale was 38.4 (SD = 19.2; range 4–92), and on the Social Function scale, 55.8 (SD = 30.1; range = 0–100). The relatives scored significantly lower on all four sub-scales (p < .0001) compared to the reference population.
(Bjørner et al., 1997). The relatives rated their own perception of quality of life as 6.4 (SD = 2.3; range = 3–10) on the VAS.

**Relatives’ emotional well-being and neuropsychological support.** A significant correlation was found between relatives’ anxiety scores at admission and the amount of support during the hospitalisation ($r = .45, p = .020$). This indicated that relatives with high anxiety scores received more neuropsychological support during the hospitalisation. This tendency was, not surprisingly, replicated for the number of sessions during hospitalisation ($r = .50, p = .009$). The amount of support per month during hospitalisation almost reached significance ($r = .38, p = .055$).

No significant correlations were found between relatives’ quality of life or depression scores at admission and amount or sessions of neuropsychological support during hospitalisation.

**Patient’s condition and neuropsychological support.** Significant correlations were found between the patient’s GCS at admission and the amount of individual neuropsychological support ($r = –.47, p = .014$) and the number of sessions of neuropsychological support during hospitalisation ($r = –.48, p = .013$). This indicated that relatives of patients with higher GCS scores at admission received less neuropsychological support during hospitalisation. However, we suspected that the length of stay could influence the association, as patients with severe injuries stay in the unit longer and their relatives receive more support. We conducted a partial correlation analysis controlling for the length of stay and found no significant association between GCS at admission and the amount of individual neuropsychological support ($r = –.29, p = .159$) or between GCS and the number of sessions of neuropsychological support during hospitalisation ($r = –.13, p = .130$).

No other significant correlations were found between the injury severity (measured by GCS initial and ISS at admission) and amount or number of sessions of neuropsychological support during hospitalisation.

No significant correlations were observed between the patients’ condition at admission assessed by FIM, EFA or RLA and the amount or number of sessions of neuropsychological support during hospitalisation.

**Patient’s condition and relative’s emotional well-being.** No significant correlations were found when investigating the patient’s condition and the relatives’ emotional well-being at admission.

We did not find an association between the number of days after injury that the relative completed the questionnaire and their emotional well-being.
DISCUSSION

As has been reported previously (Norup, Siert, & Mortensen, 2010; Novack, Bergquist, Bennett, & Gouvier, 1991; Oddy, Humphrey, & Uttley, 1978), we found significantly higher anxiety and depression scores in our sample of relatives as well as decreased quality of life compared to reference populations.

Almost all the relatives had at least one session with a neuropsychologist during their family member’s rehabilitation, and the amount of neuropsychological support decreased during the hospitalisation. This was expected, as the patient recovers the relatives start adjusting to the new changed situation in their lives. Interestingly, the decrease in number of sessions was not as clear, indicating that the relatives still had sessions with a neuropsychologist, but that the duration of these sessions shortened during the hospitalisation. We also found that more than one-third of the relatives participated in the group sessions during hospitalisation.

We found an association between the anxiety level of the relatives and the amount of support and number of sessions with a neuropsychologist during hospitalisation. These findings suggest that relatives in severe emotional distress actively seek the psychological support provided in the unit. Interestingly, no associations were found between depression, quality of life and the neuropsychological support. When investigating the different items on the depression and anxiety scales, it is evident that the anxiety scale reflects symptoms such as nervousness, tenseness, and fear as well as physiological reactions, whereas the depression scale reflects symptoms of clinical depression, such as less interest for life, lack of energy and motivation, and hopelessness. Symptoms of anxiety might be more visible to staff working in the unit and therefore staff might be more insistent on providing the necessary support. Two items on the anxiety scale reached a mean score at or above two in this sample. This was the case for “Feeling pushed to get things done” and “Feeling fearful”. “Feeling so restless you can’t sit still” reached a mean just below two.

Relatives with symptoms of anxiety might also be more support-seeking than relatives with high levels of depression as the behaviour associated with depression is more introverted. Items with high means on the depression scale were: “Worrying too much about things”, “Feeling blue”, “Feeling low in energy or slowed down”, and “Crying easily”. When experiencing a lack of energy and feeling blue, the relatives might not be able to seek the necessary support. It is important that staff are able to identify the symptoms of depression and provide the support needed. However, it is also important to point out that not all relatives are interested in seeing a neuropsychologist and some prefer to handle things themselves.

One variable related to the severity of injury, GCS score at admission, was related to the amount and number of sessions of neuropsychological support.
indicating that relatives of patients with less severe injuries received less neuropsychological support. This finding was explained by the fact that relatives of less severely injured patients were hospitalised for a shorter period.

Associations between the condition of the patient and the relative at admission has been reported earlier in a similar sample (Norup et al., 2010), but these findings were not replicated in the present study. The lack of relationship between the patient’s condition and the relatives’ emotional well-being may be the result of the small sample size and the associated low statistical power. However, it should also be observed that the current study was conducted 23 days after injury, while our previous study was conducted 36 days after injury. The sample in the current study was more homogenous since only adults and TBI patients were included.

To the authors’ knowledge, no other studies have investigated the amount and number of sessions of neuropsychological support given during sub-acute rehabilitation. A thorough literature study (Boschen et al., 2007) only identified four intervention studies of brain injury caregiver populations. Three of the studies (Carnevale et al., 2002; Sanguinetti & Catanzaro, 1987; Simmakaruppan et al., 2005) were investigating effects of educational interventions, and the last study (Singer et al., 1994) examined the effect of two types of support groups. The four studies all had a small sample size.

Kreutzer et al. (2009) recently published the preliminary results of a study investigating the effect of a family intervention programme; these results were promising, even though some uncertainties remain. Kreutzer’s sample was assessed about 18 months after injury, which is much later than our sample, and the study was conducted in an outpatient setting. It is important to investigate possible effects of early family interventions, which may prepare families for the possible consequences of brain injury and make the adjustment to a changed family life easier.

Limitations

A major limitation of this study is the small sample size, which suggests caution with respect to generalising our results. This is primarily a concern when interpreting unexpected negative findings that may be a consequence of insufficient statistical power. An example is the lack of a significant association between the relatives’ emotional well-being and the patient’s condition, since we have previously found a significant relationship (Norup et al., 2010). The small sample size only allowed simple statistical analyses, which is why we did not carry out multiple regression analysis.

Many factors may affect the well-being of the relatives and the amount of neuropsychological support given, but only a few were investigated in this study. Factors such as personality, social support, coping style, and earlier life experiences are all known to be important when experiencing an
emotionally difficult situation (Olsen et al., 2006). These factors may influence the need for and ability to benefit from psychological support.

In this study, we investigated the psychological support provided by the neuropsychologists working in the unit. However, all staff members working in the unit provide support during the patient’s hospitalisation. This type of support was not investigated in this study. Furthermore, we did not investigate the support that the relatives receive from family and friends, which may be more important than professional support.

Implications

Even when a relative receives substantial support during the sub-acute phase, she or he will be emotionally affected for years to come and an important issue is whether it is possible to provide an adequate amount of neuropsychological support during a limited period such as hospitalisation.

The present study did not investigate the relatives’ emotional well-being at the patient’s discharge or whether their well-being at this point in time was affected by the support received. The study emphasises the need for randomised controlled studies investigating the effect of psychological intervention during the critical phases in the patient’s rehabilitation process. Future studies will need to be designed using clearly defined and well-documented family interventions and matched controls. The authors are currently conducting a randomised controlled intervention study investigating the effect of psychological intervention to relatives at different times in the patient’s rehabilitation process.

REFERENCES


Depression, anxiety and quality-of-life among relatives of patients with severe brain injury: The acute phase.

Norup, A. Welling, K.L., Qvist, J., Siert, L. & Mortensen, E.L.

Depression, anxiety and quality-of-life among relatives of patients with severe brain injury: The acute phase

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Abstract
Primary objective: To investigate the emotional well-being of relatives of patients with a severe brain injury in the acute setting, as well as risk factors associated with high anxiety and depression scores and impaired quality-of-life.
Research design: Clinical convenience sample.
Methods and procedures: Participants included 45 relatives of patients with severe brain injury recruited at a NICU. All relatives completed selected scales from the SCL-90-R and SF-36 14 days after injury. Data concerning the condition of the patient were also collected.
Main outcome and results: Of the relatives, 51% and 69% reported anxiety and depression, respectively, as well as significantly impaired quality-of-life compared to normal reference populations. Regression analysis revealed that up to 20% of the variance in depression and anxiety scores could be explained by the CRASH 2 Mortality prediction.
Conclusions: The majority of the relatives had severely impaired quality-of-life and symptoms of anxiety and depression during the patient’s NICU stay. Future research is required to explore stressors and evaluate effects of psychological intervention in the acute setting.

Keywords: Emotional distress, neuro-intensive care unit, family, severe brain injury, relatives, anxiety, depression, quality-of-life

Introduction
Development in neuro-critical care during the last decades has resulted in an increasing number of patients surviving severe brain injury. A recent report by the National Board of Health [1] counted all cases of traumatic brain injury (TBI) and non-traumatic brain injury (NTBI) based on the Danish Patient Registry. The report classified the injury severity based on number of days in hospital and estimated a severe brain injury as patients staying in hospital more than 28 days. According to the report, 328 patients acquired a severe TBI and 706 a severe NTBI in Denmark in 2009. Cases of severe brain injury often cause severe physical and mental disability and result in economic strain on society as well as psychological strain on the family of the surviving patient. The emotional strain in family members has been shown to persist years after brain injury and several studies have documented the long-term impact on the relatives [2–4]. However, in the field of brain injury there is a lack of studies investigating early effects of brain injury and the family’s condition during hospitalization. Only one study has been identified, and this study investigated...
post-traumatic stress symptoms in relatives in the first weeks after severe traumatic brain injury [5]. This gap in the literature is problematic since studies have shown that the better the family cope, the better recovery for the patient [6].

Studies in intensive care medicine have investigated the families of patients staying in general intensive care units (ICU) and shown that the majority of relatives report severe symptoms of anxiety and depression [7–11]. It is very important for clinicians to be aware of these symptoms, as Kross and Curtis [12] have pointed out recently. First, the relatives serve as surrogate decision-makers for the critically ill patient. Secondly, the mental symptoms may have important long-term consequences for family members with respect to employment and quality-of-life. Thirdly, the mental state of the relative is of great importance for the patient being treated and, finally, the care provided by the ICU doctors and nurses can be influenced by the mental wellbeing of the relatives since symptoms of distress may affect the collaboration between the family and the staff resulting in a very stressful work environment.

Both short-term and the long-term consequences of severe brain injury on patients and their families emphasize the need for further research exploring the condition of the relatives in the different phases of rehabilitation in order to develop clinical guidelines for supporting the relatives whose life will often be permanently influenced by the change in the functioning of the patient.

The present study
To the authors’ knowledge, no other studies have investigated depression, anxiety and quality-of-life in a sample of relatives of patients with severe brain injury during treatment in a neuro-intensive care unit (NICU). This present study aimed at:

(1) investigating the emotional distress and quality-of-life of relatives of patients with a severe brain injury in the acute setting, as well as

(2) investigating risk factors associated with high anxiety and depression scores and impaired quality-of-life.

It was hypothesized that a sample of relatives of patients with severe brain injury treated in a NICU would report symptoms of depression and anxiety and decreased quality-of-life. It was expected that the characteristics of the patient (clinical status at admission), characteristics of the relative and characteristics related to the NICU would be associated with the reported emotional distress and quality-of-life.

Methods
Participants
The participants in the study were relatives of patients with severe brain injury admitted at a NICU. Relatives were consecutively invited to participate in the study from February 2005 to October 2009. A relative was defined as parent, spouse/cohabitant, child, sibling or boy- or girlfriend. Relatives who did not speak Danish, had a psychiatric diagnosis or a progressive brain disease were excluded. The family decided which relative should participate if more relatives were present at the NICU. Only relatives of patients with a severe brain injury, indicated by a Glasgow Coma Score (GCS) from 3–9 after ending sedation, and need for further intensive neurorehabilitation in hospital, were included. These criteria resulted in a sample comprising 45 relatives of patients with severe TBI or NTBI.

Procedure
A physician from the NICU contacted the manager of the project, when an eligible patient with a relative meeting the inclusion criteria, was admitted. The physicians monitored the condition of the patient the first 48 hours and, if the patient survived and met the GCS criterion, indicating a need for further rehabilitation, a neuropsychologist contacted the relatives and arranged a meeting in the NICU. At this meeting, the relatives received oral and written information about the study and the included relatives gave oral consent to participate. The relatives were then asked to complete a questionnaire regarding their emotional wellbeing during the patient’s stay in the NICU.

The Committees on Biomedical Research Ethics of the Capital Region of Denmark as well as the Danish Data Protection Agency approved the study.

Measures
Assessment of relatives
Relatives were asked to complete selected sub-sub-scales from the SCL-90-R [13] (Symptom Checklist) and the Short Form 36 (SF-36) [14], which have been validated on Danish normative samples. In addition, demographic information was collected.

Anxiety and depression
The relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of SCL-90-R; a self-report checklist designed to reflect the symptom patterns and level of distress [15]. Each item is
The severity of injury was assessed by two well-known and validated scales: The Glasgow Coma Score [17] and the Injury Severity Score [18]. GCS consists of values from 3–15. Patients with scores less than 9 are considered to be in a coma and patients with scores of 15 are able to follow commands, are fully oriented and have spontaneous eye opening. According to criteria for injury severity, GCS scores of 8 or less are classified as severe injuries. The initial GCS was obtained as well as the patient’s GCS score on the day where the relative completed the questionnaire (GCS questionnaire).

The treating physician estimated the Injury Severity Score (ISS), which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0–75 with higher scores indicating more severe injury. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (head, face, chest, abdomen, extremities (including pelvis) and skin). Only the highest AIS score in each region of the body is used. The scores of the three most severely injured regions are added together to produce the ISS.

### Clinical status at admission

Simplified Acute Physiology Score II (SAPS II) [19] and Acute Physiology And Chronic Health Evaluation II (APACHE II) [20] were designed to measure the severity of disease for patients above age 15. Both scores are obtained 24 hours after admission to the ICU. SAPS II includes parameters such as age, GCS, blood pressure, heart rate, body temperature, urine output amongst others and the measurement results in a predicted mortality. The APACHE score is calculated from information about previous health status, age and 12 routine physiological measurements (such as blood pressure, body temperature, heart rate, etc.) during the first 24 hours after admission and results in an APACHE II estimated risk of hospital death.

The Pediatric Index of Mortality (PIM) [21] was used instead of SAPS and APACHE in the paediatric cases. The PIM is calculated from information collected when a child is admitted to the ICU. The PIM describes how ill the child is and predicts a death rate based on the observations of blood pressure, pupil reaction, mechanical ventilation, etc.

CRASH 2 (Clinical Randomization of an Anti-fibrinolytic in Significant Haemorrhage) [22] score was only used for TBI patients. This prognostic model estimates mortality at 14 days and severe disability at 6 months in patients with traumatic brain injury (TBI). The predictions are based on the average outcome in adult patients with Glasgow Coma Score (GCS) of 14 or less, within 8 hours of injury and calculated on the patient’s age, GCS, pupil reaction, presence of major extra cranial injury and a CT scan description. The authors calculated this score retrospectively based on information collected from the patient’s file. Both the mortality rate at 14 days as well as the disability rate at 6 months were used.

The SAPS II, APACHE II and PIM scores were estimated as a part of the standard procedure at admission to the NICU. These scores as well as the CRASH 2 can be calculated online on the relevant websites and the scores used in this study were the mortality prediction in a percentage.
Other variables

Variables were registered related to the patients’ condition that was assumed to affect the emotional distress of the relative. These variables included number of surgeries, days under sedation and days treated on mechanical ventilation. Furthermore, three dichotomous variables were registered: if the patient had a craniotomy or craniectomy, intraventricular monitoring or intraventricular drainage. The length of stay (LOS) in the NICU was also registered, as this variable was expected to be related to severity of injury. Furthermore, the number of conferences with attending physician (only formal meetings documented in the patient’s chart) was registered as well as the commuting time for the relative to the hospital. The variables registered have been associated with the relatives’ condition in earlier studies conducted in critical care medicine [9, 23, 24] and were retrieved from the patients’ files.

Data analysis

Descriptive statistics (means, standard deviations and minimum–maximum range for quantitative variables) were used to describe demographics. Group comparisons were made using independent samples t-tests. Predictor variables were chosen based on the literature from critical care medicine as well as on assumptions from the physicians working in the NICU in question. For every outcome variable, Pearson’s correlation analyses were completed identifying significantly associated predictor variables. Multiple linear regression analyses were carried out to investigate associations between the significant predictor variables and the individual outcome measures. Since the participants-to-independent variables ratio was low, predictor variables were only included in regression analyses, if there were significant associations with outcome variables in the bivariate analyses. For each outcome, stepwise regression was conducted including the predictor variables with significant bivariate association with the outcome.

Statistical analysis was conducted with SPSS version 19.0. All data were analysed using two-tailed testing and \( p = 0.05 \) as a threshold for statistical significance.

Results

Description of sample

All relatives approached at the NICU agreed to participate in the study. The sample of relatives consisted of 78% females and primarily of parents (64%) and spouses (20%). Four children of patients were included (9%) and one sibling (2%). Most of the relatives (82%) were working or studying full time at time of injury and 67% of the relatives were living with the patient at time of injury.

The majority of the patients were male (73%) and working at the time of injury (81%). Most patients had sustained a TBI (80%) and other injury causes were spontaneous intracranial haemorrhage (4%), subarachnoid haemorrhage (7%), major cerebral infarction (7%) and brain tumour (2%) (see Table I).

The patients had a mean age of 30 years (SD = 18; range = 4–71). Four patients died during the stay in the NICU and one patient died after transfer to the sub-acute rehabilitation unit. Characteristics related to the patients’ injuries can be seen in Table II.

All relatives completed the questionnaire ~2 weeks after injury, ranging from 0–32 days. The patients were hospitalized in the acute setting for ~15 days. Correlation analysis did not find associations between time since injury and outcome measures and, therefore, data were treated as being homogenous.

Emotional distress

Raw scores on the depression and anxiety scale were converted into gender-adjusted T-scores according to the SCL manual [15].

Anxiety. A mean T-score of 64.58 was found on the anxiety scale. This was significantly different from a normal reference population (\( p < 0.001 \)) and 53% (24/45) of the relatives had scores above the suggested cut-off (T-score ≥ 63) [13].

Depression. A mean T-score of 64.76 was found on the depression scale. The relatives reported significantly higher depression scores (\( p < 0.001 \)) than a normal reference population [13]. Of the relatives, 69% (31/45) scored above cut-off (see Table III for standard deviations, minimum–maximum range and difference to norm population).

Derogatis [15] defined clinical caseness criteria as having a T-score of 63 or above on at least two of the Symptom Checklist sub-scales and 47% (21/45) of the relatives met this criterion.

Quality-of-life

Table III shows that the relatives obtained significantly lower mean scores than the mean reported for a Danish population sample on all four SF-36 scales [14].
Table I. Characteristics of the sample.

<table>
<thead>
<tr>
<th>Characteristics of the relatives (n = 45)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>35 (78%)</td>
</tr>
<tr>
<td>Cohabitant at time of injury</td>
<td>30 (67%)</td>
</tr>
<tr>
<td>Working at time of injury (aged 16–66)</td>
<td>37 (82%)</td>
</tr>
<tr>
<td>Relationship to the patient</td>
<td></td>
</tr>
<tr>
<td>Spouse</td>
<td>9 (20%)</td>
</tr>
<tr>
<td>Parent</td>
<td>29 (64%)</td>
</tr>
<tr>
<td>Child</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>Sibling</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

Table II. Injury-related characteristics of the patients.

<table>
<thead>
<tr>
<th>Characteristics of the patients (n = 45)</th>
<th>Mean ± SD</th>
<th>Range</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS in NICU, days</td>
<td>15.24 ± 8.02</td>
<td>4–48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days treated on mechanical ventilation</td>
<td>7.91 ± 5.13</td>
<td>1–18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCS initial</td>
<td>5.21 ± 2.93</td>
<td>3–14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCS questionnaire</td>
<td>10.00 ± 3.16</td>
<td>3–15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS (n = 36)</td>
<td>35.78 ± 11.15</td>
<td>25–66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS II (n = 36)</td>
<td>45.44 ± 10.05</td>
<td>15–60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHE II</td>
<td>19.50 ± 4.68</td>
<td>8–30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIM (n = 5)</td>
<td>37.16 ± 16.16</td>
<td>9–49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRASH 2 Mortality prediction at 14 days (TBI-patients) (n = 36)</td>
<td>28.31 ± 24.39</td>
<td>3–92.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRASH 2 Unfavourable outcome at 6 months (TBI-patients) (n = 36)</td>
<td>59.44 ± 21.61</td>
<td>16.4–96.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of operations</td>
<td>1.96 ± 1.47</td>
<td>0–6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conferences with treating physician (documented in files)</td>
<td>5.82 ± 4.00</td>
<td>0–19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commuting time to hospital, minutes</td>
<td>30.61 ± 25.28</td>
<td>2–102</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table III. Mental state of the relative: Descriptive statistics and difference (D) to Danish norms.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± SD</th>
<th>Range</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCL-90-R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety (T-score)</td>
<td>64.58 ± 8.01</td>
<td>45–80</td>
<td>14.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depression (T-score)</td>
<td>64.76 ± 6.97</td>
<td>47–80</td>
<td>14.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>28.60 ± 19.16</td>
<td>0–75</td>
<td>41.24</td>
<td>-14.11</td>
</tr>
<tr>
<td>Social Function</td>
<td>54.26 ± 29.65</td>
<td>0–100</td>
<td>37.09</td>
<td>-8.30</td>
</tr>
<tr>
<td>Mental Health</td>
<td>33.30 ± 18.49</td>
<td>0–76</td>
<td>48.47</td>
<td>-17.19</td>
</tr>
<tr>
<td>Role Emotional</td>
<td>27.19 ± 30.86</td>
<td>0–100</td>
<td>59.14</td>
<td>-11.81</td>
</tr>
</tbody>
</table>

The p-value refers to a one-sample t-test of the difference between the means of the sample of the relatives and the norms from the reference population.

SF-36, Short Form 36; SCL, Symptom Checklist.

LOS, Length of stay; NICU, neuro-intensive care unit; GCS, Glasgow Coma Scale; GCS questionnaire, GCS on the day the relative completed the questionnaire; ISS, Injury Severity Score; SAPS, Simplified Acute Physiology Score; APACHE, Acute Physiology and Chronic Health Evaluation; PIM, Paediatric index of mortality; CRASH, Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage.
Table IV. Pearson correlation analyses: Associations between predictor variables and outcome measures.

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Anxiety</th>
<th>Depression</th>
<th>SF</th>
<th>MH</th>
<th>VT</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics of the patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiving pension (n = 8)</td>
<td>−0.255</td>
<td>0.055</td>
<td>−0.349*</td>
<td>0.129</td>
<td>0.203</td>
<td>−0.186</td>
</tr>
<tr>
<td>Non-survivor (n = 5)</td>
<td>−0.287</td>
<td>−0.115</td>
<td>−0.162</td>
<td>0.185</td>
<td>−0.008</td>
<td>−0.164</td>
</tr>
<tr>
<td>Cranietcmy/craniotomy (n = 17)</td>
<td>0.148</td>
<td>0.246</td>
<td>0.096</td>
<td>−0.349*</td>
<td>−0.009</td>
<td>0.055</td>
</tr>
<tr>
<td>Intraventricular drainage (n = 23)</td>
<td>0.318*</td>
<td>0.281</td>
<td>−0.094</td>
<td>−0.260</td>
<td>−0.158</td>
<td>0.003</td>
</tr>
<tr>
<td>Characteristics of the relative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n = 10)</td>
<td>−0.292*</td>
<td>−0.213</td>
<td>0.102</td>
<td>0.087</td>
<td>0.148</td>
<td>−0.121</td>
</tr>
<tr>
<td>Not cohabiting at time of injury (n = 15)</td>
<td>−0.093</td>
<td>0.094</td>
<td>−0.309*</td>
<td>−0.017</td>
<td>−0.126</td>
<td>−0.037</td>
</tr>
<tr>
<td>Treatment in NICU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOS in NICU, days</td>
<td>0.073</td>
<td>0.160</td>
<td>−0.304*</td>
<td>−0.008</td>
<td>−0.059</td>
<td>0.186</td>
</tr>
<tr>
<td>Days treated on mechanical ventilation</td>
<td>0.179</td>
<td>0.259</td>
<td>−0.136</td>
<td>−0.223</td>
<td>−0.232</td>
<td>0.207</td>
</tr>
<tr>
<td>GCS initial</td>
<td>−0.050</td>
<td>−0.157</td>
<td>−0.176</td>
<td>−0.096</td>
<td>0.036</td>
<td>0.052</td>
</tr>
<tr>
<td>GCS questionnaire</td>
<td>−0.312*</td>
<td>−0.275</td>
<td>−0.032</td>
<td>0.170</td>
<td>−0.058</td>
<td>0.048</td>
</tr>
<tr>
<td>ISS</td>
<td>−0.131</td>
<td>−0.146</td>
<td>0.228</td>
<td>0.154</td>
<td>0.096</td>
<td>0.058</td>
</tr>
<tr>
<td>SAPS II</td>
<td>0.062</td>
<td>−0.004</td>
<td>0.001</td>
<td>0.027</td>
<td>0.056</td>
<td>0.294</td>
</tr>
<tr>
<td>APACHE II</td>
<td>−0.088</td>
<td>0.030</td>
<td>0.132</td>
<td>0.040</td>
<td>0.100</td>
<td>0.199</td>
</tr>
<tr>
<td>CRASH 2 Mortality prediction at 14 days</td>
<td>0.455**</td>
<td>0.406*</td>
<td>−0.097</td>
<td>−0.219</td>
<td>−0.070</td>
<td>0.142</td>
</tr>
<tr>
<td>CRASH 2 Unfavourable outcome at 6 months</td>
<td>0.329</td>
<td>0.349*</td>
<td>−0.047</td>
<td>−0.091</td>
<td>0.042</td>
<td>0.240</td>
</tr>
<tr>
<td>Number of operations</td>
<td>0.413**</td>
<td>0.273</td>
<td>−0.114</td>
<td>−0.315*</td>
<td>−0.223</td>
<td>0.036</td>
</tr>
<tr>
<td>Conferences with physician (doc. in files)</td>
<td>0.184</td>
<td>0.139</td>
<td>−0.173</td>
<td>−0.214</td>
<td>−0.246</td>
<td>0.182</td>
</tr>
<tr>
<td>Commuting time to hospital, minutes</td>
<td>−0.144</td>
<td>−0.133</td>
<td>0.087</td>
<td>−0.240</td>
<td>−0.211</td>
<td>0.224</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01.
1 relatives of patients having a craniectomy/craniotomy did not completed the MH-items.

Regression analysis

Bivariate associations between predictor variables and outcome measures were analysed using Pearson’s correlation analyses and results are shown in Table IV. These analyses failed to reveal significant associations between predictor variables and scores on the VT- and RE-scales. Consequently, regression analysis was not conducted on these outcome measures.

Anxiety. GCS questionnaire, number of operations and CRASH 2 Mortality were associated with anxiety scores and so were intraventricular drainage, non-survivor and gender of the relative. However, given the limited number of participants, it was chosen to include only GCS questionnaire, number of operations, CRASH 2 Mortality and intraventricular drainage in the regression analysis. Stepwise regression analyses revealed that CRASH 2 Mortality as the sole variable explained 20.7% of the variance in anxiety scores ($\beta = 0.44$, $p = 0.008$).

Depression. CRASH 2 Mortality and CRASH 2 Outcome correlated significantly with the depression scores. CRASH 2 Mortality and Outcome did, as expected, correlate mutually ($r = 0.84$, $p < 0.001$) and CRASH 2 Mortality was used in the regression analysis, since this variable showed the strongest association with depression scores. Intraventricular drainage was also included in the stepwise regression, but only CRASH 2 Mortality contributed significantly to the variance in depression scores, explaining 16.5% ($\beta = 0.41$, $p = 0.014$).

Mental health. Number of operations and craniectomy/craniotomy correlated significantly with the scores of the relatives on the Mental Health scale. Stepwise regression analysis revealed that a model consisting solely of the craniectomy/craniotomy explained 12.2% of the variance ($\beta = 0.35$, $p = 0.022$).

Social function. Number of days in the NICU, cohabitant status and patient’s employment status were significantly correlated with scores on the Social Function scale. Stepwise regression analysis showed that a model including cohabitant status explained 9.6% of the variance in Social Function scores ($\beta = 0.31$, $p = 0.041$).

Discussion

As hypothesized, high frequencies of both anxiety (53%) and depression (69%) were found in the sample of relatives, comparable to the findings from general ICUs [7, 9, 10].
This study also found severely impaired quality-of-life, which has not been investigated earlier. High frequencies of emotional distress have been reported regardless of methodological diversities such as different times of assessment, different scales and patient populations. However, inconsistencies regarding predictors of the relatives' well-being remain.

Risk factors predicting the condition of the relatives

CRASH 2 Mortality was the strongest predictor of both anxiety and depression in relatives accounting for up to 21% of the variance. Another injury-related variable craniotomy/craniectomy accounted for 12% for up to 21% of the variance. Another injury-related both anxiety and depression in relatives accounting.

The clinical variables, CRASH 2 and craniotomy/craniectomy, predicted anxiety, depression and Mental Health scores to some extent and correlations between relatives' anxiety and depression scores and the patient's level of consciousness and function have previously been demonstrated, indicating an association between the patient's physical condition and the relative's well-being [25]. This relationship has not been observed in studies with long-term follow-up, where the primary predictors of the relatives' distress have been personality and emotional changes in the brain-injured patient and not the physical deficits [26, 27]. In contrast, most patients in the acute setting are unconscious and this may explain why the emotional distress of the relatives is more influenced by the physical condition than by the personality or emotional condition of the patient.

The Social Function scale describes how the relative functions socially. One's social life is naturally affected when having a critical ill family member and staying at the NICU most of the time. Relatives, not living with the patient, had lower scores on the Social Function scale. One possible interpretation is that these relatives were more affected in their daily life than those relatives who were cohabiting and spend time with their relative every day. Another reason might be that relatives living with the patient already scored higher on this scale before the patient's injury.

Earlier studies, consisting of regular ICU patients, have reported associations between SAPS II, APACHE II and the condition of the relatives [8]. SAPS II and APACHE II reflect deviations from normal physiologic parameters and the presence of chronic illnesses. Trauma patients generally score low on these parameters, because they are healthy before entering the NICU and much younger than ICU patients. Therefore, SAPS II and APACHE II are not as useful in predicting outcome (death) in trauma patients as in regular ICU patients. CRASH 2 was developed to predict outcome in head trauma patients and was found to be an important predictor of emotional distress amongst relatives in the study.

The age of the patient was not related to the relatives' emotional distress, as reported earlier [9, 23]. This study took place in a NICU and not in a general ICU, thus this sample was younger than the patients in the Pochard et al. [9, 10] studies. This study was unable to confirm the results of other studies indicating that the relationship to the patient was related to the well-being of the relatives [9, 11, 25], but two out of three relatives were parents and the negative finding may be the result of low statistical power.

Earlier studies have reported associations between the outcome measures and commuting time and conferences with the treating physicians [9, 23–25] and this study did not replicate these findings. In the NICU in question, visiting hours are free and most relatives stay at the hospital all the time when the patient's condition is critical. This may explain why commuting time was not associated with the relatives' condition. Formal conferences were registered with the treating physician. This number of meetings may be misleading as an expression of information given, since the doctors often have informal talks with the relatives during rounds and in the hallway. This may be the reason why previous studies were not replicated, showing an association between information received and the relatives' well-being [9, 24].

Limitations

The single-centre design is an obvious limitation and a small sample size yields low statistical power and warrants caution with respect to generalizing the results. This is particularly important when comparing groups with unequal distribution.

Another aspect affecting the generalizability of the results is the heterogeneity of the sample. It was chosen to include TBI and NTBI patients as well as both children and adult patients. It can be argued that the relatives of TBI and NTBI patients face different situations and this may influence their emotional condition. However, in this study no significant difference was found in relation to the aetiology of brain injury. This might be due to the different size of the two groups, as the NTBI group only consisted of nine relatives compared to the 36 in the TBI group. The inclusion of relatives of both children and elderly patients make the sample heterogeneous and it is possible that the experiences of the relatives are different depending on the
patients’ age, although these results do not support this hypothesis.

This study investigated the presence of anxiety, depression and quality-of-life in the relatives, but previous life events and social support were not investigated and these are known to have an impact on emotional well-being [16].

Clinical implications

As Kross and Curtis [12] pointed out, it is important to be aware of symptoms of emotional distress, when working with families in the acute setting. The distress that families experience influences the collaboration between the clinicians and the family. High scores of depression and anxiety may affect the ability to remember and retain the information given by clinicians. This can cause frustration in both the affected families as well as the staff working at the NICU. Information needs to be repeated several times and if possible in a more quiet setting than during rounds or in the hallway. It is important for clinicians to make sure that the family understands information given regarding treatment and prognosis.

A structured approach regarding the conferences with the family may be recommended, as regular meetings providing information about treatment and prognosis may reduce the distress and psychological symptoms experienced by the family. By meeting the families regularly, the clinicians can assess the needs of the family and make relevant referrals to meet these needs (e.g. psychological support, economic and social counselling). This is also expected to reduce distress in families and may indirectly reduce the stressful work-environment in the NICUs.

Conclusion

The relatives had a high prevalence of depression and anxiety and reported significantly impaired quality-of-life. The mental distress of the relatives is a consequence of the stress and trauma of experiencing a sudden and severe disease in a close relative. Although the traumatic and life-threatening experience itself cannot be prevented, it is important to attempt to minimize the psychological effects on the families by developing and evaluating interventions in the acute setting. It seems that factors related to the condition of the patient are highly associated with the well-being of the relatives in the acute setting.

As pointed out previously [25], further research is required to explore stressors in NICUs and to evaluate the effect of interventions in the acute setting. Early intervention might reduce the emotional distress experienced by relatives in the acute setting as well as later in the process of rehabilitation.

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References


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Neuropsychological intervention in the acute phase: a controlled trial investigating the emotional wellbeing of relatives of patients with severe brain injury.

_in manuscript._
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Short title: acute neuropsychological intervention.

Key words: acute neuropsychological intervention, relatives, severe brain injury, controlled trial, anxiety, depression, quality of life.

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Acknowledgements and disclosure of conflicts of interest

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ABSTRACT

This study investigated the effects of acute neuropsychological intervention to relatives of patients with severe brain injury. Participants were enrolled in an intervention group consisting of 39 relatives, and a control group comprising 47 relatives. The intervention consisted of supportive and psycho-educational sessions with a neuropsychologist in the acute care setting. The intervention group completed self-report scales in the acute setting and after the intervention at admission to sub-acute rehabilitation. The control group completed the scales only at admission to sub-acute rehabilitation. Outcome measures included selected scales from the Symptom Checklist Revised 90 (SCL-90-R), the Short Form 36 (SF-36) and a visual analogue quality of life scale. The intervention group showed a significant decrease in anxiety scores from the acute to the sub-acute setting ($t=2.70, p=0.010, d=0.30$). In the sub-acute setting, an ANCOVA model showed a borderline significant difference between the intervention and the control group on the anxiety scale ($p=0.066, d=0.59$). Any effects of the acute neuropsychological intervention were limited, and further research is needed to explore effects of different interventions in more homogenous and larger groups of relatives.
INTRODUCTION

Quite a few studies in the field of brain injury have documented emotional strain and distress in relatives of patients with brain injury (Harris, Godfrey, Partridge, & Knight, 2001; Machamer, Temkin, & Dikmen, 2002; Norup, Siert, & Mortensen E.L, 2010; Oddy, 1985; Panting & Merry, 1972; Perlesz, Kinsella, & Crowe, 2000; Ponsford, Olver, Ponsford, & Nelms, 2003; Schonberger, Ponsford, Olver, & Ponsford, 2010; Thomsen, 1974). The majority of studies have focused on the long-term impact on family members, and there has been a lack of studies investigating early effects of brain injury and the family’s condition during hospitalization. Only two studies have been identified investigating relatives of patients with severe brain injury in the early phases of hospitalization (Pielmaier, Walder, Rebetez & Maercker, 2011; Norup, Welling, Qvist, Siert & Mortensen, 2012). Pielmaier et al. (2011) reported that more than half of the relatives of patients with severe TBI admitted to critical care had clinically significant posttraumatic stress symptoms shortly after the injury, which is in concordance with our findings in an NICU reporting high frequencies of anxiety and depression (Norup et al., 2012). These results are consistent with research investigating the condition of the relatives with longer follow-up (Douglas & Spellacy, 1996; Turner et al., 2010; Marsh, Kersel, Havill, & Sleigh, 1998b; Marsh, Kersel, Havill, & Sleigh, 1998a; Ponsford et al., 2003).

A review concerning the emotional condition of relatives of critically ill patients in ICUs and NICUs found that most relatives needed ‘to have questions answered honestly’ and ‘to know specific facts regarding what is wrong with the patient and the patient’s progress. The review concluded that information was the most important need identified in critical care, when the patient’s situation is unstable. The families seeked honest and frequent information about progress, status and prognosis (Hickey, 1990).
Despite the knowledge about the distress and needs of families of patients admitted to NICU’s, no studies have investigated and evaluated intervention to families of brain injury survivors in the early phases of rehabilitation. The intervention studies conducted have investigated interventions to families of brain injury survivors in outpatient centers years after injury and the majority has only proved limited effects on relatives’ distress and emotional condition (See Table 1). Only two (Rivera, Elliott, Berry & Grant, Singer, Glang, & Nixon, 1994) of five RCT’s conducted (Rivera et al., 2008; Singer et al., 1994; Carnevale, Anselmi, Busichio & Millis, 2002; Sanguinetti & Catanzaro, 1987; Backhaus, Ibarra, Klyce, Trexler & Malec, 2012) found significant effects of the administered interventions on anxiety, depression and health complaints. Rivera et al (2008) also found effects on dysfunctional problem-solving, and Backhaus found an intervention effect on Perceived Self-Efficacy, but not on experienced distress. The third RCT found an effect on knowledge about brain injury and cognitive problem (Sanguinetti & Catanzaro, 1987), and the forth reported no significant findings (Carnevale et al., 2002). Sinnakaruppan and coworkers (2005) conducted a pilot study and found significant improvement in severe depression in the intervention group.

The rest of the intervention studies conducted had a pretest-posttest quasi-experimental design revealing mixed results. Acorn (1995), Liamaki & Bach (2003) and Morris (2001) reported no significant findings of their administered interventions (e.g. support groups and an information booklet). Two studies by Kreutzer and colleagues (Kreutzer, Stejskal, Ketchum, Marwitz, Taylor & Menzel, 2009; Kreutzer, Stejskal, Godwin, Powell & Arango-Lasprilla; 2010) and Albert, Brenner, Smith & Waxman (2002) reported a significant decrease on subjective measures primarily on Likert type scales. Kreutzer et al. (2009/2010) also used standardized measures, but did not find any improvements on these. Perlesz & O’Louglan (1998) and Brown, Pain, Berwald, Hirschi, Delehanty & Miller (1999) were the only two of the quasi-experimental studies, who were able to report
significant improvements on standardized scales. Improvements were found in relation to family cohesion and conflict as well as psychological distress. Nevertheless, it is difficult to assess effects of the quasi-experimental studies, as no control group (in one case a historical control group (Albert, Brenner, Smith & Waxman, 2002)) have been included, and the reported effects could be due to time. Nevertheless, most authors do conclude that the carers have benefited from the different programs, even though the results of the reviewed studies are not convincing in terms of reducing experienced distress.

*Insert Table 1*

Moreover, many of the findings have been based on self-report measures, sometimes constructed by the authors themselves. No consensus exists on important outcome measures or which methodology that is most appropriate. In most studies, samples were small and in some cases biased, as they were recruited from diverse support groups, which were not representative for the whole population. Most authors do not comment on the situation and condition of the patient, which is maybe one of the most important factors, when evaluating the status of the caregivers.

Despite this recent focus on intervention to the family and the knowledge about the needs of families in the acute care setting, no studies have been conducted investigating effects of psycho-educational and supportive intervention in the early phases of rehabilitation, even though the relatives explicitly request information and neuropsychological support in the acute care setting (Hickey, 1990; Norup et al., 2010; Norup et al., 2012).

The present study was designed in an attempt to meet the needs of the relatives in the early phases of rehabilitation (Oddy & Herbert, 2003) and investigate effects of interventions to relatives in the early phases of rehabilitation.
The purpose of the study was to investigate the effects of neuropsychological intervention to relatives of patients with severe brain injury in the acute care setting. The intervention consisted of supportive sessions with a trained neuropsychologist, and the sessions were a flexible mixture of both psycho-education and emotional support. The sessions were individualized and focused primarily on the family’s immediate situation with a close family member in hospital.

The aims of the study were to investigate whether:

1) a group of relatives receiving neuropsychological intervention in the acute setting experienced a decrease in symptoms of anxiety and depression and an increase in quality of life

2) the group receiving intervention had significantly fewer symptoms of anxiety and depression and better quality of life compared to a control group.

MATERIALS AND METHODS

Participants

Two groups of relatives of patients with a severe brain injury were included: an intervention group receiving acute neuropsychological intervention and a control group receiving no intervention in acute care. The intervention group initially comprised 46 relatives, but because four patients died and three relatives did not return follow-up questionnaires at admission to rehabilitation, data will only be reported for 39 relatives.

The group consisted primarily of parents (61%) and spouses (20%), and most were female (80%). The majority of the relatives (59%) was living with the patient at time of injury and most (87%) was working at time of injury. The majority of the patients was male (80%) and had sustained a traumatic brain injury (80%). A fifth of the intervention group had sustained a non-traumatic brain
injury (NTBI) caused by spontaneous intracranial hemorrhage (2.5%), subarachnoid hemorrhage (5%), brain tumor (2.5%) and major cerebral infarction (10%). The mean age in the intervention group was 31 years (SD 17; 4-71) (See Table 2).

Insert Table 2 about here

The control group consisted of 47 relatives who only completed the questionnaires when included at admission to sub-acute rehabilitation. This group consisted primarily of females (69%), and most relatives were spouses (44%) or parents (27%). The majority of the relatives (58%) were living with the patient at time of injury, and the majority (83%) was working at time of injury.

Most patients in the control group were male (68%) and had acquired a TBI (66%). Of the patients in the control group, 16 had acquired a NTBI caused by cardiac arrest (8%), spontaneous intracranial hemorrhage (4.5%), subarachnoid hemorrhage (4.5%), major cerebral infarction (11%), tumor (2%) and meningitis (2%). The mean age of the patients in the control group was about 46 years (SD 20; 1-82) (Table 2).

All patients had severe brain injury and a need for intensive neurorehabilitation. The patients had to fulfill one of the following admission criteria:


2) Patients with a GCS > 9 with severe focal neurological deficits such as aphasia, hemi paresis or agitation.

3) Patients with severe cognitive deficits as well as paresis or agitation.
Relatives, who did not speak Danish, had a psychiatric diagnosis or a progressive brain disease, were excluded from the study.

**Procedure**

The two groups of relatives were included at two different time points. The intervention group was included at the Neuro Intensive Care Unit (T1), when the patient’s condition was stabilized, and the control group was included at admission to the sub-acute rehabilitation (T2). Patients were only included when fulfilling the criteria above, and if the relative did not meet any of the exclusion criteria. Both groups were admitted for intensive neurorehabilitation in the sub-acute phase at the Traumatic Brain Injury Unit (See Figure 1).

*Insert Figure 1*

Oral consent to participate was obtained by a neuropsychologist, when the relative was included. If more than one relative was present at time of inclusion, the family decided which relative should participate in the study.

The relatives in the intervention group completed questionnaires regarding emotional wellbeing in the acute phase (T1) on average 16 days ($SD$ 6; 5-32) after injury and once again when the patient was transferred to sub-acute rehabilitation (T2) about 24 days ($SD$ 8; 11-41) after injury. The patients in the intervention group were admitted to rehabilitation 17 days ($SD$ 6; 7-34) after injury. The patients in the control group were admitted to sub-acute rehabilitation 24 days ($SD$ 16; 8-68) after injury on average, and their relatives completed the questionnaires at admission to sub-acute rehabilitation (T2) 35 days ($SD$ 18; 9-77) days after injury.
Potential effects of the intervention were evaluated by comparing the results obtained in the two groups at admission to sub-acute rehabilitation (T2).

The study was approved by The Committees on Biomedical Research Ethics of the Capital Region of Denmark (journal number H-KF-311150) as the Danish Data Protection Agency (journal number 2007-41-0583).

**Intervention**

*Method:* The intervention group received neuropsychological support during acute care conducted by neuropsychologists trained in dealing with psychological trauma and having years of experience in the field of brain injury rehabilitation. The sessions were not manualized, as the emotional condition and consequently the needs of relatives differed considerably. In each session the neuropsychologist decided on the most beneficial structure of the session according to the needs of the relatives balancing between psychological support and psycho-education. This method was chosen after conducting a few pilot sessions facing the very different situations and needs of the families. The intervention was administered during the first three weeks after the injury.

*Purpose and expected benefits:* The purpose of the intervention was twofold and consequently it was a flexible mixture of both emotional support and psycho-education. The sessions were targeted on the family’s immediate situation with a close family member severely ill in hospital. The first purpose of the intervention was providing psychological support to the family in terms of dealing with the distressing situation of having a critically ill family member. The primary objective for the neuropsychologist was to listen and to instill hope in the families by identifying progress in the patient’s condition and personal strengths in the relatives. This was expected to help families regain
hope in the future and indirectly causing emotional relief. The second purpose of the session was psycho-educational providing information about treatment in the acute setting and consequences of brain injury. Giving needed information was expected to improve understanding of the patient’s condition and reduce anxiety and more general symptoms of distress. The relatives were only given information they requested, and in each session the neuropsychologist carefully evaluated how much information the relatives were capable of receiving without causing further distress.

Content and topics: The specific topics of the sessions depended on the relatives’ specific needs. Every session began with the neuropsychologist asking the family how they experienced the accident, if they witnessed it or were involved. In cases where the relatives had not been present, they were asked to share how they received the message about the accident. The relatives often needed immediate psychological support to help them deal with their own emotional reactions and needs during the first critical phases of the patient’s stay in the acute setting. Topics often addressed in the supportive part of the sessions were how to handle each day with a close family member in hospital, feelings of isolation, guilt and emotional distress. The second part of the sessions was psycho-educational, and the relatives were able to ask all questions regarding treatment in the acute setting, the first period of unconsciousness, post-traumatic amnesia, consequences of brain injury and recovery from brain injury.

In some cases, the relatives were had obvious symptoms of anxiety being tense, physically restless and almost unable to sit still. In such sessions, the focus remained on the immediate situation and how to handle this. In cases where the families were more calm and able to receive information, the neuropsychologist tried to answer the relatives’ questions about prognosis, treatment in the acute setting. However, it was very important that each session was finished properly making sure that the relatives had no further questions or queries.
**Outcome measures:** Effects of the intervention were assessed by having the relatives complete standardized questionnaires regarding anxiety, depression and quality of life (information regarding the specific measures is given below). Anxiety and depression were chosen, as these symptoms have been described in families of brain injury survivors for years (Oddy, 1985; Livinston, Brooks & Bond, 1985, Marsh, Kersel, Havill & Sleigh, 2002). We expected anxiety to be more sensitive to the intervention, as information is known to be able to reduce anxiety.

A quality of life measure was also included; as research has shown that quality of life can be high in caregivers despite high levels of distress (Wells, Dywan, & Dumas, 2005).

**Amount of intervention:** The duration of the sessions was one to one and a half hours depending on the relatives, and the majority of the relatives (67.4%) received one session. Of the relatives, 17.4% had two sessions, 13.0% had three sessions and one relative had four sessions (2.2%).

An independent samples t-test showed no difference in the relatives’ emotional wellbeing on T2 depending on whether or not the relative received more than one session of intervention.

*Insert Table 3*

**Measures**

Assessment of relatives

Outcome measures were administered at T1 and T2 in the intervention group and at T2 in the control group:
**Quality of life:** Each relative was asked to complete the Short Form 36 (SF-36), a measure of self-reported health-related quality of life. The questionnaire comprises 36 items addressing eight dimensions of health. Scores in each domain of the SF-36 range from 0-100 with higher scores indicating better health. Only four scales were used in the present study: Role Emotional (RE), Social Function (SF), Mental Health (MH) and Vitality (VT). Low scores on the RE-scale means problems with work or other daily activities as a result of emotional problems, and high scores indicate no problems in these areas. Low scores on the SF-scale indicate extreme and frequent interference with normal social activities due to physical and emotional problems, and high scores indicate no problems. On the MH-scale, low scores indicate feelings of nervousness and depression, and high scores mean that the respondent feels happy, peaceful and calm. On the VT-scale, low scores refers to feeling tired and worn out, and high scores refer to feeling full of pep and energy (Ware, Jr. & Sherbourne, 1992).

The scores of the relatives were evaluated in terms of available Danish norms (Bjørner, Damsgård, Watt, & Bech, 1997). This normative study showed high Cronbach’s alpha coefficients on all the subscales used in this study ranging from 0.75 to 0.85 (Bjørner et al., 1997).

The relatives were also asked to rate their own perception of quality of life on a visual analogue scale (VAS) with a range from 0 to 10, 0 indicating “very dissatisfied” and 10 indicating “very satisfied”.

**Anxiety and depression:** The relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of Symptom Check List 90 Revised (SCL-90-R); a self-report checklist designed to reflect the symptom pattern and level of distress (Olsen, Mortensen & Bech, 2007). Each item is scored on a scale of 0 (‘not at all’) to 4 (‘extremely’) indicating the degree of distress for that particular item. The respondents are asked to answer each item according to their condition during
the past seven days. Raw-scores were converted into T-scores, and evaluated in terms of the gender-specific norms for a Danish sample (Olsen, Mortensen & Bech, 2007). This Danish population study revealed high alpha coefficients on all the SCL subscales, and in particular for the depression and anxiety scales used in this study ($\alpha=0.91$ and $\alpha=0.86$ respectively) (Olsen et al., 2006).

**Social support and life events**: Questions regarding the relatives’ social support included a question about how often they had contact with different people (parents, children, other family, colleagues after work, neighbors, childhood friends, other friends, professional caregiver), and how satisfied the relative was with this contact. The relatives also reported how many people they were able to share very personal matters with.

Questions about traumatic life events over the past year and over the entire life span included five work related questions (unemployment, not being promoted, conflicts with colleagues, superiors or subordinates) and seven questions related to events in the family (children severely ill, severe educational problems for children, severe conflicts with grown-up children, severe problems in marriage, own severe illness, severe illness or death among relatives, severe economical problems). We counted the total amount of traumatic events in the past year and over the entire life.

The questions were modified versions of questions used in the Copenhagen City Heart Study and were administered, when the relatives were enrolled (Sethi, Nordestgaard, Agerholm-Larsen, Frandsen, Jensen & Tybjerg-Hansen, 2001).

**Assessment of patients**

As a standard procedure during admission, relevant data were collected regarding the patient’s condition: severity of injury, level of consciousness and function.
Severity of injury: The severity of injury was assessed by two well-known and validated scales: The Glasgow Coma Score (Teasdale & Jennett, 1974) and the Injury Severity Score (ISS) (Baker, O'neill, Haddon, & Long, 1974). GCS is scored from 3 to 15. Patients with scores less than nine are considered to be in coma, and patients with scores of 15 have spontaneous eye opening, are able to follow commands and are fully oriented. According to criteria for injury severity, GCS scores of eight or less are classified as severe injuries. The treating physician assessed GCS at admission to the Traumatic Brain Injury Unit. The treating physician also estimated the Injury Severity Score (ISS), which consists of an anatomical scoring system that provides an overall score for patients with multiple traumatic injuries. The ISS ranges from 0 to 75. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (head, face, chest, abdomen, extremities (including pelvis) and external). Only the highest AIS score in each region of the body is used. The scores of the three most severely injured regions are added together to produce the ISS. The ISS was only assessed for patients with a traumatic brain injury.

Level of consciousness: Rancho Los Amigos (RLA) score (Hagen, Malkmus, & Durham, 1972; Hagen, 1984) was assessed by a neuropsychologist at admission to sub-acute rehabilitation. This score ranges from level one, which describes a comatose condition with no observable response, to level eight, which is a condition with purposeful and appropriate responses. This scale was designed for use on patients with a traumatic brain injury.

Functional level: The patient’s functional level at admission was assessed with the Early Functional Abilities (EFA) and the Functional Independence Measure (FIM).
The EFA is an assessment tool for patients with severe cerebral impairments in the early neurological rehabilitation stage, which describes clinically observable changes in a patient’s early functional abilities (Heck, Schmidt & Steiger-Bachler, 2000). The EFA Scale contains 20 items and assesses early basic abilities related to four functional areas: vegetative, face and oral, sensory-motor and sensory cognitive functions. Each item is rated on a five-point scale from “not obviously observable” to “no essential functional limitation”. The total score is the sum of the item scores ranging from 20 to a maximum of 100. High scores indicate better functional ability.

The FIM (Keith, Granger, Hamilton, & Sherwin, 1987) is an 18-item rating scale assessing activities of daily living (ADL): self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a seven-point scale from “total assistance” to “complete independence”. A total FIM score ranges from 18 to 126 with higher scores indicating greater independence. The FIM Scale has been shown to be valid and reliable for measuring functional outcome after TBI.

Both FIM and EFA scores assessed by physio- and occupational therapists, who were trained users of the scales.

**Data Analysis**

Descriptive statistics were used; results are presented as percentages and means with standard deviation and range. Categorical and ordinal data were analyzed using chi-square and Mann-Whitney tests. Changes in the relatives’ emotional condition between T1 and T2 were analyzed with paired t-tests and the emotional condition of the intervention and control group were compared using independent samples t-tests. ANCOVA was used to adjust for the relatives’ gender and for the observed group differences on variables with significantly different distributions in the two patient groups. We calculated Cohen’s $d$ to estimate effect size.
All data was analyzed using two-tailed testing and $p=0.05$ as a threshold for statistical significance. The statistical software used was SPSS version 19.0.

**RESULTS**

The condition of the relatives in the two groups were assessed and compared to the relevant Danish norms (Bjorner et al., 1997; Olsen et al., 2007) using one-sample t-tests. The relatives in both groups had significantly higher scores on the depression and anxiety scales and significantly lower quality of life at T2 compared to Danish norms and this was also the case for the intervention group at T1. Means, standard deviations, range can be seen in Table 4.

*Insert Table 4 about here*

### Changes in emotional wellbeing from T1 to T2

**Quality of life:** The intervention group became significantly worse from T1 to T2 ($t=2.12$, $p=0.043$, $d=0.40$) on the RE scale, but a trend towards improvement on the VT-scale was found ($t=-2.02$, $p=0.051$, $d=0.18$). No change from T1 to T2 was observed on the MH-scale and SF-scale. On the visual analogue scale, the relatives in the acute group rated their quality of life slightly better on T2 compared to T1 (See Table 4).

*Emotional distress:* The intervention group experienced significantly less anxiety at T2 compared to T1 ($t=2.70$, $p=0.010$, $d=0.30$), and also scored lower on depression at T2 compared to T1, although not significantly lower ($t=1.77$, $p=0.085$, $d=0.29$) (Table 4).

### Comparisons between the intervention and the control group
*Group differences:* The control group was admitted to rehabilitation and completed the
questionnaires later than the intervention group (See Table 2). The groups did not differ
significantly in regards to occupational status, cohabitation status or gender distribution.
The relative’s relationship to the patient was recoded into three categories; parents, spouses and
others (siblings, children, boy-/girlfriends), and a chi-square test showed that the relatives’
relationship to the patient was distributed significantly different in the two groups (See Table 2).
The groups did not differ significantly in regards to social support or experienced life events.
The patients in the intervention group were significantly younger than the control group, and the
intervention group had a significantly higher ISS score than the control group indicating that
patients in the intervention group had more severe injuries (see Table 2 for results regarding group
differences).

*Quality of life:* A significant difference was found on the Role Emotional scale; the control group
had significantly better scores on T2 ($t=-1.99$, $p=0.05$, $d=0.39$) than the intervention group. No
difference was observed between the two groups on the MH-, SF- or VT-scale.
No difference was found when comparing the VAS scores of the intervention group with the VAS
scores of the control group scores at T2 (see Table 4).

*Emotional distress:* No difference was found in regards symptoms of anxiety or depression, when
comparing the two groups at T2 (see Table 4).

*Adjusted differences between groups*
An ANCOVA model was used to adjust for gender and variables showing significantly different
distribution in the intervention and the control group. The model adjusted for the relative’s gender,
the relatives’ relationship to the patient (spouse vs. other), the patient’s age and the number of days after injury that the relatives completed the questionnaire. The model also adjusted for the ISS, and this reduced our sample, as it is only applicable to patients with TBI (See Table 5 for raw and adjusted means). The control group obtained higher anxiety \((p=0.066, d=0.59)\) and depression scores \((p=0.338, d=0.31)\) than relatives in the intervention group at T2, but not significantly higher. With regards to quality of life, the control group showed lower adjusted VAS scores \((p=0.351, d=0.30)\), but non-significant, and this was also the case on the MH-scale \((p=0.070, d=0.61)\). Scores on the anxiety and Mental Health scale were borderline significant. Table 5 shows that the control group obtained higher scores on the remaining SF-36 scales, however non-significant.

*Insert Table 5 about here*

**Supplementary analyses**

The age of the patient was significant in the model, and consequently possible interactions between the age of the patient and the effect of the intervention were tested. However, no interactions were significant, and analyses including only patients above the age of 15 years showed results similar to those obtained for the full sample.

However in the full sample, the age of the patient was important in relation to anxiety \((p<0.001)\) and depression \((p<0.001)\) indicating that relatives of older patients experienced less anxiety and depression. The relatives of older patients had higher scores on the VAS \((p=0.001)\), RE- \((p=0.001)\), MH- \((p<0.001)\) and the VT-scale \((p<0.001)\) indicating better quality of life.

We also found that spouses had higher levels of depression \((p<0.001)\) and anxiety \((p=0.001)\) and reported lower quality of life at MH- \((p=0.002)\) and VT-scale \((p=0.007)\) compared to other relatives.
DISCUSSION

Changes in emotional wellbeing from T1 to T2

We found a significant decrease in symptoms of anxiety from T1 to T2 and a decrease in symptoms of depression, however this decrease was not significant. We found a borderline significant increase in Vitality scores, but the only significant change on the SF-36 scales was a decrease in Role Emotional scores from T1 to T2 indicating lower quality of life at T2.

Anxiety probably reflects acute worries about the patient and the future, and these symptoms may decrease faster than symptoms of depression, as other studies have shown that symptoms of depression can persist years after injury (Machamer et al., 2002; Douglas & Spellacy, 1996; Marsh et al., 1998b; Marsh, Kersel, Havill, & Sleigh, 2002; Perlesz et al., 2000; Ponsford et al., 2003; Schonberger et al., 2010). The decrease in symptoms of anxiety and depression and improvement in vitality could be caused by the intervention, but it is very likely that the decrease is a consequence of a more spontaneous improvement in the emotional state of the relatives related to the patient’s more stable and perhaps improved condition.

Low scores on the RE scale reflects problems with work or other daily activities as a results of emotional problems. It is very likely that relatives rate this score lower at T2 because they at this point realize the severity of the injury and the long-term care and rehabilitation needed.

Because of the intervention as well as the stabilization of the patient’s condition, an improvement in the condition of the relatives from T1 to T2 was anticipated, and the control group was included in an attempt to obtain a more realistic picture of the effects of the intervention.

Comparisons between the intervention and the control group
The control group was included at admission to rehabilitation in hospital and had not received any kind of intervention in the acute setting. Unfortunately, there were many differences between the two groups: the intervention group completed the questionnaire earlier, the patients were younger and had more severe injuries, and the distribution of parents and spouses was significantly different in the two groups. When adjusting for these differences more anxiety and depression were found in the control group as well as lower VAS and MH-scores. The results regarding anxiety and the scores on the MH-scale were borderline significant, but the others were non-significant. We also found a non-significant tendency towards higher scores on the RE- and SF-scale in the control group.

The results are somewhat mixed when comparing the two groups, but it is clear that any effects of the intervention were small. Other factors appeared to be more important since the age of the patient and the relatives’ relationship to the patient overrode any effects of the intervention.

This result was unexpected and in contrast to what most relatives had expressed since the majority did spontaneously express satisfaction with the information and support received during the sessions. However, it is likely that the intervention should have been provided even earlier than it was administered. Many relatives pointed out that their need for psychological support as well as information had been more critical earlier during the patient’s stay in acute care. Moreover, in most cases the intervention was limited to only one session, and this may not be enough to produce detectable effects.

To the authors’ knowledge, this study is the only one investigating the effect of an early intervention study and therefore adds to the knowledge available regarding the condition of the relatives in the early phases of rehabilitation. Nevertheless, the intervention conducted only had limited effects on emotional distress. As discussed in the introduction, the intervention studies
previously conducted regarding psychological support have also had difficulties proving effects on standardized measures of psychological distress (Kreutzer et al., 2009; Backhaus et al, 2012; Acorn, 1995; Liamaki & Bach, 2003). Intervention effects seem to be more detectable on more subjective measures (Kreutzer et al, 2010; Sander, Clark, Atchison & Rueda, 2009; Albert et al., 2002).

Methodological considerations

The aim of this study was to examine effects of neuropsychological intervention in the acute setting, but a variety of circumstances influenced our data collection and the two groups differed on a number of key variables.

In many cases, one of several eligible relatives volunteered to participate at the critical time of enrolment, and it was not deemed justifiable to ask specific members of the families to participate. Of course, this choice may have resulted in bias, as we might primarily have included resilient and emotionally strong relatives, which may indirectly have influenced the effects of intervention. Additionally, this choice also made it impossible to stratify the relatives according to their relationship to the patient.

Our samples were relatively small, and it is likely that statistical power was not sufficient to detect small effects of the intervention. This is particularly the case for the comparison of the intervention and control groups since Cohen’s $d$ was 0.59 and 0.31 for anxiety and depression, but the group differences were not significant.

It is also a limitation that we used general measures of mental symptoms and quality of life since it is possible that outcome measures specifically aimed at detailed description of the immediate emotional distress and concrete worries and concerns of the relatives may be more sensitive to the effects of interventions.
Implications

The study emphasized the emotionally straining situation of families of brain injury survivors in the early phases of rehabilitation and the need for early intervention. No other studies have investigated effects of early psychological intervention in a controlled design despite the call for early supportive interventions has been demonstrated in previous research (Mauss-Clum & Ryan, 1981; Pielmaier et al., 2011; Norup et al., 2010; Norup et al., 2012).

Future research should focus on obtaining larger samples and investigate intervention characteristics such as timing, number of sessions and follow-up time. Randomized studies should be considered, but if this is considered unethical, efforts should be made to obtain a more comparable intervention and control groups than we were able to obtain in the present study. Larger samples should enable better statistical control of background variables, but individual matching is also a possibility. Choice of outcome measures as well as follow-up time after intervention should be considered thoroughly, as distress might require a longer follow-up time in order to be measurable.

CONCLUSIONS

In the intervention group, a decrease in symptoms of anxiety and depression from T1 to T2 was observed and this group also showed less anxiety than the control group. However, most effects were small, and consequently the study did not demonstrate convincing effects of a short neuropsychological intervention administered early in the acute phase. Despite the negative results, psychological intervention of sufficient duration is likely to reduce emotional strain and distress, and this possibility should be further explored in future studies.
Reference List


<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention/measure</th>
<th>Design</th>
<th>Time of assessment</th>
<th>Significant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morris (2001)</td>
<td>Information booklet/HADS &amp; GHQ</td>
<td>Quasi-experimental (pretest-posttest) I1 (n=11): booklet I2 (n=15): booklet Allocated to groups depending on time since injury (2-9 mth vs&gt;12 mth).</td>
<td>Inclusion: I1: 2-9 mth post injury I2: &gt;12 mth post injury Follow-up: 3-4 weeks after intervention</td>
<td>No significant findings</td>
</tr>
<tr>
<td>Sanguinette (1987)</td>
<td>2 videotapes addressing cognitive and physiological problems at discharge/ rating on cognitive extrapolation test</td>
<td>RCT I (n=20): both tapes C (n=9): only the tape addressing physiological problems</td>
<td>Inclusion: at discharge from hospital. Follow-up: after intervention</td>
<td>I-group were more informed about consequences of brain injury</td>
</tr>
<tr>
<td>Albert (2002)</td>
<td>Caregiver education at discharge, designated social worker/ Likert scale assessing burden, satisfaction &amp; mastery</td>
<td>Quasi-experimental I (n=27): education + social worker C (n=29): historical cohort</td>
<td>Inclusion: at discharge Follow-up: 1, 2-4, 5-7 or 8-13 mth after discharge</td>
<td>Significantly lower burden, better quality of life</td>
</tr>
<tr>
<td>Carnevale (2002)</td>
<td>Behaviour management (8x2 hours) and education (4x2 hours) administered by psychologist and behaviour technician/QRS &amp; MBI</td>
<td>RCT I1 (n=9): education +behavioural intervention I2 (n=8): education (offered behavioural intervention at end of study) C (n=10): standard care (offered I1 at end of study)</td>
<td>Inclusion: I1: 7.8 yrs since injury I2: 10 yrs since injury C: 8.5 yrs since injury Follow-up: 1, 5 and 14 wks after intervention.</td>
<td>No significant findings</td>
</tr>
<tr>
<td>Sinnakaruppan (2005)</td>
<td>8 sessions of didactic presentation with a neuropsychologist: written material, role play, discussion etc. addressing memory, emotional, executive problems/HADS, GHQ, RSE &amp; COPE</td>
<td>Pilot study (RCT) I (n=25→23): intervention described C (n=25→19): received I at the end of the study.</td>
<td>Inclusion: I: 2-97 mth C: 7-84 mth Follow-up: 3 mth after intervention</td>
<td>I-group showed significantly improvement compared to controls in terms of severe depression (GHQ).</td>
</tr>
<tr>
<td>Sander (2009)</td>
<td>Web-based videoconference (6 sessions of 15-20 minutes): education and interactive problem-solving/Satisfaction survey</td>
<td>Feasibility study n=15</td>
<td>Inclusion: 2 wks after discharge (~7.1 mth after injury). Follow-up: 18 mth after the last training</td>
<td>High overall satisfaction: gained knowledge was applicable to everyday problems</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Type of Support Group</td>
<td>Setting/Duration</td>
<td>Design</td>
<td>Intervention Group Details</td>
</tr>
<tr>
<td>-------------</td>
<td>-----------------------</td>
<td>------------------</td>
<td>--------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Singer (1994)</td>
<td>2 types of support groups (9 sessions of 2 hours): stress management group and a information and support group/ BDI &amp; STAI</td>
<td>RCT</td>
<td>I1 (n=7): Stress management group  I2: (n=8): Information and support group</td>
<td>Inclusion: I1: 3-66 mth  I2: 9-34 mth Follow-up: Immediately after intervention</td>
</tr>
<tr>
<td>Acorn (1995)</td>
<td>10 hours of education and support in groups/JCS, LSIZ &amp; RSE</td>
<td>Quasi-experimental (pretest-posttest)</td>
<td>I1 (n=11)/ I2 (n=8): Both groups received all 10 modules</td>
<td>Inclusion: 8 mth to 10 years Follow-up: 1 and 2 mth post intervention</td>
</tr>
<tr>
<td>Perlesz (1998)</td>
<td>Family therapy, different lengths of counselling/GHQ, POMS, SBS, SASSR &amp; FES</td>
<td>Quasi-experimental (pretest-posttest)</td>
<td>I (n=32): 1-22 sessions (mean 8.4 sessions). Time in therapy 1-18 mth (mean 9.5 mth).</td>
<td>Inclusion: 6-108 mth Follow-up: 12 &amp; 24 mth.</td>
</tr>
<tr>
<td>Brown (1999)</td>
<td>Support group (9-10×1.5-2 hours): on-site vs. phone groups led by social worker or psychology professionals/POMS, CBI, FAD</td>
<td>Quasi-experimental (pretest-posttest)</td>
<td>I1 (n=52): phone group  I2 (n=39): on-site groups</td>
<td>Inclusion: I1: 2.6 yrs since injury  I2: 1.9 yrs since injury Follow-up: 6 mth after intervention</td>
</tr>
<tr>
<td>Liamaki (2003)</td>
<td>Support group (six hourly sessions) providing education and possible sharing/PSS, WOC, GHQ &amp; CBI.</td>
<td>Quasi-experimental (pretest-posttest)</td>
<td>I (n=6): support group</td>
<td>Inclusion: 10.5 mth Follow-up: Immediately after intervention</td>
</tr>
<tr>
<td>Kreutzer (2009/2010)</td>
<td>Ten week program (BIFI) with interactive format addressing issues as communication, problem solving &amp; goal setting/FNQ, SOS, FAD, BSI &amp; SWLS</td>
<td>Quasi-experimental (pretest-posttest)</td>
<td>n=53/76 caregivers and survivors</td>
<td>Inclusion: 1.2-185 mth since injury (mean 30.2) Follow-up: 3 mth after intervention</td>
</tr>
<tr>
<td>Backhouse (2010)</td>
<td>CBT 16 x 2 hours including supportive psychotherapy, psychoeducation, stress management, problem-solving skills/ BSI &amp; BICSQ</td>
<td>RCT</td>
<td>I: CBT (n=20) C: waitlist (n=20)</td>
<td>Inclusion: 85% &lt;1 yrs since injury Follow-up: immediately &amp; 3 mth after</td>
</tr>
</tbody>
</table>

‘I’ refers to intervention/experimental group. ‘C’ refers to control group. ^ Only including parents of children with ABI. # The range refers to the number of months that the participants had carer for the TBI survivors as time since injury was not provided in the study. HADS: Hospital Anxiety and Depression Scale, GHQ: General Health Questionnaire, QRS: Questionnaire on Resources and Stress, MBI: Maslach Burnout Inventory, RSE: Rosenberg Self-esteem Scale, CED-S: Center for Epidemiologic studies Depression-Scale, SWLS: Satisfaction with Life Scale, PILL: Pennebaker Inventory for Limbic Languidness, CBS: Caregiver Burden Scale, POMS: Profile Of Mood States, CBI: Caregiver Burden Inventory, FAD: Family Assessment Device, PSS: Perceived Stress Scale, WOC: Ways Of Coping, BIFI: Brain Injury Family Intervention, FNQ: Family Needs Questionnaire, SOS: Services Obstacles Scale, BSI: Brief Symptom Inventory, BICSQ: Brain Injury Coping Skills Questionnaire.
Table 2: Characteristics of the relatives and the patients retrieved at baseline

<table>
<thead>
<tr>
<th>Characteristics of the relatives</th>
<th>Intervention group (n= 39)</th>
<th>Control group (n=47)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (80%)</td>
<td>32 (69%)</td>
<td>0.211</td>
</tr>
<tr>
<td>Cohabitant at time of injury</td>
<td>23 (59%)</td>
<td>28 (58%)</td>
<td>0.820</td>
</tr>
<tr>
<td>Working at time of injury (age 16 to 66)</td>
<td>34 (87%)</td>
<td>40 (83%)</td>
<td>0.683</td>
</tr>
<tr>
<td>Relationship</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse</td>
<td>8 (20%)</td>
<td>21 (44%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Parent</td>
<td>24 (61%)</td>
<td>13 (27%)</td>
<td></td>
</tr>
<tr>
<td>Sibling</td>
<td>1 (3%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td>5 (13%)</td>
<td>8 (17%)</td>
<td></td>
</tr>
<tr>
<td>Boy/girlfriend</td>
<td>0 (0%)</td>
<td>3 (6%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (3%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>Very satisfied</td>
<td></td>
<td></td>
</tr>
<tr>
<td>People to talk with about personal matters</td>
<td>82%</td>
<td>80%</td>
<td>0.855</td>
</tr>
<tr>
<td>Life events</td>
<td>Last year</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 (0-2)</td>
<td>1 (0-4)</td>
<td>0.434</td>
</tr>
<tr>
<td></td>
<td>Entire life</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (0-5)</td>
<td>2 (0-5)</td>
<td>0.651</td>
</tr>
<tr>
<td>Completion of questionnaires</td>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
<td></td>
</tr>
<tr>
<td>T1: NICU, days after injury</td>
<td>16 ± 6 (5-32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2: Sub-acute rehab, days after injury</td>
<td>24 ± 8 (11-41)</td>
<td>35 ± 18 (9-77)</td>
<td>0.001</td>
</tr>
<tr>
<td>Characteristics of the patients</td>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31 (80%)</td>
<td>32 (68%)</td>
<td>0.145</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>31 (80%)</td>
<td>31 (66%)</td>
<td>0.211</td>
</tr>
<tr>
<td>Clinical status at adm. to rehabilitation</td>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
<td></td>
</tr>
<tr>
<td>Admision, number of days after injury</td>
<td>17 ± 6 (7-34)</td>
<td>24 ± 16 (8-68)</td>
<td>0.013</td>
</tr>
<tr>
<td>Age</td>
<td>31.35 ± 17.02 (4-71)</td>
<td>45.51 ± 19.62 (1-82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>10.44 ± 2.96 (4-15)</td>
<td>11.05 ± 3.25 (5-15)</td>
<td>0.402</td>
</tr>
<tr>
<td>Early Functional Abilities</td>
<td>42.47 ± 17.42 (23-90)</td>
<td>44.80 ± 19.81 (22-91)</td>
<td>0.784</td>
</tr>
<tr>
<td>Functional Independence Measure</td>
<td>22.11 ± 12.06 (18-74)</td>
<td>24.36 ± 13.82 (18-68)</td>
<td>0.451</td>
</tr>
<tr>
<td>Rancho Los Amigo</td>
<td>3.86 ± 1.68 (2-8)</td>
<td>4.00 ± 1.39 (2-7)</td>
<td>0.805</td>
</tr>
<tr>
<td>Injury Severity Scale</td>
<td>34.90 ± 10.94 (25-66)</td>
<td>28.58 ± 7.09 (10-43)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*p-values from student's t-test for continuous data, from Chi-square tests (or Fisher's exact test) for categorical characteristics and Mann-Whitney for ordinal data.
Figure 1: Procedure of inclusion

T1: The acute phase

Control

T2: The sub-acute phase

n=47

n=39

n=46

Intervention
### Table 3: Overview of intervention

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Objective</th>
<th>Expected benefits</th>
<th>Examples of topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional support</td>
<td>Identifying progress in the patient’s condition and emotional strength in the relative by listening and instilling hope</td>
<td>Regain hope in the future and indirectly causing emotional relief</td>
<td>Handling each day with a family member in hospital</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feelings of isolation, guilt and distress.</td>
</tr>
<tr>
<td>Psycho-education</td>
<td>Improve understanding of the patient’s condition by providing information</td>
<td>Reduce anxiety and general symptoms of distress</td>
<td>Treatment in the acute setting; monitoring of intracranial pressure, decompressive surgery etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>The first period of unconsciousness, vegetative and minimally conscious state</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Post-traumatic amnesia, consequences and recovery from brain injury</td>
</tr>
</tbody>
</table>
Table 4: The emotional condition of the relatives at T1 and T2

<table>
<thead>
<tr>
<th></th>
<th>The intervention group</th>
<th>The control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1 (n=39)</td>
<td>T2 (n=39)</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT</td>
<td>28.38 ± 19.62</td>
<td>0-75</td>
</tr>
<tr>
<td>SF</td>
<td>53.62 ± 30.05</td>
<td>0-100</td>
</tr>
<tr>
<td>MH</td>
<td>33.58 ± 17.61</td>
<td>4-76</td>
</tr>
<tr>
<td>RE</td>
<td>26.01 ± 31.38</td>
<td>0-100</td>
</tr>
<tr>
<td>VAS</td>
<td>6.40 ± 3.01</td>
<td>1-10</td>
</tr>
<tr>
<td>Emotional distress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCL-90-R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>64.08 ± 7.75</td>
<td>45-80</td>
</tr>
<tr>
<td>Depression</td>
<td>64.00 ± 6.94</td>
<td>47-80</td>
</tr>
</tbody>
</table>

*Significant decrease from T1 to T2, p=0.043, Cohen’s d=0.40. Δ Significant decrease from T1 to T2, p=0.010, Cohen’s d=0.30. △ Significant difference comparing the groups at T2, p=0.05, Cohen’s d=0.39. SF-36: Short Form 36, VT: Vitality, SF: Social Function, MH: Mental Health, RE: Role Emotional, VAS: Visual Analogue Scale. SCL-90-R: Symptom Checklist Revised.
Table 5: Raw and adjusted means for emotional distress and quality of life at T2

<table>
<thead>
<tr>
<th>Quality of life</th>
<th>The intervention group</th>
<th>The control group</th>
<th>p-values*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Raw mean</td>
<td>Adjusted mean*</td>
<td>Raw mean</td>
</tr>
<tr>
<td>VT (n=59)</td>
<td>30.86</td>
<td>34.34</td>
<td>38.00</td>
</tr>
<tr>
<td>SF (n=61)</td>
<td>47.17</td>
<td>53.24</td>
<td>62.50</td>
</tr>
<tr>
<td>MH (n=58)</td>
<td>32.87</td>
<td>37.05</td>
<td>32.76</td>
</tr>
<tr>
<td>RE (n=47)</td>
<td>15.94</td>
<td>22.45</td>
<td>31.94</td>
</tr>
<tr>
<td>VAS (n=59)</td>
<td>6.46</td>
<td>6.81</td>
<td>6.38</td>
</tr>
<tr>
<td>Emotional distress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety (n=61)</td>
<td>61.73</td>
<td>59.46</td>
<td>62.03</td>
</tr>
<tr>
<td>Depression (n=61)</td>
<td>62.17</td>
<td>61.02</td>
<td>61.90</td>
</tr>
</tbody>
</table>

* Adjusted for the relative’s gender and relationship to the patient (spouse vs. other), the patient’s age, number of days after injury that questionnaire was completed and the patient’s the injury severity score. * Unadjusted p-values calculated from independent t-tests. VAS: Visual Analogue Scale
Norup, A., Petersen, J., Siert. L. & Mortensen, E. L.

Relatives of patients with severe brain injury: Growth curve analysis of the first year after injury.

*In manuscript.*
Relatives of Patients with Severe Brain Injury: Growth Curve Analysis of the First Year after Injury

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ABSTRACT

Objective: To investigate changes in the emotional condition of relatives of patients with a severe brain injury during the first year after injury.

Study design: A prospective longitudinal study investigating emotional distress in relatives of patients with severe brain injury at four time points during the first year after injury.

Participants: 88 relatives of patients with severe brain injury admitted for intensive sub-acute rehabilitation in hospital.

Main outcome measures: Outcome measures were the anxiety and depression scales from the Symptom Checklist-90-Revised (SCL-90-R).

Data analysis: Latent variable growth curve models were employed.

Results: The development in anxiety and depression was described by two different trajectories. Anxiety symptoms showed a steeper decline during the first three months and a continued decrease at a slower pace during the rest of the year. Depression symptoms decreased significantly over the first six months, and the decline continued the last six months, although not significantly. The initial level of anxiety and depression were associated with characteristics related to the patient, but over time this association disappeared.

Conclusion: Anxiety is associated with the immediate experience after the injury, and the recovery process is faster than the trajectory seen for depression.

Keywords: Relatives, severe brain injury, anxiety, depression, growth curve modeling, and early rehabilitation.
INTRODUCTION

The condition of families living with traumatic brain injury (TBI) has been investigated thoroughly the last decades (e.g., Boschen, Gargaro, Gan, Gerber, & Brandys, 2007; Gan, Campbell, Gemeinhardt, & McFadden, 2006; Kreutzer, Marwitz, & Kepler, 1992; Lezak, 1978; Turner et al., 2010). Most research conducted has been cross-sectional in nature and have underlined the difficult and distressing situations of these families at different points in time after the injury (Livingston, Brooks, & Bond, 1985a; Novack, Bergquist, Bennett, & Gouvier, 1991; Oddy, 1985; Pielmaier, Walder, Rebetez, & Maercker, 2011; Thomsen, 1983). However, it is evident that the condition of the relatives changes over time as the condition of the patient improves and the family adjusts to the changed situation of life.

Earlier studies have investigated the condition of relatives over time and have reported specific frequencies of distress, anxiety and depression at different time points (Brooks, Campsie, Symington, Beattie, & McKinlay, 1986; Livingston, Brooks, & Bond, 1985b; McKinlay, Brooks, Bond, Martinage, & Marshall, 1981; Novack et al., 1991; Oddy, 1985; Turner et al., 2010). Moreover, the authors have investigated correlations between characteristics of the patient and relative at the specific time points. However, trajectories of changes in emotional distress have not been described previously.

Predictors of the long-term condition of the relatives have been identified such as neurobehavioral changes and emotional changes in the patient. Recent work has examined predictors of emotional wellbeing of relatives in early rehabilitation and found predictors related to the patient’s physical condition to be important (Norup, Siert, & Mortensen E.L., 2010; Norup, Kristensen, Siert, Poulsen, & Mortensen, 2011; Pielmaier et al., 2011), but change in the condition of the relatives during the process of rehabilitation has not been investigated further. This is of interest in order to reduce sick
leave, early retirement and improve the long-term wellbeing and quality of life of both the patient and the relatives.

To our knowledge, only three longitudinal studies have been conducted using techniques such as path analysis, structural equation modeling and latent growth curve modeling, when investigating the relationship between the patient and the relative’s condition (Schonberger, Ponsford, Olver, & Ponsford, 2010; Berry, Elliott, Grant, Edwards, & Fine, 2012; Winstanley, Simpson, Tate, & Myles, 2006). Winstanley et al. found that family functioning decreased, and that distress experienced by relatives was not a direct result of the neurobehavioral deficits since the effect was mediated by the degree of community participation achieved by the individual with the TBI (Winstanley et al., 2006).

Schönberger et al. tested a model of the relationship between neurobehavioral status, family functioning and relatives’ emotional status at two and five years follow-up and found that behavioral and mood changes in the injured person at a two year follow-up predicted low family functioning and the presence of clinically significant levels of anxiety in the relative. Furthermore, anxiety and depression symptoms at the two year follow-up predicted the same symptoms as well as poor family functioning at a five year follow-up. The authors conclude that there seemed to be a reciprocal relationship between family functioning and anxiety and depression in relatives (Schonberger et al., 2010).

A very recent study investigated effects of a problem-solving training administered to family caregivers of patients with severe disabilities (amongst others TBI) employing a latent growth model framework (Berry et al., 2012). The study found that the training significantly improved problem-solving skills and lessened depression. The study was conducted in the chronic phase and on average the caregiver had cared for their family member more than ten years.
No longitudinal studies have explored the changes in the emotional condition during the early phases of rehabilitation or possible predictors of change. When exploring changes over time growth curve analyses allows for longitudinal analyses at both patient and group level, as Jackson (2010) pointed out a few years ago (Jackson, 2010). Moreover, growth curve analyses enables us to model the relationship between outcome and time with more than one parameter, taking possible changes in this relationship into account. Another benefit of this type of analysis is the inclusion of cases with missing data.

For these reasons, we chose this framework for our analyses in the current study.

The present study aimed at investigating:

1) Changes in the emotional condition of the relatives during the first year after the patient’s injury

2) Predictors of changes in the emotional condition of the relatives during the first year after injury.

METHODS & MEASURES

Participant recruitment

Participants were patients and relatives recruited at admission to sub-acute rehabilitation¹ and the patients had to fulfill the following criteria:

1: Adults: GCS 3-9

¹ Half of the participants were included in the acute phase, but fulfilled the same criteria as the participants recruited in the sub-acute phase. The sample recruited earlier has been described in detail in an earlier study (Norup, Welling, Qvist, Siert, & Mortensen, 2012).
Children < 5 years: GCS 3 – 9

Children 5 – 15 years: GCS 3 – 11

2: Patients with GCS > 9 with severe focal neurological deficits such as aphasia, hemiparesis or agitation

3: Patients with severe cognitive deficits as well as paresis or agitation

When patients were admitted, the relatives were asked to participate in the study. Consent to participate was obtained by a neuropsychologist. If more than one relative were present at time of inclusion, the family decided who should participate. Relatives who did not speak Danish, had a psychiatric diagnosis, or a progressive brain disease were excluded from the study.

The condition of the relatives

Anxiety and depression: The relatives’ symptoms of anxiety and depression were evaluated by the relevant scales of Symptom Checklst-90-Revised (SCL-90-R), a self-report checklist designed to reflect the symptom pattern and level of distress. Each item was scored on a scale of 0 (‘not at all’) to 4 (‘extremely’) indicating the degree of distress for this particular item. The respondents were asked to answer each item according to their condition during the past seven days (Bech, Olsen, Poulsen, Mortensen, & Munk, 2006). The scales have been validated in Danish (Olsen, Mortensen, & Bech, 2004), and a population study revealed high alpha coefficients on all the SCL subscales and in particular for the depression and anxiety scales used in this study ($\alpha=0.91$ and $\alpha=0.86$ respectively) (Olsen, Mortensen, & Bech, 2006).
Social support: Questions regarding the relatives’ social support included a question about how often they had contact with different people (parents, children, other family, colleagues after work, neighbors, childhood friends, other friends, professional caregiver), and how satisfied the relative was with this contact (‘very’, ‘fairly’ or ‘not at all’ satisfied). The relatives also reported how many people they were able to share very personal matters with. The questions were modified versions of the questions used in the Copenhagen City Heart Study (Sethi et al., 2001) and were administered at the baseline assessment.

Life events: Questions about traumatic life events over the past year included five work-related questions (unemployment, not being promoted, conflicts with colleagues, superiors or subordinates) and seven questions related to events in the family (children severely ill, severe educational problems for children, severe conflicts with grown-up children, severe problems in marriage, own severe illness, severe illness or death among relatives, severe economical problems). These questions were also modified from the Copenhagen City Heart Study (Sethi et al., 2001) and were administered at baseline. We counted the total amount of traumatic events in the past year.

The condition of the patients

As a standard procedure during admission, relevant data were collected regarding the patient’s condition: severity of injury, level of consciousness and function. Assessments were conducted by the relevant professionals at admission and discharge.

Severity of injury: The severity of injury was assessed by a well-known and validated scale: The Glasgow Coma Scale (Teasdale & Jennett, 1974). GCS is scored from 3 to 15. Patients with scores less than nine are considered to be in coma, and patients with scores of 15 are able to follow
commands, are fully oriented, and have spontaneous eye opening. According to criteria for injury severity, GCS scores of eight or less are classified as severe injuries.

The treating physician assessed GCS at admission to sub-acute rehabilitation.

**Level of consciousness:** Rancho Los Amigos (RLA) score (Hagen, Malkmus, & Durham, 1972; Hagen, 1984) was assessed by a neuropsychologist at admission and at discharge. This score ranges from level one, which describes a comatose condition with no observable response, to level eight, which is a condition with purposeful and appropriate responses. This scale was designed for use on patients with a traumatic brain injury.

**Functional level:** The patient’s functional level at admission was assessed with the Early Functional Abilities (EFA) (Heck G., Schmidt T., & Steiger-Bachler G., 2000) and the Functional Independence Measure (FIM™) (Keith, Granger, Hamilton, & Sherwin, 1987).

The EFA is an assessment tool for patients with severe cerebral impairments in the early neurological rehabilitation stage, which describes clinically observable changes in a patient’s early functional abilities. The EFA scale contains 20 items and assesses early basic abilities related to four functional areas: vegetative, face and oral, sensory-motor and sensory cognitive functions. Each item is rated on a five-point scale from “no function” to “practically full function”. The total score is the sum of the item scores ranging from 20 to a maximum of 100. High scores indicate better functional ability.

The FIM is an 18-item rating scale assessing activities of daily living: self-care, bowel and bladder management, mobility, communication, cognition, and psychosocial adjustment. Each item is rated on a seven-point scale from “total assistance” to “complete independence”. A total FIM score ranges from 18 to 126 with higher scores indicating greater independence. The FIM scale has been
shown to be valid and reliable for measuring functional outcome after TBI (Cohen & Marino, 2000; Dodds, Martin, Stolov, & Deyo, 1993).

Both FIM and EFA scores were obtained by physio- and occupational therapists at admission and discharge.

**Data analysis**

Descriptive analyses of data were presented as percentages and medians. To investigate whether anxiety and depression were similar for relatives of TBI vs. NTBI patients, we conducted independent samples t-tests for each of the four time point.

Latent growth curve models were used to describe the development in anxiety and depression experienced by the relatives during the first year. The latent growth curve model for each latent variable (anxiety and depression) consisted of two components: 1) A component modeling the latent variable by the items of the SCL; and 2) a component that models the development in the latent variable over time. The development in the latent variables are modeled by random coefficients; one describing the intercept of the growth curve (initial level at admission), and the slopes describing the development in the latent variable.

Anxiety and depression were modeled separately. For each of the outcome measures we conducted the following analysis:

*Initial exploratory analyses:* To investigate whether the outcome were measured similarly for the four time points by the items, we did an exploratory item response analysis at each of the four time points. Moreover, to validate whether the time development for each of the items were similar, we made a growth curve model for each of the items. The time points were fixed. We fixed these at 0, 3, 6 and 12, as we chose to set the admission to the sub-acute rehabilitation unit to 0. Discharge was
fixed at 3 months based on the median number of days that the patient stayed in hospital. Relatives were assessed three months after discharge, so the third assessment was fixed at 6 months. The last assessment was one year after injury, and so this loading was fixed at 12.

To evaluate the development over time of the latent depression and anxiety outcome variable, we fitted a latent growth curve model without covariates modeling piecewise linear slope parameters.

**Final models:** Subsequently, two separate models were fitted one with the covariates describing characteristics of the patient (age, GCS at admission, EFA at admission/discharge and RLA at admission/discharge) and one with covariates related to the relatives (gender, relationship to the patient, social contacts and experienced life events). EFA as well as RLA were included as time-varying covariates. The covariates were assumed to affect both the level as well as the slope of the curve. In these models, missing data were modeled by missing at random (MAR).

Model fit was assessed with chi-square, root mean square error of approximation (RMSEA) and comparative fit index (CFI). Smaller values of chi-square and RMSEA (particularly values below .06) indicate better model fit. Values of CFI that are close to 1 indicate better fit.

The statistical software used was Mplus version 5.1 developed by Muthén and Muthén (Muthén & Munthén, 2007). SPSS version 19 was used to conduct the standard analyses.

**RESULTS**

**Demographics**

*Patients: The majority of the patients were male (72.7%), and the sample consisted of 64 patients (72.7%) with a traumatic brain injury and 24 (27.3%) with a non-traumatic brain injury (For further
sample characteristics see Table 1). The non-traumatic brain injuries were caused by cardiac arrest (4.5%), spontaneous intracranial hemorrhage (3.4%), subarachnoid hemorrhage (5.7%), brain tumor (2.3%), meningitis (1.1%) or major cerebral infarction (10.2%). The patients were admitted to rehabilitation about three weeks after injury (Median= 18 days; IQR=13-22.75).

Relatives: The sample of relatives consisted primarily of females (73.9%) and the majority of the relatives were working at time of injury (85.2%). About half of the relatives (59.1%) were living with the patient, when he or she was injured. Most of the relatives were spouses (33.0%) or parents (43.2%), and the remainders were siblings (3.4%), children (14.8%) or boy-or girlfriends/partners not cohabiting (3.4%). In two cases (2.3%) the relatives included were aunts of the patients, as they were the closest relatives.

Insert Table 1

Administration: The relatives completed the questionnaire four times; at admission to sub-acute rehabilitation (T1), at discharge from sub-acute rehabilitation (T2), three months after discharge (T3) and one year after injury (T4). Table 2 shows the number of days after injury that the questionnaires were completed and mean scores on the two outcome measures.

Insert Table 2

Modeling the latent variables
First, we examined the comparability of relatives of patients with TBI vs. NTBI using independent samples t-tests. Anxiety and depression scores of the two groups of relatives were compared, and no significant differences were found at any of the four time points. Consequently, the total sample was treated as being homogeneous in the following analyses.

Mean raw scores at the four different time points are shown in Table 2 for both anxiety and depression.

**Depression:** Preliminary investigations of data showed that on the later assessments (T3 and T4), several items had only one or two observations in the higher categories. In order to be able to fit the model, we chose to collapse categories ‘A lot’ and ‘Extremely’ on all items. The development over time for each of the items and the raw scores are depicted in Figure 1.

*Insert Figure 1*

Descriptive investigations of the changes in scores on the 13 items over time showed that all the items seemed to develop uniformly over time (see Figure 1), except for the item 12 ‘Thoughts of ending your life’, where no decrease was observed. Further, the initial explorative item response analyses showed that the discrimination and location parameters coefficients were similar over time, once again with the exception of item 12. After these initial analyses, we chose to exclude this item. After removing item 12, we found that the discrimination parameters were similar among items, and consequently the component of the model measuring the latent variable were modeled by Rasch models.
Initial descriptive analysis of raw scores over time (Table 2), the plotted mean raw scores against time (Figure 1), and modeling the latent growth curve model without covariates (Table 3) showed a steeper decline from T1 to T3 (s1) than from T3 to T4 (s2), and consequently we chose to model the development over time as a piecewise linear function ($\chi^2=124.772$, $p<0.000$, RMSEA=0.130, CFI=0.900). S1, describing the development in depression from the patient’s admission to sub-acute rehabilitation (T1) to three months after discharge (T3), had the steepest decline ($\beta=-0.074$, $p<0.000$). S2, the decline from three months after discharge (T3) to one year after injury (T4), was not significantly different from zero ($\beta =0.014$, $p=0.338$) (Table 3).

Insert Table 3

Fitting the full latent growth curve model with covariates, we found that relatives of patients with higher level of consciousness reported less depression scores initially ($p=0.019$) (Table 3). Patient’s level of consciousness seemed to have some effect on slope 1 ($p=0.160$) indicating that relatives of patients with a higher level of consciousness experienced a steeper decrease in depression scores, but this effect disappeared on slope 2 ($p=0.995$). We also found that relatives reporting having more personal contacts had a steeper decrease in depression scores at s1 ($p=0.010$) indicating that relatives with a better social network recovered faster from the symptoms of depression (See Table 3).

Anxiety: Preliminary examinations of data showed that many items had few observations on the later assessments (T3 and T4), so we chose to collapse categories three and four on the rest of the
items to be able to fit the model. When investigating frequencies of observations in each category, we found that the items “Feeling that familiar things are strange and unreal”, “Trembling” and “ Spells of terror and panic” had low scores on all assessments. Consequently, these items were dichotomized. The development over time for each of the items and the raw scores are depicted in Figure 2.

*Insert Figure 2*

We investigated the distribution of scores on each item over time and found that the 11 items had similar development over time (Figure 2). Moreover, the initial explorative item response analyses showed that the discrimination and the location parameters were similar over time. Consequently, the component of the model measuring the latent variable was modeled by Rasch models.

Further, initial descriptive analysis (Table 2), the plotted mean raw scores over time (Figure 2), and modeling the latent growth curve without covariates showed (Table 3) that the steepest decline was from T1 to T2, so we constructed a baseline model describing piecewise growth, and the model had a good fit ($\chi^2=67.12$, $p=0.036$, RMSEA=0.067, CFI=0.971).

As shown in Table 3, both slopes were significantly different from zero. The steepest decline was found during the patient’s hospitalization ($\beta=-0.154$, $p<0.000$). After the patients’ discharge, the decline continued, but not as steep as during the first three months ($\beta=-0.055$, $p<0.000$).

When fitting the full latent growth curve model including covariates, we found that relatives of older patients experienced less anxiety initially ($p=0.052$). We also found that the decline in anxiety
was steeper in relatives of younger patients (p=0.014), but this effect disappeared at slope 2 (p=0.247) (Table 3).

Once again, we found that relatives of patients with a higher level of consciousness experienced less anxiety initially (p=0.066). However, this finding was only borderline significant. Patient’s level of consciousness also had a borderline significant effect on slope 1 (p=0.056) indicating that relatives of patients with a higher level of consciousness experienced a steeper decrease in anxiety scores. But this effect disappeared completely on slope 2 (p=0.099).

Relatives who had experienced more significant life events during the last year scored significantly higher on anxiety initially (p=0.002) and had a steeper decline during the first three months (p<0.000). After discharge, the curve leveled off, and relatives with less life events had a steeper curve (p=0.002).

**Dropout analysis**: We investigated if relatives dropping out of the study had higher anxiety and depression scores initially. We compared the baseline scores of relatives completing vs. not completing at T3 (anxiety; t=0.299, p=0.766, depression; t=-0.067, p=0.946) and T4 (anxiety; t=0.138, p=0.890; depression t=0.864, p=0.390). Thus relatives, not completing questionnaires, did not have higher anxiety or depression scores at baseline. We also wanted to investigate if dropout was associated with the condition of the patient and compared the condition of patients of dropouts and non-dropouts. Patients of relatives not returning the questionnaire at discharge had significantly lower level of function (FIM; t=-2.126, p=0.037) (e.g. Figure 3).
The condition of the patients was not assessed three months after discharge, but we used the assessment made at discharge and found that patients of relatives, not completing the questionnaire three months after discharge, had a significantly lower level of consciousness (RLA; t=-2.503, p=0.020) at discharge. At T4, one year after injury, the same pattern was observed; the patients had significantly lower RLA scores (t=-2.248, p=0.032) in the group of relatives not completing the questionnaire.

DISCUSSION

Changes in the emotional condition of the relatives during the first year

The present study found an improvement in both anxiety and depression in the 12 months study period and identified the most substantial improvement during the first six months.

Our analysis revealed different trajectories for anxiety and depression. Anxiety had a significant decrease during the first three months, and a less steep decrease during the last nine months. The decrease found in depression was significant during the first six months, and the decline continued, but was not significantly different from zero the last six months. Symptoms of depression remained for a longer period than anxiety. It seemed that symptoms of anxiety were a more immediate reaction, which also recovered faster. Other authors have found that symptoms of anxiety wear off faster than depression in a sample of caregivers (e.g. Turner et al., 2010). This finding is not surprising, as anxiety is normally associated with an acute reaction to a stressful or traumatic event, whereas depression is a more general and often long-term condition. The anxiety that relatives experience is most likely associated with the uncertainty about the patient’s condition in the early
phases of rehabilitation. When the condition of the patient is stabilized, the uncertainty passes, but worries about the future emerges, as deficits after brain injury appears, and the symptoms of depression are maintained.

**Predictors of changes in the emotional condition of the relatives**

Relatives of patients with a lower level of consciousness experienced more depression and anxiety initially. This finding is consistent with previous cross-sectional findings (Norup et al., 2010; Norup, Welling, Qvist, Siert, & Mortensen, 2012; Pielmaier et al., 2011). Our results also confirmed results from cross-sectional studies showing how relatives of younger patients experience more anxiety (Pochard et al., 2001; Pochard et al., 2005). Better social network seemed to increase the recovery process of depression, as relatives having more personal contacts experienced a steeper decrease in depression at slope 1. Previously cross-sectional studies have also found that more perceived social support was related to lower levels of depression (Pelletier, Alfano, & Fink, 1994) and emotional distress (Sander, High, Jr., Hannay, & Sherer, 1997).

Relatives who experienced more serious life events the last year had higher initial anxiety scores. An association between traumatic life events and high scores on the anxiety scale had been reported in a normal population (Olsen et al., 2006), but interestingly, these relatives had a more rapid decline in anxiety scores. Most likely the distress of these relatives reflects both life events and the condition of the patients, and this may influence the fall in anxiety scores.

Longitudinal studies conducted by other authors (Schonberger et al., 2010; Winstanley et al., 2006) showed that long-term distress in relatives was predicted by family function and neurobehavioral changes in the patient, and that caregivers are likely to benefit from problem-solving training (Berry et al., 2012). No previous longitudinal studies have investigated predictors in the early phases of
rehabilitation, and we found predictors related to the patient (age and level of consciousness) to have an effect on anxiety and depression. Interestingly, the effect was significant initially, but disappeared at slope 2. This suggests that factors related to the patient directly affect the condition of the relatives initially, and that later on in the process personal characteristics related to the relative are more important.

**Dropout analysis:** We expected that relatives dropping out were experiencing more anxiety and depression at baseline (e.g. dropouts to be characterized by greater emotional distress), but this was not the case. Dropout analysis revealed the relatives dropping out of the study were relatives of patients with lower level of function and consciousness. These relatives may not be completing the questionnaire because of lack of time and energy being tied up with practical tasks. Some relatives may also refuse to participate further because due to a disappointing outcome of the rehabilitation.

**Clinical implications**

Our analyses indicated that distress experienced by family members of brain injury survivors persists during the first year, in particular symptoms of depression. It is important that professionals working with the families are aware of the draining situations of relatives of brain injury survivors. The emotional condition of the relatives might very well influence the collaboration between professionals and the families.

Our results also indicated that families of younger patients and patients with a lower level of consciousness experienced more symptoms of anxiety and depression in the early phases of rehabilitation. This is important for professionals to recognize, as these families might need more
psychological support initially. Moreover, our results indicate that social support is associated with faster recovery from depression, and professionals working in the rehabilitation setting should encourage families to use their social network whenever possible.

Our analyses of attrition emphasized how clinicians should pay attention to relatives not being able to meet appointments, complete assessments and so on, as they may very well be families needing professional support.

Methodological limitations and implications for further research

A limitation of this study is the small sample size, which only allowed analyses of single predictors of changes over time. This was due to the large drop out at the later assessment. A larger sample would have allowed a model including all the associated predictor variables, but this was not possible due to lack of statistical power.

Future research should employ personality and coping measures later in the process of rehabilitation as well as characteristics related to the patient in order to investigate the effect of different types of covariates over time.

CONCLUSION

Two different trajectories were found in the development of anxiety and depression in relatives of patients with severe brain injury during the first year after injury. Anxiety symptoms decreased faster than symptoms of depression. Moreover, the initial level of symptoms and decrease in both
anxiety and depression were related to the characteristics of the patient, but this association disappeared over time.
Reference List


Ref Type: Unpublished Work


Table 1: Sample characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency/Median</th>
<th>Mean ± SD</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (n=88)</td>
<td>Male</td>
<td>72.7%</td>
<td></td>
</tr>
<tr>
<td>Injury (n=88)</td>
<td>Traumatic</td>
<td>72.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-traumatic</td>
<td>27.3%</td>
<td></td>
</tr>
<tr>
<td>Age (n=88)</td>
<td></td>
<td></td>
<td>39.19 ± 19.65</td>
</tr>
<tr>
<td>ISS (n=63)</td>
<td></td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>GCS adm. (n=79)</td>
<td></td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>EFA (n=76)</td>
<td></td>
<td></td>
<td>38.50</td>
</tr>
<tr>
<td>FIM (n=76)</td>
<td></td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>RLA (n=59)</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Adm. rehab. days after injury (n=80)</td>
<td></td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>LOS, days (n=68)</td>
<td></td>
<td></td>
<td>113.50</td>
</tr>
<tr>
<td>Gender (n=88)</td>
<td>Female</td>
<td>73.9%</td>
<td></td>
</tr>
<tr>
<td>Relationship (n=88)</td>
<td>Spouse</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parent</td>
<td>43.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>14.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Siblings</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boy-/girlfriends</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Occupational status (n=88)</td>
<td>Full time work</td>
<td>85.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pension</td>
<td>10.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>4.5%</td>
<td></td>
</tr>
<tr>
<td>Cohabitant status (n=88)</td>
<td>Cohabiting</td>
<td>59.1%</td>
<td></td>
</tr>
<tr>
<td>Social support (n=39) *</td>
<td>Very satisfied</td>
<td>79.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fairly satisfied</td>
<td>20.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>People sharing</td>
<td>4</td>
<td>3.88 ± 1.69</td>
</tr>
<tr>
<td></td>
<td>personal matters</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life events (n=40) *</td>
<td>Last year</td>
<td>1</td>
<td>0.88 ± 1.02</td>
</tr>
<tr>
<td></td>
<td>Entire life</td>
<td>2</td>
<td>1.85 ± 1.44</td>
</tr>
</tbody>
</table>

* The questions regarding social support and life events were included in the data collection after starting the enrollment, therefore not all participants were asked to complete these questions.
Table 2: Completion of questionnaires; raw mean scores on the different time points.

<table>
<thead>
<tr>
<th>Time point</th>
<th>Completion of questionnaires (days after injury)</th>
<th>Depression (raw score)</th>
<th>Anxiety (raw score)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Mean ± SD</td>
<td>IQR</td>
</tr>
<tr>
<td>T1 (n=85)</td>
<td>27</td>
<td>29.82 ± 14.33</td>
<td>20-34</td>
</tr>
<tr>
<td>T2 (n=70)</td>
<td>141</td>
<td>139.53 ± 55.19</td>
<td>94.75-170.50</td>
</tr>
<tr>
<td>T3 (n=59)</td>
<td>224</td>
<td>226.10 ± 59.22</td>
<td>175-263</td>
</tr>
<tr>
<td>T4 (n=57)</td>
<td>389</td>
<td>396.30 ± 29.61</td>
<td>378.50-405.50</td>
</tr>
</tbody>
</table>

T1, Admission to TBI Unit; T2, Discharge from TBI-Unit; T3, 3 months after discharge; T4, 1 year after injury.
The lines illustrate the raw score on each item at the four different time points. The bold line indicates the estimated mean.
Table 3: Univariate analysis of predictor variables in the latent growth curve models

<table>
<thead>
<tr>
<th></th>
<th>Intercept</th>
<th>Slope 1</th>
<th>Slope 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>S.E.</td>
<td>p-value</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline model</td>
<td>---------------</td>
<td>Fixed---------------</td>
<td>-0.074</td>
</tr>
<tr>
<td>Patient age</td>
<td>-0.008</td>
<td>0.005</td>
<td>0.107</td>
</tr>
<tr>
<td>GCS adm</td>
<td>-0.031</td>
<td>0.026</td>
<td>0.246</td>
</tr>
<tr>
<td>EFA adm/dis</td>
<td>-0.001</td>
<td>0.005</td>
<td>0.823</td>
</tr>
<tr>
<td>RLA adm/dis</td>
<td>-0.0134</td>
<td>0.057</td>
<td>0.019</td>
</tr>
<tr>
<td>Gender</td>
<td>0.079</td>
<td>0.200</td>
<td>0.693</td>
</tr>
<tr>
<td>Spouse</td>
<td>0.199</td>
<td>0.180</td>
<td>0.268</td>
</tr>
<tr>
<td>Talk personal</td>
<td>-0.053</td>
<td>0.061</td>
<td>0.383</td>
</tr>
<tr>
<td>Life events year</td>
<td>0.040</td>
<td>0.110</td>
<td>0.717</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline model</td>
<td>---------------</td>
<td>Fixed---------------</td>
<td>-0.154</td>
</tr>
<tr>
<td>Patient age</td>
<td>-0.008</td>
<td>0.004</td>
<td>0.052</td>
</tr>
<tr>
<td>GCS adm</td>
<td>-0.033</td>
<td>0.026</td>
<td>0.286</td>
</tr>
<tr>
<td>EFA adm/dis</td>
<td>-0.001</td>
<td>0.005</td>
<td>0.867</td>
</tr>
<tr>
<td>RLA adm/dis</td>
<td>-0.115</td>
<td>0.063</td>
<td>0.066</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.121</td>
<td>0.179</td>
<td>0.500</td>
</tr>
<tr>
<td>Spouse</td>
<td>0.198</td>
<td>0.171</td>
<td>0.246</td>
</tr>
<tr>
<td>Talk personal</td>
<td>0.004</td>
<td>0.061</td>
<td>0.951</td>
</tr>
<tr>
<td>Life events year</td>
<td>0.280</td>
<td>0.092</td>
<td>0.002</td>
</tr>
</tbody>
</table>

In the depression model slope 1 is from admission to rehabilitation to three months after discharge, and slope 2 is from three months after discharge to one year after injury. In the anxiety model slope 1 is from admission to rehabilitation to discharge, and slope 2 is from discharge to one year after injury. The time-varying covariates EFA and RLA (admission and discharge) were included only at the relevant slope (EFA and RLA admission at slope 1, EFA and RLA discharge at slope 2).
Figure 2: Anxiety; raw scores on each item over time.

The lines illustrate the raw score on each item at the four different time points. The bold line indicates the estimated mean.
Figure 3: FIM scores at discharge; comparing relatives completing and not completing at T2.

The figure shows the FIM score at discharge in two groups of relatives. The number 0 indicates relatives not completing the questionnaire, and 1 indicates relatives completing the questionnaire at discharge.