Late cognitive and vocational outcome of traumatic brain injury:  
A neuropsychological follow-up study

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If our brains were so simple that we could understand them,
we would be so simple that we could not
(Anonymous)

To my family
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ABSTRACT

Traumatic brain injury (TBI) is caused by an external mechanical force causing damage to the head. Two thirds of major TBI’s are sustained in motor-vehicle accidents. The latest estimate of people currently living with disabilities resulting from TBI is at least 2% of the Finnish population. Poor employment outcomes following TBI have grave personal consequences for the mainly young and middle-aged population and cause significant financial and social burden to the society.

The main aim of this study was to investigate the very long-term cognitive and psychosocial sequelae of TBI in relation to vocational outcome. Neuropsychological data were retrospectively collected from 114 moderate to severe TBI patients who had been injured more than a decade ago in mostly motor-vehicle related accidents and referred to Kauniala Hospital’s out-patient clinic between 1978 and 1993. A subgroup of patients with preschool TBI were followed-up until midlife. The second follow-up with neuropsychological, neurological and psychosocial assessment was performed in 2001 at the Finnish Institute of Occupational Health. The patients' vocational outcome in young adulthood (N = 33) was compared to that of middle-age (N = 27). In addition, the late cognitive and neurobehavioural indicators of employment status were studied.

TBI severity at the acute stage as measured by the level or length of unconsciousness was not directly related to late cognitive or vocational outcome, nor was school performance. Intellectual capacity or memory performance did not unambiguously predict late vocational outcome although they were partly related to it. Complex performance speed, flexibility and strong sense of identity were found to be associated with positive long-term employment status. Between young adulthood and middle-age, 74% of the patients had no change in employment status. Patients working full-time also reported less neuropsychiatric symptoms than the patients not at work.

In conclusion, although moderate to severe TBI seems to cause some life-long deficits in cognitive performance, it is possible for a subgroup of patients with sufficient intellectual and social skills and lack of major neurobehavioural problems to live a normal productive life as assessed more than three decades post-injury. Interestingly, the patients who had entered work life in young adulthood continued working at middle-age. This highlights the importance of developing vocational rehabilitation and support services to escort young TBI patients into work life.
ABBREVIATIONS

ANOVA = analysis of variance
CT = computed tomography
DAI = diffuse axonal injury
EEG = electroencephalography
FTW = full-time work
GCS = Glasgow coma scale
GOS = Glasgow outcome scale
ICF = international classification of functioning
IQ = intelligence quotient
LOC = length of coma
MRI = magnetic resonance imaging
NGW = not at gainful work
NRS = Neurobehavioural Rating Scale
POMS = Profile of Mood States
PTA = posttraumatic amnesia
TBI = traumatic brain injury
WAIS-R = Wechsler Adult Intelligence Scale - Revised
WMS-R = Wechsler Memory Scale - Revised
LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following publications which are referred to in the text by their Roman numerals I-V:


INTRODUCTION

1. INTRODUCTION

The latest estimate of people currently living with disabilities resulting from traumatic brain injury (TBI) is at least 2% of the U.S. population (Millis & Wood, 2005), corresponding the estimated prevalence (2.3%) of people with TBI-related problems in Finland (Guideline, 2003). Thus traumatic brain injuries contribute to a substantial number of permanent disability annually. Poor employment outcomes following TBI represent a global health dilemma resulting in significant financial and social burden to the society. TBI has been recognized a major public health problem with grave personal consequences to the mainly young and middle-aged population (Engberg & Teasdale, 2004).

Employment outcome represents one of the best indicators of real world functioning (Sherer et al., 2002). Loss of employment potential has many personal consequences which can lead to loss of self-identity, autonomy and emotional well-being. Thus, the prediction of vocational outcome is important in many contexts including rehabilitation planning and the development of vocational support services (Ownsworth & McKenna, 2004).

In TBI patients, studies on the relationship between cognition as measured with neuropsychological tests and outcome have revealed reduced capacity for new learning and memory (Vilkki et al., 1988; Zec et al., 2001), slowed information and speed processing (Clifton et al., 1993; Girard et al., 1996) fluency and disruption in executive function (Atchison et al., 2004; Clifton et al., 1993; Hanks et al., 1999; Johnstone et al., 1999; Mathias et al., 2004; Vilkki et al., 1994). In addition, level of depression has been associated with vocational outcome (Franulic et al., 2004; Ryan et al., 1992), even more than 10 years later (Hoofien et al., 2001; Koponen et al., 2002).

Age at injury is a well-documented predictor of outcome in TBI (Anderson et al., 2000; Asikainen et al., 1996; Kriel et al., 1989). The findings suggest that children sustaining severe TBI in early childhood may be particularly at risk for residual problems post-injury (Levin et al., 1993; Taylor & Alden, 1997).

In a TBI population, tracking down patients post injury becomes more challenging year after year which greatly limits the number of long-term follow-up studies. Very few studies have followed children with TBI until adulthood. Klonoff et al. (Klonoff et al., 1993) found in their 23 year follow up of 159 individuals with mostly (90%) mild head injuries that subjective sequelae was reported by 31% of the sample. The long-term outcome was related to the extent of head injury, initial IQ and current measures of social adaptation.

In the present study we were interested in the very long-term cognitive and vocational outcome of moderate to severe TBI. Performance speed was focused on as it affects several types of cognitive aspects in work tasks. In addition, the clinical
and cognitive indicators of functional and vocational outcome of moderate to severe childhood TBI were investigated. We also wanted to study the stability of vocational outcome which is poorly known (Olver et al., 1996) between young adulthood and middle-age. Given that the average life expectancy of persons with severe TBI is several decades post-injury, very long-term follow-up studies are important both from epidemiological as well as rehabilitative and clinical points of view.
2. REVIEW OF THE LITERATURE

2.1. Traumatic brain injury (TBI)

2.1.1. Epidemiology

An operational definition of TBI stated in the Finnish Adult (≥ 15 years) TBI guidelines (2003) incorporates a verified history of trauma to the head (an external mechanical force causing damage to the head) followed by at least one of the following conditions 1) altered consciousness no matter how brief 2) any kind of memory loss before or after the trauma 3) alteration of mental functioning (eg. confusion, desorientation) in connection to the trauma or 4) temporary or permanent neurological deficit indicating local brain damage (Guideline, 2003).

In western countries injuries are the leading cause of death under the age of 45 years of which up to half are due to head injuries. On the other hand these account for most cases of permanent disability post-injury (Jennett, 1996). In the United States (U.S.), motor vehicle accidents cause most head injuries (50 %), followed by falls (20 %-30 %) and violence (15%; 7-45% depending on the population studied) (Millis & Wood, 2005; Smith et al., 1998). In Finland, falls account for 65 % and traffic accidents 20 % of all TBI cases treated in hospitals followed by 5 % caused by violence. At working age, however, traffic accidents are the leading cause of TBI. In Finland, about half of the TBI cases have been under the influence of alcohol at the time of injury and almost as many have a history of heavy alcohol use (Guideline, 2003).

Incidence reports in epidemiological studies vary depending on the inclusion criteria: are all grades of severity included or is the study limited to hospital admissions, are deaths counted etc. Reliable statistics are difficult to discover from routinely collected data (Jennett, 1996). Based on hospital admissions, the incidence in Finland during years 1991-2000 was 100 per 100 000 (Guideline, 2003). A review of the annual incidence figures in the U.S. found an acceptable estimate for a typical community of average rate of 200 per 100 000 (minimum in Maryland 132/100 000, maximum in Chicago 367/100 000) (Hillier et al., 1997). Rates reported in the United Kingdom (Jennett & MacMillan, 1981) and France (Tiret et al., 1990) are somewhat higher, 270-310/100 000 and 281/100 000, respectively.

In an epidemiological study carried out in south-western Sweden based on hospital admissions during a five-year period (1987-1991) the mean incidence rate of paediatric (0-17 years) TBI was 12/100 000 and mortality was 2.6/100 000. Traffic was the dominant external cause (60%), followed by falls (22%). At discharge, 48% suffered from functional impairment and 52% suffered from two or more impairments. It was concluded that although the incidence rate of TBI is low in Sweden
the mortality accounts for almost 70% of postneonatal accidental deaths in Sweden and causes permanent functional impairment in 6/100 000 cases every year (Emanuelson & v. Wendt, 1997).

2.1.2. Mechanisms of TBI

There are two major types of brain injuries: penetrating and closed. Both types involve primary mechanisms that occur at impact and secondary mechanisms, cascades of later effects (Smith et al., 1998). The patterns of injury are divided into focal and diffuse lesions and in many patients, the distribution of lesions is multi-focal (Asikainen, 2001). The TBI mechanisms are shown in Table 1 (Smith et al., 1998).

Diffuse axonal injury (DAI) is a very common lesion in TBI (Adams et al., 1989). Meythaler et al. (Meythaler et al., 2001) suggest that in the U.S., DAI is the predominant mechanism of injury in 40% to 50% of TBIs requiring hospital admission. A component of DAI is believed to be present in all motor vehicle crash related TBI cases where the patient has lost consciousness. The neuropathology of DAI in humans is characterized histologically by widespread damage to the axons of the brainstem, parasagittal white matter of the cerebral cortex, corpus callosum, and the gray-white matter junctions of the cerebral cortex (Meythaler et al., 2001). It is yet unclear which clinical, computed tomography (CT) and magnetic resonance imaging (MRI) constellations are related to neuropathologically defined DAI (Fork et al., 2005). The relationship to neuropsychological complications is not clear, although several studies suggest that DAI may be responsible for the lion’s share of the global cognitive deficits after TBI (Meythaler et al., 2001). Markers of DAI, such as generalized ventricular enlargement and corpus callosum and hippocampal atrophy have been associated with cognitive problems (Mathias et al., 2004; Vilkki et al., 1992). On the other hand, there is some evidence that traumatic DAI would result in mainly transient neuropsychological deficits in mild-to-moderate TBIs (Wallesch et al., 2001).

Table 1. TBI mechanisms (modified from Smith et al., 1998). 1 = Primary, 2 = Secondary.

<table>
<thead>
<tr>
<th>Focal</th>
<th>Diffuse</th>
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<tbody>
<tr>
<td>1. Contusion</td>
<td>1. DAI</td>
</tr>
<tr>
<td>1. Laceration</td>
<td>1. Haemorrhage</td>
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<tr>
<td>1. Depressed skull fracture</td>
<td>2. Increased ICP</td>
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<tr>
<td>1. Cavitation from PHI</td>
<td>2. Hydrocephalus</td>
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<tr>
<td>2. Haematoma</td>
<td>2. Neurochemical changes</td>
</tr>
<tr>
<td>2. Localized swelling</td>
<td>2. Generalized swelling</td>
</tr>
<tr>
<td>2. Infarction</td>
<td>2. Hypoxia/ischemia</td>
</tr>
<tr>
<td>2. Herniation</td>
<td>2. Herniation</td>
</tr>
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PHI = penetrating head injury  
DAI = diffuse axonal injury  
ICP = intracranial pressure
2.1.3. Defining TBI severity

Traumatic brain injury covers a wide range of severity, from patients dying before they are admitted to the hospital to those with so mild brain injuries that they never attend the health care system. In between are the patients in coma, either related to TBI or secondary complications and those who are hospitalized for different periods of time and subsequently sent back home. In defining injury severity, changes in consciousness at the acute stage, usually at hospital admission are the basis of most approaches. The Glasgow Coma Scale (GCS), which separately assesses eye opening response (max score 4), best motor response (max score 6) and best verbal response (max score 5) is widely accepted (Teasdale & Jennett, 1974). The scores of different components are summed to an overall coma score ranging from 3-15, with this total coma score providing the basis for classification (Teasdale, 1976): GCS 3-8 severe injury, 9-12 moderate injury and 13-15 mild injury. Moderate to severe TBIs account for approximately 20% to 25% of all injuries (Hillier et al., 1997).

In less severe injuries (GCS 13-15), however, the GCS is insensitive. In these cases, the duration of amnesia after injury, post-traumatic amnesia (PTA) is a widely accepted index. An Extended Glasgow Coma Scale (GCS-E) (Nell et al., 2000) offers a combined tool to the initial assessment of especially milder TBI. The amnesia scale gives a numeric value between 7 (no amnesia) and 0 (amnesia greater than 3 months) to differing durations of amnesia, higher scores indicating better performance as in GCS. The Finnish Adult TBI Guideline (2003) recommends the use of both GCS and length of PTA. The following categories are suggested by the Guideline instead of the older ones in parenthesis (Russell & Smith, 1961): mild < 24 hours (< 1 hour), moderate 1-7 days (1-24 hours), severe > 7 days (1-7 days), very severe > 4 weeks. Duration of PTA measured prospectively with the Galveston Orientation Amnesia Test (GOAT) has been shown to be a useful variable in predicting functional outcome after TBI (Zafonte et al., 1997). PTA has been found to be only moderately correlated with coma length and patients with prolonged PTA (> 7 days) have shown more extensive brain damage on MRI and more neuropsychological impairment in comparison with a group with short coma and PTA (Wilson et al., 1994). In paediatric TBI the PTA is difficult to reliably reconstruct post-injury, and length of coma (cut-off point for severe injury 24 hours) has been used as a severity indicator (Hennes et al., 1988).
2.2. Late cognitive and psychosocial outcome

2.2.1. Adults

The neuropsychological consequences of TBI in adults have been extensively documented (Atchison et al., 2004; S. Dikmen et al., 1983; Levin, 1995; Sherer et al., 2002). The most frequently observed deficits are impairments of attention, memory, information processing ability and speed. Tests of mental flexibility and programming have been shown to be the best predictors of psychosocial recovery 1-2 years after TBI (Leon-Carrion et al., 1998; Vilkki et al., 1994). Cognitive flexibility and mental programming play a major role in adjustment to the community, living independently, and coping with variable and unstructured situations. Persistent impairment of executive functions and speed of psychomotor processing are suggested to be the major factors associated with the loss of social autonomy (Mazaux et al., 1997).

A general conclusion from the literature is that most survivors of moderate to severe TBI will initially demonstrate significant neuropsychological deficits across a range of functions (Smith et al., 1998).

At least 2 years post-injury, moderate to severe TBI subjects have been found to remain impaired in a number of neuropsychological functions compared with a control group (Dikmen et al., 1990). However, long-term (≥ 5 years) neuropsychological recovery is less well understood. Millis and co-workers (Millis et al., 2001) found impairments in learning and memory, complex attention and processing speed 5 years after injury in 182 persons with complicated mild to severe TBI. Half of the sample had impaired performance in the Rey Auditory Verbal Learning test, but on a more structured memory task (Logical Memory) less than 20% had significant difficulty. Similarly, less than 25% of patients demonstrated marked impairments on the Block design test of the WAIS-R. Somewhat surprisingly, the mean performance (perseverative errors) on a problem solving task, the Wisconsin Card Sorting Test (WCST) was not deficient. They also compared the test performance at one year with 5 year post-injury performance and found that for a subset of persons with moderate to severe TBI, neuropsychological recovery may continue several years after injury. Improvement was most apparent on cognitive speed, visuoconstruction and verbal memory. Verbal memory tests have been found to correlate significantly with everyday memory problems (Kaitaro et al., 1995).

Studies examining the very long-term (≥ 10 years) sequelae of TBI are limited in number (Hoofien et al., 2001). The studies have found impaired memory and learning (Himanen et al., 2005; Thomsen, 1984) and psychomotor slowness (Hoofien et al., 2002). Hoofien et al. (2001) reported a significant advantage of verbal IQ compared with performance IQ, which they interpreted as the general slowing in psychomotor ability and processing speed. However, as they conclude, very long-term follow-up studies of cognition using neuropsychological tests are scarce.
2.2.2. Children

Suggestions of brain plasticity during development led some investigators to ask if it is better to have your brain lesion early in life (Schneider, 1979). However, a number of studies have shown that persistent cognitive and behavioural deficits follow also paediatric TBIs (Anderson et al., 2000; Anderson et al., 1997; Taylor et al., 2002). A recent 2-year follow-up suggested that children sustaining severe TBI are particularly vulnerable to impairments in executive functions. While some recovery took place with time since injury, deficits remained 2 years post-injury and were suggested to have an impact on ongoing development (Anderson & Catroppa, 2005).

Children with moderate to severe TBI have displayed poorer outcomes compared to children with orthopedic injuries in all neuropsychological domains at an extended (mean 4 years) follow-up. Some recovery occurred during the first year post-injury, but recovery reached a plateau after that time. Further recovery was uncommon after the first year (Yeates et al., 2002). After paediatric TBI, negative social outcomes are exacerbated by lower socioeconomic status and poor family functioning. Executive functions, pragmatic language skills, and social problem solving accounted for long-term social outcomes (Yeates et al., 2004).

There are hardly any follow-up studies of childhood TBI until adulthood. A 23-year follow-up of 159 paediatric head injury patients (mean age at study 31.4 years, mean age at injury 7.96) revealed that injury severity is the primary contributory factor in the prediction of long-term outcome. However, 90% of the injuries were mild (loss of consciousness ≤ 30 minutes). IQ recorded at the post-acute phase was a reliable predictor of long-term outcome. 31% of the sample reported subjective sequelae related to the extent of the head injury and initial IQ. Significant relationships were also found between subjective sequelae and psychosocial measures of adaptation, including educational lag, unemployment, current psychological/psychiatric problems and relationships with family members (Klonoff et al., 1993).

A 7-year follow-up study of 18 adolescents with TBI (mean age at injury 13.9 years) suggested that as a group they performed significantly subnormally in gross and fine motor tests and perception tasks. The basic intellectual functions were relatively well preserved within a broad normal range but only 28% had a functional outcome within normal limits. The most disabling component was social integration (Emanuelson et al., 1998).
2.3. Vocational Outcome

2.3.1. Overview of the concept

The literature on vocational or employment outcome after TBI is confounded by varying classification of employment status and social outcome. Also, the clinical severity of TBI is not always well-documented. There are two main reviews of the subject. The first one covers in addition to the authors’ own study the main 11 studies published post-war until 1980 (Humphrey & Oddy, 1980). The authors included all studies with 50 patients and a follow-up time for at least 12 months. They found a marked variation in the number of patients returning to work after TBI, ranging from 50% to 99%. The authors consider the studies included to be quantitative rather than qualitative and not lending themselves to comparison. They point out the crudity of return to work as an index of social recovery, which includes also leisure activities, social relationships and family life. Other factors influencing outcome discussed are age, previous personality and occupational level, personality changes, general and specific abilities and current social circumstances. The authors conclude that a study in depth of even a smaller number of TBI patients would be most valuable.

The other critical review of factors related to employment outcome following TBI covers the studies published between January 1980 and December 2003 (Ownsworth & McKenna, 2004). The first stage of the review considered 85 studies which were evaluated and rated by two independent evaluators according to the quality of their methodology based upon nine criteria. 50 studies met the criteria for inclusion in the second stage of the review. The factors most consistently associated with employment outcome included pre-injury occupational status, functional status at discharge, global cognitive functioning, perceptual ability, executive functioning, involvement in vocational rehabilitation services and emotional status.

Ownsworth and McKenna (2004) indicated that the effects of demographic, injury related and neuropsychological factors in relation to employment outcome after TBI have been extensively investigated in the literature. They highlighted the need for future research to investigate the role of social environment, emotional and metacognitive (the person’s awareness of, and control over his or her own cognitive functions and capabilities) in relation to employment outcome. The authors presented a conceptual model of the broad range of factors associated with vocational outcome (Figure 1).

Many studies have suggested poor stability of employment outcome after TBI (Hoofien et al., 2001; Kreutzer et al., 2003; Olver et al., 1996). It is suggested that particular attention should be paid to the long-term consequences of reduced capacity to work in these patients and that providing long term counseling may be necessary, even for individuals with good recovery (Possel et al., 2001).
2.3.2. Pre-injury and injury variables

According to the recent review on factors related to employment outcome after TBI, the most common pre-injury and demographic predictors examined in the literature include age, gender, race, marital status, pre-injury education level and occupational status. Of these, the effect of gender has a low level and pre-injury occupational status a moderate level of empirical support, all the other predictors having inconsistent findings (Ownsworth & McKenna, 2004).
Age at the time of injury in relation to employment outcome has been investigated in a number of studies (Asikainen et al., 1996; Dikmen et al., 1994; Keyser-Marcus et al., 2002; Ponsford et al., 1995). In their follow-up study of 5 or more years post-injury, Asikainen et al. (1996) found that individuals’ age at the time of injury was significantly related to work status. Patients in the youngest age group (7 years or younger) with severe TBI were more likely to have poor employment outcome than other age groups (8-16 years, 17-25 years and ≥ 26 years). Patients ≥ 26 years with a moderate to severe TBI were less likely to have competitive work status than individuals aged 8-25. Other studies have not included a range of younger age groups and therefore the findings of Asikainen et al. cannot be compared (Asikainen et al., 1996). Keyser-Marcus et al. (Keyser-Marcus et al., 2002) found that individuals aged between 18-39 years at time of injury were more likely to return to work between 1-4 years post-injury compared with individuals aged 40-55 years. This finding is consistent with the research by Ponsford et al. (Ponsford et al., 1995) who found that individuals aged 40 or over at injury were less likely to be employed 2 years post-injury than individuals under 40. Ownsworth et al. found the level of empirical support for relationship between age at injury and employment outcome inconsistent. However, they concluded that studies with different age groups were more likely to produce consistent findings which indicated that poor employment outcome is associated with age ≤ 7 or ≥ 40 years at time of injury (Ownsworth & McKenna, 2004).

Regarding severity of injury a number of studies have found a relationship between longer periods of coma and poor employment outcome (Cifu et al., 1997; Goran et al., 1997; Kreutzer et al., 2003; Ruff et al., 1993). It has been suggested that there may not be a critical threshold for coma duration and return to work (Crépeau & Scherzer, 1993). The findings of PTA duration and employment outcome are somewhat controversial. Many studies have found a relationship (Ponsford et al., 1995; Sherer et al., 2002) while some have failed to provide support (Ownsworth & McKenna, 2004). Similarly, the findings with studies between GCS score and employment outcome are inconsistent and it has been suggested that severity of injury may be more reliable in predicting survival and specific aspects of neuropsychological functioning than psychosocial outcomes (Ownsworth & McKenna, 2004).

Brain scan studies have mainly focused upon the presence or absence of trauma-related brain scan findings as predictor of vocational outcome (Ownsworth & McKenna, 2004). Rao et al. (Rao et al., 1990) found that individuals who returned to work were more likely to have a normal brain scan or unilateral damage than those who failed to return to work. Grosswasser et al. (Grosswasser et al., 2002) studied retrospectively war veterans 12-14 years post-injury to find radiologic predictors of long-term work outcome. They found widening of the third ventricle to be the best predictor of poor employment outcome.
REVIEW OF THE LITERATURE

predictor of employment outcome after penetrating head injury. The present level of empirical support was found to be controversial for prognostic value of brain scan results and employment outcome. Functional status measured at hospital discharge was the best predictor of employment outcome and more reliable than injury severity incidences (Ownsworth & McKenna, 2004).

2.3.3. Neuropsychological variables

Sherer et al. (Sherer et al., 2002) conducted an extensive review of neuropsychological factors related to employment outcome. They found more conclusive evidence to support the relationship between early cognitive impairment and poor employment outcome. The studies of late neuropsychological assessment and employment outcome and studies of concurrent neuropsychological assessment and employment outcome were inconclusive and had significant limitations regarding the study type, small sample size or adequacy of methodology. Atchison et al. (Atchison et al., 2004) found that neuropsychological test performance at one year post-injury provides important information regarding the ability of TBI patients to return to productive activity assessed at the same time point. Sherer et al. also pointed out that neuropsychological assessment makes a contribution to outcome prediction that is not redundant to that made by medical indices of injury severity. In view of the wide range of neuropsychological measures used in various studies and the minimal overlap in measures between the studies the authors did not attempt to determine which measures may be the best predictors of employment outcome but suggested further investigation with a large sample size (Sherer et al., 2002).

Ownsworth and McKenna (Ownsworth & McKenna, 2004) identified seven areas of neuropsychological functioning, based on common classifications (Lezak et al., 2004) as follows: 1. estimated premorbid IQ, 2. general intellectual or global cognitive functioning, 3. verbal or language functioning, 4. perceptual or visuo-spatial ability, 5. memory functioning, 6. attention and processing speed (including motor speed) and 7. executive functioning (including higher order attention). Of these, impaired executive functioning reached the level of moderate to strong empirical support regarding the prognostic value of employment outcome, defective general intellectual or global cognitive functioning and visuospatial ability were at the level of moderate support and verbal and memory functioning and attention/processing speed had inconsistent findings. Estimated premorbid IQ was insufficiently investigated and the findings indicated a insignificant relationship with employment outcome (Ownsworth & McKenna, 2004).

Gil et al. (Gil et al., 1996) found aphasia in 11.1% of a group of 351 patients with severe TBI. The commonest form was amnestic aphasia (56%), followed by expressive and receptive aphasia (10.3% and 10.5%, respectively). The study suggested
that 84.4% of severe TBI patients who also suffered from aphasia were able to return to gainful employment and thus the presence of aphasia did not have negative prognostic implications for occupational outcome.

2.3.4. Social variables

In the International Classification of Functioning, Disability and Health (ICF), environmental factors represent a key component in order to highlight the dynamic interaction between health and environment and personal factors (World Health Organization, 2004). The significance of social and environmental factors for individual’s functioning is being increasingly recognized. Family support has been identified to be associated with vocational re-entry (Rao et al., 1990). Vogenthaler et al. (Vogenthaler et al., 1989) found that the strength of an individual’s informal social support systems was positively associated with employment outcome at 4-7 years post-injury. A recent population-based study suggested that an important factor influencing outcome after TBI seemed to be whether relations to family and friends could be maintained at pre-injury level (Engberg & Teasdale, 2004). It has been suggested on the other hand that once family relations are established, they remain stable as no change in marital status was found 10 years post-injury (Franulic et al., 2004).

Involvement in vocational rehabilitation services is suggested to be an indicator of employment status with a moderate level of empirical support (Ownsworth & McKenna, 2004). Malec et al. (Malec et al., 2000) have found that vocational interventions (Medical/Vocational Case Coordination system) optimized vocational outcome after TBI. Introducing a Vocational Case Coordinator who served as a liaison to community-based services resulted in community-based employment for 81% of the patients and 53% were working independently in the community one year post-injury. Johnstone et al. found that the provision of vocational guidance and counseling and on-the-job training predicted vocational outcome while demographic, injury severity, and neuropsychological variables did not (Johnstone et al., 2003). With severe TBI patients Wehman et al. (Wehman et al., 1993) have reported an increase in the monthly employment ratio from 13% after injury with no supported employment to 67% with supported employment services.

2.3.5. Behavioural and emotional variables

Emotional and behavioural disturbance has been consistently recognized as a significant factor limiting individual’s capacity to find and sustain work but has rarely been investigated in employment outcome studies. Research in this area has mainly focused upon examining the relationship between measures of depression and
employment outcome (Ownsworth & McKenna, 2004). In a longitudinal study Ruff et al. (Ruff et al., 1993) found that individuals who displayed a higher level of depressive symptoms at 6 months post-injury were less likely to be employed at one year post-injury. It has also been suggested that TBI causes especially mood and anxiety disorders (van Reekum et al., 1996; van Reekum et al., 2000) and that in some individuals TBI may cause decades-lasting vulnerability to psychiatric illness (Koponen et al., 2002). Hoofien et al. (Hoofien et al., 2001) have also found 10-20 years after TBI high rates of depression with a 60% employment rate and low stability at work in low-level technological and clerical professions.

Self-awareness is an integrative cognitive and emotional construct which is considered to be the highest of all mental abilities, affecting functioning, quality of life, and psychological well-being in many ways. It is the end product of two, sometimes opposing perceptions of the subjective self and the objective reality (Hoofien et al., 2004). Impaired awareness of the effects of brain injury is a commonly observed and poorly understood finding after TBI. Nonetheless, it has been identified as a major factor determining outcome after TBI (Sherer et al., 1998). Self-awareness comprises three distinct but interlinked aspects: unawareness to the mere existence of the disability, unawareness to the functional implications of the disability, and unawareness of the disability when setting future goals i.e. inability to set realistic goals (Fleming et al., 1996). It is assumed that self-awareness is mostly related to injuries in the frontal lobes or the tip of the temporal lobes, in which executive functions are affected (Hoofien et al., 2004; Ownsworth et al., 2002).

In relation to vocational outcome, the self-awareness studies have suggested somewhat controversial findings. Malec et al. (Malec et al., 2000) found that the discrepancy score between health professionals and patient ratings on a standardized measure of functional status was significantly correlated with months to employment placement but not with the level of vocational independence at initial placement or 1-year follow-up. Sherer et al. (Sherer et al., 2003) investigated the relationship between early impaired awareness, as rated by clinicians and employability at discharge from inpatient rehabilitation for 129 patients. The findings indicated that early impaired awareness significantly predicted employability after adjusting for the effects of demographic and injury severity variables. In a recent study of 61 TBI patients and 34 family members awareness was found to be significantly related to psychiatric symptomatology and partially associated with behavioural disturbances and daily functioning but not with vocational outcomes (Hoofien et al., 2004).
3. AIMS OF THE STUDY

The general purpose of this study was to evaluate and describe the late cognitive and vocational outcome of TBI patients.

The specific aims of the present study were:

* To find out what kind of differences in performance speed are associated with long-term functional and vocational outcome in moderate to severe TBI patients on the average 12 years post-injury (Study I)

* To study the clinical and cognitive indicators of functional and vocational outcome of severe childhood TBI in young adulthood (Studies II and III)

* To study the stability of vocational outcome between young adulthood and midlife (Study IV)

* To study the middle-age cognitive performance and social variables in patients with moderate to severe childhood TBI (Study V)
4. METHODS

4.1. Subjects

Study I

Altogether 1,500 patients with traumatic brain injury (TBI) and post-injury problems in education and employment were referred to neurological examination to Kauhala Hospital's outpatient clinic between 1978-1993. The accidents were mostly motor-vehicle related and had occurred between 1950 and 1988. This study on long-term outcome of TBI included patients that had been followed-up by the Insurance Rehabilitation Association for at least 5 years. This criterion was fulfilled by 508 patients.

After a neurological examination of this population, 496 patients were evaluated to have a brain injury that could be defined. Of these patients, the neuropsychological data was collected retrospectively using original test documents from patients referred to the clinic during the years 1985, 1987, 1989, 1991 and 1993. Before the year 1985, a standardized test battery had not been in use.

The neuropsychological data included 140 patients of whom 114 patients had been exposed to severe (N = 92) or moderate (N = 22) TBI and were included in this study (see Figure 2). The severity of brain injury was estimated by using the Glasgow Coma Scale (GCS) scores (Teasdale & Jennett, 1974) on emergency hospital admission. If the scores were not given directly in patient reports, they were collected retrospectively from the physicians’ and nurses' notes. This method has been validated earlier (Katz & Alexander, 1994). The GCS scores 3-8 were considered to represent severe and 9-12 moderate brain injuries. The 114 patients were subdivided into three groups on the basis of age at injury; age ≤ 7 years (N=33), 8-16 years (N=49) and age > 16 years (N=32). The mean follow-up time was 12 years (SD 5.2 years, range 5-32 years). Patients with moderate or severe motor weakness of the dominant hand were excluded from the motor performance tests.

At the acute stage the patients were treated at local hospitals, with rehabilitation and follow-up provided both by general practitioners and by neurologists. The patients were referred to a rehabilitation programme provided by the Insurance Rehabilitation Association. An individual rehabilitation plan was made for each patient. The patients’ rehabilitation programme was a loose network of out-patient rehabilitation services according to the patient’s needs at different levels of recovery including intensive rehabilitation and adaptation courses in rehabilitation clinics and educational and occupational counselling of the patients and family members.
METHODS

Figure 2. Schema of the studies.

Studies II and III

Studies II and III concern a subgroup of patients of Study I (see Figure 2), including patients with childhood TBI only. Fifty-five patients were referred to the Insurance Rehabilitation Association during 1959-1969. The patients had been injured in traffic accidents at the age of ≤ 7 years (mean 5.2 years, range 2-7) with severe TBI, 90% as pedestrians. Three of the 55 patients were incapacitated to the extent of being unable to participate in the study, 10 refused because their medical impairment had previously been evaluated 100% and three did not reply. Of the remaining 39 patients, long-term follow-up was made by a neurologist, neuropsychologist and a social worker at the Kauniala hospital’s outpatient clinic during 1980-1982.

The criteria for grading head injury severity at the acute phase were: (1) unconsciousness lasting 24 hours or more (34/39 patients) or (2) unconsciousness lasting less than 24 hours plus presence of penetrating injury (2 patient), focal neurological deficit (2 patients) or evidence of increased intracranial pressure (1 patient).
Table 2. Clinical data of patients in Studies II and III. Outcome was graded on a seven-point scale in Study II. 1 = academic education and work, 2 = full-time work; skilled labour (professional), 3 = full-time work; unskilled labour, 4 = part time work at a sheltered work place, 5 = lives independently at home, 6 = lives at home with support, 7 = lives at an institution. In Study III the outcome was graded on a 3-point scale. 1 = full-time work, 2 = part-time or sheltered/subsidized work, 3 = not at work.

<table>
<thead>
<tr>
<th>Patient number and sex</th>
<th>Age at injury</th>
<th>Length of coma (LOC; days)</th>
<th>Complications (Fractures)</th>
<th>CT ca/co</th>
<th>EEG</th>
<th>Outcome Study II</th>
<th>Outcome Study II</th>
</tr>
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<td>Depressed</td>
<td>-/-</td>
<td>-</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
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<td>-/-</td>
<td>+</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
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<td>7</td>
<td>-/-</td>
<td>-</td>
<td>2*</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4. F</td>
<td>3.0</td>
<td>4</td>
<td>Basal</td>
<td>ND</td>
<td>ND</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>5. F</td>
<td>2.6</td>
<td>28</td>
<td>-/-</td>
<td>-</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
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<td>&lt; 1</td>
<td>Frontal, open</td>
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<td>-</td>
<td>6</td>
<td>3</td>
</tr>
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<td>7.6</td>
<td>1</td>
<td>-/-</td>
<td>-</td>
<td>2*</td>
<td>1</td>
<td></td>
</tr>
<tr>
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<td>4.6</td>
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<td>Depressed</td>
<td>-/-</td>
<td>-</td>
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<td>3</td>
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<td>-</td>
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<td>3</td>
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<tr>
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<td>-/+</td>
<td>3*</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. F</td>
<td>6.3</td>
<td>4</td>
<td>Basal, blind #</td>
<td>-/-</td>
<td>2*</td>
<td>1</td>
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</tr>
<tr>
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<td>7.3</td>
<td>&lt; 1§</td>
<td>-/-</td>
<td>-</td>
<td>2*</td>
<td>1</td>
<td></td>
</tr>
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<td>3.1</td>
<td>&lt; 1§</td>
<td>Depressed, open</td>
<td>5/-</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
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<td>6.8</td>
<td>30</td>
<td>Frontal</td>
<td>-/-</td>
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<td>2</td>
<td></td>
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<td>-/-</td>
<td>-</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
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<td>5.5</td>
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<td>-/-</td>
<td>-</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>17. F</td>
<td>5.4</td>
<td>&lt; 1</td>
<td>Papilledema</td>
<td>+/-</td>
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<td>3</td>
<td></td>
</tr>
<tr>
<td>18. F</td>
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<td>Depressed, open</td>
<td>-/-</td>
<td>3*</td>
<td>1</td>
<td></td>
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<td>6.8</td>
<td>14</td>
<td>-/-</td>
<td>-</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>20. M</td>
<td>2.4</td>
<td>14</td>
<td>1/-</td>
<td>-</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>21. M</td>
<td>5.9</td>
<td>21</td>
<td>Frontal, open</td>
<td>+/-</td>
<td>5</td>
<td>3</td>
<td></td>
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<tr>
<td>22. M</td>
<td>4.4</td>
<td>21</td>
<td>-/-</td>
<td>-</td>
<td>3*</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>23. F</td>
<td>4.5</td>
<td>21</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<td>3</td>
</tr>
<tr>
<td>24. F</td>
<td>6.8</td>
<td>21</td>
<td>Basal</td>
<td>-/-</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>25. F</td>
<td>5.0</td>
<td>21</td>
<td>Right parietal, open</td>
<td>24/-</td>
<td>3*</td>
<td>1</td>
<td></td>
</tr>
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<td>26. M</td>
<td>7.3</td>
<td>14</td>
<td>Depressed, open</td>
<td>88/+</td>
<td>4</td>
<td>2</td>
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</tr>
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<td>27. M</td>
<td>5.8</td>
<td>9</td>
<td>-/-</td>
<td>+</td>
<td>5</td>
<td>3</td>
<td></td>
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<tr>
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<td>-</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>29. M</td>
<td>6.1</td>
<td>&lt; 1§</td>
<td>-/-</td>
<td>-</td>
<td>1*</td>
<td>1</td>
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<td>30. M</td>
<td>7.2</td>
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<td>Left parietal</td>
<td>-/-</td>
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<td>3</td>
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<tr>
<td>31. M</td>
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<td></td>
</tr>
<tr>
<td>32. M</td>
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<td>-</td>
<td>5</td>
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</tr>
<tr>
<td>33. M</td>
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<td>11</td>
<td>6/-</td>
<td>-</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

§ = focal neurologic deficit; # = right eye blind; * = full-time work; ND = not known.

CT ca/co = presence + (moderate; volume in millimeters) or absence - (none or mild) of cavity or cortical atrophy.

EEG, presence + (moderate) or absence - (none or mild) of abnormality.
METHODS

Detailed neuropsychological assessment was carried out in 33/39 patients, 19 male (Study III). Because during the time of the follow-up some of the patients were still too young to be at work, it was completed with a questionnaire about the employment outcome when the youngest patients were 21 years old (1985), 16-30 years after the injury (Studies II and III). There were 18 children (55%) who had been unconscious for more than 2 weeks, the mean length of coma was 17 days, range 1-90. The clinical data of the patients is given in Table 2.

Studies IV and V

Of the first follow-up (Study III) patients, 22 out of 33 were clinically reassessed in 2001 (Studies IV and V). The causes of the 11 drop-outs between the first and second follow-up were: one died, one emigrated, two did not participate because of permanent full-pension due to severe post-traumatic epilepsy. Seven refused to participate in the clinical study of which five were reached by telephone and interviewed on their vocational outcome and were included in the analysis of stability of vocational status.

The criteria for grading head injury severity at the acute phase were the same as in Study II. The patient characteristics are shown in Table 3.

After the clinical assessment, every patient received a written report of their neuropsychological test results, neurological status and a social worker's comment on their level of social functioning with possible recommendations for support activities. The patients' status was clinically compared with that of the first follow-up for almost two decades previously.

4.2. Measures

4.2.1. Neuropsychological tests

The neuropsychological results were collected retrospectively from original test protocols in Studies I-III. Neuropsychological assessment included tests of general intelligence from the WAIS (Wechsler, 1955), verbal memory and learning from the WMS (Wechsler, 1954) and visual memory measured by the Benton Visual Retention Test, BVRT (Benton, 1974). The Wisconsin Card Sorting Test (WCST) (Heaton, 1981) and the Stroop test (Stroop, 1935) were used as measures of executive function and attention. Motor speed was measured by the Purdue Pegboard Test (Tiffin, 1968) and the Simple Auditory and Visual Reaction Time tests (De Renzi 1965). Simple reaction times were measured with both visual (a patient had to press a button placed in front of him with his dominant index finger as soon as a lamp was switched on), and auditory (a buzzer signal was used) stimuli. (Table 4)
METHODS

In the second follow-up (Studies IV and V) the neuropsychological assessment was performed by the author. In addition to the tests in Studies I-III, the Digit Symbol test from the WAIS-R (Wechsler 1981) measuring psychomotor performance and sustained attention and the Trail-Making B test (Army, 1944) measuring motor speed and cognitive flexibility were performed. The Stockings of Cambridge (SOC) test measuring the ability to plan actions in advance and the Intradimensional/Extradimensional shift test (IED) measuring flexibility were included in the test battery. Both tests are from the Cambridge Neuropsychological Test Automated Battery (CANTAB) and were administered according to the standard test protocol (CANTAB, 1999) (Table 4).

<table>
<thead>
<tr>
<th>Patient (N=27)</th>
<th>Sex</th>
<th>Age at injury (y)</th>
<th>Age at study (y)</th>
<th>LOCdays</th>
<th>Education (y) / vocational training</th>
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<td>12</td>
<td>P</td>
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<td>11</td>
<td>S</td>
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<tr>
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<td>7</td>
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<td>A</td>
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<td>21</td>
<td>9 S</td>
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<td>41</td>
<td>90</td>
<td>7 /no</td>
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</table>

LOC = length of coma; P = professional; S = skilled; A = academic; * = change in vocational outcome, TEL = not clinically studied, vocational status via telephone.

Table 3. Patient characteristics of Studies IV and V.
### METHODS

#### Table 4. The neuropsychological tests, rating scales and questionnaires.

<table>
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<th>TEST</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
<th>Study V</th>
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<td>(WAIS or WAIS-R*)</td>
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<td>Arithmetics</td>
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<td>+</td>
<td>+*</td>
<td>+*</td>
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<tr>
<td>Similarities</td>
<td>+</td>
<td>+</td>
<td>+*</td>
<td>+*</td>
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</tr>
<tr>
<td>Picture Completion</td>
<td>+</td>
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<tr>
<td>Block design</td>
<td>+</td>
<td>+</td>
<td>+*</td>
<td>+*</td>
<td></td>
</tr>
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<td>Digit Symbol</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+*</td>
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<td></td>
<td></td>
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<tr>
<td>Logical Memory; Immediate</td>
<td>+</td>
<td></td>
<td>+*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and Delayed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associative Learning</td>
<td>+</td>
<td></td>
<td>+*</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Visual Memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(BVRT, modified in Study V)</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Executive functions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-M b</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stockings (Cantab)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ID/ED (Cantab)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Motor Speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peg Board</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple Reaction Times</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(auditive&amp;visual)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rating Scales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale (GCS)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Outcome Scale (GOS)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Structured and Scaled Interview to Assess Maladjustment (SSIAM)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol Use Disorders</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identification Test (AUDIT-C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Profile of Mood States (POMS)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurobehavioural Rating Scale (NRS)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

29
4.2.2. Rating scales and questionnaires

The severity of brain injury in Study I was estimated by using the Glasgow Coma Scale (GCS) scores (Teasdale & Jennett, 1974) on emergency hospital admission. If the scores were not given directly in patient reports they were collected retrospectively from the physicians’ and nurses’ notes. This method has been validated earlier (Katz & Alexander, 1994). The GCS scores 3-8 were considered to represent severe, 9-12 moderate and 13-15 mild brain injuries.

The Glasgow Outcome Scale (GOS) (Jennett et al., 1981) was used in Study I at the end of the follow-up to assess functional outcome of the patients. A GOS score of 1 represents good recovery, a GOS score of 2 moderate disability and a GOS score of 3 severe disability. Employment status at the end of follow-up was divided into three categories: independent employment on the open job market, subsidized employment including sheltered activity, less demanding work or part-time work, and not capable of working. Patients who were judged to be capable of independent employment according to the neurological examination made by our team, but who were temporarily unemployed because of lack of jobs, were included in the category termed independent employment in Study I. The patients (N=20) who were at junior high school at the end of follow-up (age <16 years) or who were older, but continued their studies with no work experience (N=16), were excluded from the employment outcome variable.

In Studies II and III the sense of identity was graded by a theme interview based on the Social Functioning Exam, (Starr et al., 1982) and the Structured and Scaled Interview to Assess Maladjustment (SSIAM) (Gurland et al., 1972). In addition, the patient’s personal achievements were evaluated by their parents and compared with that of their siblings. Identity was scaled on a 5-point scale as follows: 1. Strong identity, 2. Struggle for identity, 3. Uneven identity, 4. Sense of identity not developed, 5. Evaluation was not possible because of problems in communication.

During the interview the patients were still too young to be at work and the study was completed by a questionnaire, when the youngest patients were 21 years old, 16-30 years after the injury in Studies II and III in 1985. The final outcome, employment status and ability to live independently in adulthood, was graded on a seven-point scale in Study II, where 1 indicates academic education and work, 2 full-time work (skilled labour), 3 full-time work (unskilled labour), 4 work part time (sheltered work), 5 lives independently at home, 6 lives at home with support, 7 lives at an institution. Because of small sample sizes, in Study III we used first a 4-point scale as follows: 1. fulltime work, 2. subsidized work, 3. lives independently at home and 4. needs help/support with daily living at home or an institution. Groups 3 and 4 were finally combined in Study III as a group not able to work.
METHODS

In Studies IV and V only two vocational outcome categories were used, i.e. full-time work and not-at-gainful work because there were only 2 patients who had subsidized work and they were merged in the not-at-gainful work group. All the clinically studied patients were first interviewed by a nurse using a structured questionnaire including detailed questions about work history and life style including standardized questions of alcohol use (AUDIT-C) (Bush et al., 1998). A social worker’s interview was included in order to assess the level of social functioning of the patient, and to provide support activities when needed. In addition, the Profile of Mood States Questionnaire (POMS) (McNair et al., 1981) and the Neurobehavioural Rating Scale (NRS) (Levin et al., 1987) were used to study the possible behavioural problems.

4.2.3. Neurological examination, neuroradiological and neurophysiological methods

A detailed neurological examination and interview was carried out to every patient. In Studies IV and V the specific aim of the neurological assessment was to reveal possible progression in the post-traumatic state or other concomitant diseases. Computed tomography (CT) of the head was included routinely in the investigation protocol of all the Study I patients. The CT scans of 37/39 of the Study II patients were available and were evaluated for abnormal absorption values and changes in tissue density by an experienced neuroradiologist.

Electroencephalography (EEG) was performed on 37/39 Study II patients, also with photic stimulation and hyperventilation when the eyes were closed (see Table 2).

The specific aims, indicators of outcome and outcome variables in Studies I-V are summarized in Table 5. In Studies IV and V a 2-point scale is used for employment status because of small group sizes.
METHODS

Table 5. Summary of aims, indicators and outcome variables in Studies I-V.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>AIM</th>
<th>INDICATORS</th>
<th>OUTCOME VARIABLE</th>
</tr>
</thead>
</table>
| I     | To find out if injury severity and age at injury are related to late performance speed after TBI and to determine which components of performance speed are associated with late functional and vocational outcome. | - Glasgow Coma Scale  
- Age at injury  
- Simple Reaction Time  
- Peg Board  
- Stroop | Glasgow Outcome Scale and employment status, 3-point scale  
(independent employment, subsidized employment, incapacity for work) |
| II    | To determine the young adulthood outcome of severe preschool TBI with focus on neurological predictors. | - Length of Coma (LOC)  
- Computed Tomography findings  
- School type  
- IQ (four subtests from the WAIS, Table 4) | Functional/vocational outcome, 7-point scale  
(academic education, full-time skilled, full-time unskilled, part-time/sheltered work, lives independently at home, lives at home with help, lives at an institution) |
| III   | To find out the cognitive indicators of vocational outcome after severe childhood TBI and evaluate the sense of identity | - Intellectual, memory and executive tests (Table 4)  
- Identity (5-point scale) | Employment status, 3-point scale  
(full-time work, subsidized work, not at work) |
| IV    | To find out if there is a change in vocational outcome between young adulthood and midlife with focus on executive function and social factors | - Executive tests (Table 4)  
- LOC  
- AUDIT-C  
- Stability of employment status | Employment status as in Study III. In the data analysis a 2-point scale  
(full-time work, not-at-gainful work) was used combining subsidized work and not at work. |
| V     | To find out the cognitive outcome in middle-age with neurobehavioural variables in relation to employment status | - Intellectual and memory tests (Table 4)  
- POMS (memory and depression)  
- NRS  
- Marital status  
- Driving licence | As in Study IV. |

IQ = Intelligence Quotient, WAIS = Wechsler Adult Intelligence Scale, Audit-C = Alcohol Use Disorders Identification Test, POMS = Profile of Mood States, NRS = Neurobehavioural Rating Scale
4.3. Statistical methods

One- and two-way ANOVAs were used for comparing the means of patients’ neuropsychological test performance grouped by injury severity (GCS scores 3-8 representing severe, 9-12 moderate and 13-15 mild brain injuries) and age at injury (≤ 7, 8-16 and >16 years). Also the interaction was tested between injury severity and age at injury. A logarithmic transformation was used before the analysis in case of skewed distributions. A trend analysis was used to measure the significance of the declining trend in performance speed measured with the PB test between the independent, sheltered and not at work patient groups (Study I).

One-way ANOVA with Tukey HSD post-hoc multiple comparisons, Pearson chi-square test and Fisher’s Exact test were used in Studies II and III.

To test the vocational outcome change between the first and second follow-up the Wilcoxon Signed Ranks Test was used (Study IV). For the comparisons between the full-time work and not-at gainful work groups, the Pearson’s chi-square test was used for categorial variables and the Mann-Whitney U-test for continuous variables (Studies IV and V). In addition, the Discriminant Function Analysis was used to test the predictive value of the variables in relation to work status (Study V).
5. RESULTS

5.1. Performance speed after moderate to severe TBI (Study I)

No statistically significant (p > 0.05, two-way ANOVA) differences in test performance (the Stroop test, the Purdue Pegboard test and Simple Visual and Auditive Reaction Times) were detected between the patients, grouped either by injury severity (severe injury GCS 3-8, N = 92 and moderate injury GCS 9-12, N = 22) or age at injury (≤ 7 years, N = 33, 8-16, years N = 49 and > 16 years, N = 32), and additionally, interactions between these two parameters were not significant. For this reason we studied the moderately and severely injured patients combined in the further analysis of outcome.

Performance speed of the patients with moderate to severe TBI in the Stroop test was significantly associated with functional outcome, as measured by the GOS, the severe disability group (GOS score 3) being the slowest (p=.0046, one-way ANOVA), compared with the outcome groups of the GOS scores of 1 and 2. Test performance of patients in the GOS score groups of 1 and 2 was similar. The PB test differentiated significantly between the GOS scores of 1 to 2 and the GOS score of 3 (p=.0413, one-way ANOVA), with the slowest performance for the worst outcome (Table 6).

<table>
<thead>
<tr>
<th>GOS score</th>
<th>Stroop test (s)</th>
<th>Peg Board test (sum of 3 trials)</th>
<th>Simple visual RT (ms)</th>
<th>Simple auditive RT (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOS score 1 good recovery</td>
<td>69 (19)</td>
<td>44 (11)</td>
<td>352 (163)</td>
<td>366 (104)</td>
</tr>
<tr>
<td></td>
<td>n = 12</td>
<td>n = 12</td>
<td>n = 12</td>
<td>n = 12</td>
</tr>
<tr>
<td>GOS score 2 moderate disability</td>
<td>70 (21)</td>
<td>44 (7.9)</td>
<td>297 (124)</td>
<td>251 (76)</td>
</tr>
<tr>
<td></td>
<td>n = 61</td>
<td>n = 51</td>
<td>n = 51</td>
<td>n = 51</td>
</tr>
<tr>
<td>GOS score 3 severe disability</td>
<td>85 (27) **</td>
<td>39 (9.4)</td>
<td>346 (139)</td>
<td>274 (99)</td>
</tr>
<tr>
<td></td>
<td>n = 45</td>
<td>n = 31</td>
<td>n = 31</td>
<td>n = 31</td>
</tr>
</tbody>
</table>

Test results are means (SD). [ ] indicates geometrical means.
** p < .01, one-way ANOVA
* p < .05, one-way ANOVA
RT = Reaction Time
ms = milliseconds
RESULTS

At the end of the follow-up 79 patients were at working age (> 16 years). When they were grouped by their capacity for work (independent employment, subsidized employment and inability to work) the Stroop test and the PB test differentiated significantly (p = 0.0015, one-way ANOVA and p = 0.032, trend-test), respectively, between the patients capable of independent or subsidized employment and those incapable of work (Table 7), the groups of patients who were unable to work being the slowest in both tests.

Simple Visual and Auditive Reaction Times did not differentiate between the GOS scores of our patients with moderate to severe TBI at the end of follow-up (Table 6), and neither did they differentiate between the three categories of capacity for work (Table 7).

Table 7. Employment status and neuropsychological test results in Study I.

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Stroop test (s)</th>
<th>Pegboard test (sum of 3 trials)</th>
<th>Simple visual RT (ms)</th>
<th>Simple auditive RT (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent work</td>
<td>68.9 (20.8)**</td>
<td>44.9 (9.0)*</td>
<td>323 (124)</td>
<td>275 (99)</td>
</tr>
<tr>
<td>Sheltered work</td>
<td>69.6 (12.2)</td>
<td>42 (6.1)</td>
<td>310 (194)</td>
<td>249 (77)</td>
</tr>
<tr>
<td>Not at work</td>
<td>88.5 (30.2)</td>
<td>38.8 (9.3)</td>
<td>325 (104)</td>
<td>251 (73)</td>
</tr>
</tbody>
</table>

Test results are means (SD). [ ] indicates geometrical means.
** p < 0.01, one-way ANOVA
* p < .05, Trend -test
RT = Reaction Time
ms = milliseconds

At the end of the follow-up 79 patients were at working age (> 16 years). When they were grouped by their capacity for work (independent employment, subsidized employment and inability to work) the Stroop test and the PB test differentiated significantly (p = 0.0015, one-way ANOVA and p = 0.032, trend-test), respectively, between the patients capable of independent or subsidized employment and those incapable of work (Table 7), the groups of patients who were unable to work being the slowest in both tests.

Simple Visual and Auditive Reaction Times did not differentiate between the GOS scores of our patients with moderate to severe TBI at the end of follow-up (Table 6), and neither did they differentiate between the three categories of capacity for work (Table 7).

5.2. Functional and cognitive outcome of childhood TBI in young adulthood (Studies II - III)

In Study II, five of the nine patients (56%) with unconsciousness lasting less than 1 week at the time of the injury were able to work full-time compared to 4/30 patients with unconsciousness lasting one week or longer (p < .01). Two patients with unconsciousness of 3 weeks at the time of injury were working full-time (unskilled jobs) (see Table 2).
RESULTS

The results of a detailed neurological examination were normal in 9/39 patients but did not correlate with final outcome except that patients living at home and not at any kind of work always had neurological deficits.

Slight cortical or central atrophy on CT had no prognostic significance. Moderate cortical atrophy was always associated with poor outcome, as was the presence of cavities (1-88 mL) within the brain tissue. The EEG did not have any prognostic significance at follow-up (Table 2). Posttraumatic epilepsy developed in 8/39 (21%) patients 3 months to 16 years after the injury but was transient in four (10%).

Intellectual capacity was within normal range (IQ ≥ 95) in 13/37 (35%) and at low normal level (IQ 86-94) in 10/37 (27%) of the patients, so altogether 62% fell within normal range. The mean IQ of the group was 85. An IQ of 100 or higher was associated with good outcome (p < 0.05) but did not directly indicate it. On the other hand, patients with an IQ 80 or less were not working full-time (Figure 3).

In Study III, 9/33 patients (27%) worked full time, seven had subsidized work (21%), 12 (37%) managed independently at home and five (15%) needed help with everyday functions. Attending normal school was associated with full-time employment (p < 0.05) but did not without reservations predict vocational outcome in adulthood: nine of 21 patients were unable to work after completing normal school (Table 8).

Figure 3. The relationship between outcome (squares) and IQ (triangles). The final outcome was graded on a seven-point scale. 1 = academic education and work, 2 = full-time work; skilled labour (professional), 3 = full-time work; unskilled labour, 4 = part time work at a sheltered work place, 5 = lives independently at home, 6 = lives at home with support, 7 = lives at an institution. ? = missing information.
RESULTS

The Wisconsin Card Sorting Test (WCST) performance was highly significantly associated with adulthood vocational outcome ($F = 10.4$, $p = 0.00$), the performance of the full-time working (FW) group being significantly superior to that of the subsidized (SW) and not-at work (NW) groups. The only memory test being significantly associated with vocational outcome was the Benton Visual Retention Test (BVRT) ($F = 6.13$, $p = 0.006$). The NW group made significantly more errors in the colour-word discrepancy part of the Stroop test ($F = 3.74$, $p = 0.035$) than the FW and SW groups. The performance of the FW group was highly significantly faster in the Pegboard (PB) test ($F = 8.80$, $p = 0.001$). No significant differences appeared in the WAIS verbal subtests. The performance in the Picture Completion test, however, was nearly significantly better in the FW group ($F = 3.12$, $p = 0.057$) and there was a trend for better performance in this group also for the Block Design test. (Table 9) The degree of identity was highly significantly associated with late vocational outcome ($F = 8.29$, $p = 0.001$). All the patients in FW group had a strong sense of identity (see Table 9). The sense of identity appeared independent of all other parameters, it correlated with none of the neuropsychological tests.

Age at injury was not significantly associated with vocational outcome. However, none of the seven children under 4 years of age at the time of injury were able to work fulltime (see Table 2).

5.3. Midlife vocational outcome and cognition (Studies IV-V)

In Study IV, the overall employment between the first (1985) and second (2001) follow-up had not changed as 20/27 (74%) of the patients had no change in vocational status ($p=0.603$). Nine patients (33%) were able to work full-time of whom six had been full-time workers also in the first follow-up (Table 10). 13/27 (48%) of the patients had vocational education (Table 3). Of the full-time working patients one participant had a M.Sc. degree and was working as a system engineer, 2 had professional education (a project leader and a photographer) and 4 were skilled workers.

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Normal school</th>
<th>School for disabled</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulltime work (FW)*</td>
<td>8</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Subsidized work (SW)</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Not able to work (NW)</td>
<td>9</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>12</td>
<td>33</td>
</tr>
</tbody>
</table>

* $p < 0.05$, Pearson chi-square test

The degree of identity was highly significantly associated with late vocational outcome ($F = 8.29$, $p = 0.001$). All the patients in FW group had a strong sense of identity (see Table 9). The sense of identity appeared independent of all other parameters, it correlated with none of the neuropsychological tests.

Age at injury was not significantly associated with vocational outcome. However, none of the seven children under 4 years of age at the time of injury were able to work fulltime (see Table 2).
RESULTS

Table 9. Test and identity scores in different employment status groups in Study III.

<table>
<thead>
<tr>
<th>Test performance</th>
<th>Full-time work (FW) N=9</th>
<th>Subsidised work (SW) N=7</th>
<th>Not at work (NW) N=17</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>WAIS / Arithmetics</td>
<td>9.9</td>
<td>2.7</td>
<td>8.1</td>
</tr>
<tr>
<td>WAIS / Similarities</td>
<td>9.8</td>
<td>1.4</td>
<td>9.4</td>
</tr>
<tr>
<td>WAIS / Picture Completion</td>
<td>9.8</td>
<td>2.3</td>
<td>5.9</td>
</tr>
<tr>
<td>WAIS/Block Design</td>
<td>10.8</td>
<td>2.2</td>
<td>8.1</td>
</tr>
<tr>
<td>WMS/LM; immediate</td>
<td>10.6</td>
<td>4.2</td>
<td>7.3</td>
</tr>
<tr>
<td>WMS/LM; delayed</td>
<td>7.6</td>
<td>2.6</td>
<td>6.7</td>
</tr>
<tr>
<td>WMS/Ass. Learning</td>
<td>15.7</td>
<td>3.2</td>
<td>14.0</td>
</tr>
<tr>
<td>BVRT**</td>
<td>7.8</td>
<td>1.6</td>
<td>4.6</td>
</tr>
<tr>
<td>PB**</td>
<td>49.0</td>
<td>5.6</td>
<td>35.9</td>
</tr>
<tr>
<td>WCST (number of cards)**</td>
<td>39.3</td>
<td>16.0</td>
<td>60</td>
</tr>
<tr>
<td>Stroop (errors)*</td>
<td>0.6</td>
<td>0.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Identity***</td>
<td>1.0</td>
<td>0.0</td>
<td>2.1</td>
</tr>
</tbody>
</table>

*p<0.05; ** p < 0.01; ***p < 0.001, one-way ANOVA

(a plumber, an electrician, a farmer and a carpenter). The greatest change was detected in those who were in subsidized work. Of the six patients with subsidized jobs in the first follow-up two had become unemployed, two had reached full-time work and only two were still doing supported work.

All the clinically studied 22 patients were independent in their domestic activities of daily living, and one patient was in need of a trustee because of extreme use of money. 8/22 patients had mild to moderate posttraumatic left-sided physical disability and 4/22 had mild to moderate right-sided physical weakness. One patient with mild left-sided physical disability and one with moderate right-sided disability were able to work gainfully. The clinical neurological examination revealed no overall change in posttraumatic state. Minor clinical peripheral neuropathy due to excessive alcohol consumption (two patients) or diabetes mellitus (one patient) was detected. In the neuropsychological assessment, there was no change in general cognitive performance in any of the patients between the first and the second follow-up.

In Study V the full-time work (FTW) group was significantly better in all WAIS-R subtests than the not-at-gainful-work (NGW) group (Table 11). In the Benton Visual Retention Test measuring visual memory the difference between the groups did not reach statistical significance, although there was a trend for better performance in the FTW group. In the Associative Learning test, the performance did not differ between the groups. However, both groups scored more than 1.5 SD below the Finnish age standards.
### Results

Table 10. Vocational outcome in the 1st (Study III) and 2nd (Study IV) follow-up and functional outcome variables in Study IV.

<table>
<thead>
<tr>
<th>Patient (N=27)</th>
<th>Sex</th>
<th>Age at injury (y)</th>
<th>Outcome 1st follow-up</th>
<th>Outcome 2nd follow-up</th>
<th>Driver’s licence</th>
<th>Marital status</th>
<th>AUDIT (max 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>6,1</td>
<td>FTW</td>
<td>FTW</td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>3,1</td>
<td>SW</td>
<td>FTW *</td>
<td>+</td>
<td>+</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>5,3</td>
<td>FTW</td>
<td>FTW</td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>7,3</td>
<td>FTW</td>
<td>FTW</td>
<td>+</td>
<td>+</td>
<td>6</td>
</tr>
<tr>
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<td>M</td>
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<td>NW</td>
<td>NW</td>
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</table>

**Mean 5,1**

| 23 TEL         | F   | 5                 | FTW                   | FTW                   |
| 24 TEL         | M   | 7,6               | FTW                   | FTW                   |
| 25 TEL         | F   | 6,8               | NW                    | NW                    |
| 26 TEL         | F   | 4,3               | NW                    | NW                    |
| 27 TEL         | F   | 3                 | NW                    | NW                    |

FTW = full-time work, SW = subsidized work, NW = not at work; * = change in vocational outcome, TEL = not clinically studied, vocational status via telephone. AUDIT = The AUDIT Alcohol Consumption Questions (AUDIT-C); + = living in marital relationship; - = living alone
RESULTS

In the Logical memory test (Table 11), the FTW group performed significantly better than the NGW group both in immediate and delayed recall (p=.010 and p=.001, respectively). Both the FTW and NGW groups had very little subjective memory complaints in the Profile of Mood states questionnaire (POMS). The POMS did not reveal depression above cut-off level in either group, but the NGW group reported significantly more depressive symptoms (p=.005).

The discriminant function was statistically significant (Wilks’ Lambda = 0.261, Chi-square = 24.20, df = 4, p<0.001) and the canonical correlation was 0.860 for four variables: the Digit Symbol and the Block Design tests from the WAIS-R, the Logical Memory-Delayed test from the WMS-R and the POMS depression score. Adding any other variable included in Table 10 did not enhance the discriminative power, although there were also more (p=.014) neurobehavioral symptoms in the NGW group than in the FTW group detected by the Neurobehavioural Rating Scale (NRS). All but one patient in the NGW group were correctly classified.

The FTW group was significantly better (p = .005) than the NGW group in the Intradimensional/Extradimensional shift test measuring flexibility. In the Stockings of Cambridge test, no difference between the groups was detected. In the Trail Making-b test, the NGW group performed slower than the FTW group (p=.046). In the Stroop test, no significant difference was found between the groups, although the FTW group showed a trend for better performance.

Difference in the length of coma did not reach statistical significance (p = 0.078) between the FTW and NGW groups in Study IV but at group level there was a clear trend for longer coma for the patients not working; mean length of coma for the NGW group was 18.7 days (SD = 13.4 days) and for the FTW group 8.4 days (SD = 8.0 days), respectively.

Having a driver’s license and living in a marital relation were significantly associated with the employment status (p = .015 and p = .000, respectively, see Table10). Alcohol consumption by AUDIT-C did not differ at group level (Table 11) but, however, there were risk drinkers (score ≥ 4) in both groups (Table 10).
### RESULTS

Table 11. The objective and subjective evaluation of cognition and neuropsychiatric symptoms in Study V.

<table>
<thead>
<tr>
<th>Tests</th>
<th>Vocational outcome</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Arithmetics (WAIS-R)</td>
<td>FTW (N = 7)</td>
<td>17.7 (4.0)</td>
<td>11-22</td>
<td>.010</td>
</tr>
<tr>
<td></td>
<td>NGW (N = 15)</td>
<td>11.5 (5.1)</td>
<td>1-19</td>
<td></td>
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<td>2. Similarities (WAIS-R)</td>
<td>FTW</td>
<td>28.7 (2.4)</td>
<td>26-32</td>
<td>.010</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>22.7 (6.0)</td>
<td>9-31</td>
<td></td>
</tr>
<tr>
<td>3. Block Design (WAIS-R)</td>
<td>FTW</td>
<td>36.6 (6.2)</td>
<td>27-46</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>21.3 (10.0)</td>
<td>7-38</td>
<td></td>
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<tr>
<td>4. Digit Symbol (WAIS-R)</td>
<td>FTW</td>
<td>48.7 (6.9)</td>
<td>40-59</td>
<td>.001</td>
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<tr>
<td></td>
<td>NGW</td>
<td>30.5 (9.9)</td>
<td>19-50</td>
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<tr>
<td>5. BVRT (number of correct figures, max 26)</td>
<td>FTW</td>
<td>21.6 (3.0)</td>
<td>18-26</td>
<td>.082</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>18.0 (4.6)</td>
<td>7-24</td>
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<tr>
<td>6. Associative Learning (WMS-R)</td>
<td>FTW</td>
<td>13.6 (3.6)</td>
<td>8-17</td>
<td>.178</td>
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<tr>
<td></td>
<td>NGW</td>
<td>11.1 (5.1)</td>
<td>1-20</td>
<td></td>
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<tr>
<td>7. Logical Memory Immediate (WMS-R)</td>
<td>FTW</td>
<td>24.4 (5.7)</td>
<td>18-34</td>
<td>.010</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>15.3 (5.8)</td>
<td>7-24</td>
<td></td>
</tr>
<tr>
<td>8. Logical Memory Delayed (WMS-R)</td>
<td>FTW</td>
<td>23.7 (4.6)</td>
<td>18-31</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>12.1 (6.4)</td>
<td>3-22</td>
<td></td>
</tr>
<tr>
<td>9. IED (perseverative errors)</td>
<td>FTW</td>
<td>17.4 (6.4)</td>
<td>11-28</td>
<td>.005</td>
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<td></td>
<td>NGW</td>
<td>35.4 (14.8)</td>
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<tr>
<td>10. SOC (optimally solved problems/12)</td>
<td>FTW</td>
<td>8.3 (3.1)</td>
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<td></td>
<td>NGW</td>
<td>8.0 (2.3)</td>
<td>3-11</td>
<td></td>
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<tr>
<td>11. Stroop (color-word discrepancy; number of errors)</td>
<td>FTW</td>
<td>0.43 (0.79)</td>
<td>0-2</td>
<td>.443</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>1.3 (1.86)</td>
<td>0-5</td>
<td></td>
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<tr>
<td>12. TMT-b (time sec)</td>
<td>FTW</td>
<td>104.7 (38.0)</td>
<td>60-160</td>
<td>.046</td>
</tr>
<tr>
<td></td>
<td>NGW</td>
<td>153.1 (52.1)</td>
<td>85-255</td>
<td></td>
</tr>
</tbody>
</table>

**Subjective Questionnaire**

| 9. POMS (memory; max 12)                   | FTW                | 3.6 (2.0)  | 1-6      | .452      |
|                                            | NGW                | 4.2 (2.5)  | 0-7      |           |
| 10. POMS (depression; max 28)              | FTW                | 1.4 (2.3)  | 0-6      | .005      |
|                                            | NGW                | 8.0 (5.7)  | 0-21     |           |
| 11. Present alcohol consumption (AUDIT-C; maximum score 12) | FTW | 4.1 (4.0) | 0-10 | .680   |
|                                            | NGW                | 4.7 (3.7)  | 0-10     |           |

**Examiner’s evaluation**

| 12. NRS (total sum; max 189)              | FTW                | 47.3 (9.7) | 34-59    | .014      |
|                                            | NGW                | 59.7 (7.6) | 47-71    |           |

SD= standard deviation, FTW= full-time work; NGW= not at gainful work; BVRT = Benton Visual Retention Test; IED, the Intradimensional/Extradimensional shift test; SOC, the Stockings of Cambridge test; TMT-b, the Trail-Making Test-b; POMS = the Profile of Mood States Questionnaire; AUDIT-C, Alcohol Use Disorders Identification Test; NRS = the Neurobehavioural Rating Scale
6. DISCUSSION

The length of unconsciousness was not unambiguously related to outcome. Moderate cortical atrophy on CT was always associated with poor outcome. School performance did not without reservations predict vocational outcome and intellectual capacity was only partly related to it. In a group of preschool TBI patients, age at injury was not associated with vocational outcome in young adulthood but the sense of identity was associated with being able to work full-time.

Complex performance speed was associated with functional and vocational outcome in the average 12 years after moderate to severe TBI. The overall employment did not change between young adulthood and middle-age. All the clinically studied preschool TBI patients were independent in their daily activities when their mean age was 40 years. Patients working full-time in middle-age were better in all tests measuring intellectual capacity, logical memory and tests of executive function measuring flexibility. Interestingly, the patients working and not working performed equally poorly in the word association learning test. Both groups had very little subjective memory complaints. The not working patients reported more depressive symptoms and had more neuropsychiatric symptoms than the patients at work. Alcohol consumption did not differ at group level. Having a driver’s licence and living in a marital relation were significantly associated with full-time work.

6.1. Diagnostic issues

Severity of brain injuries cannot be unambiguously defined. In Study I we used the GCS scores (Teasdale & Jennett, 1974) at the time of emergency admission to the hospital. Because the GCS score is strictly descriptive and not an objective measure more specific information and data was needed from the acute patient reports. This made the retrospective construction of the GCS scores possible also in cases where the scores were not given directly in patient reports, as well as comparable with those scores given directly (Katz & Alexander, 1994). Acute GCS has been found to be of limited value in predicting functional and cognitive outcome of TBI patients (Zafonte et al., 1996), especially in mild to moderate brain injuries (van der Naalt et al., 1999). However, in Study I most patients (81%) had a severe TBI (GCS 3-8). In Studies II-V the injuries had taken place during 1959-1969, before the time GCS was published. The length of coma (LOC) alone is not the best indicator of pediatric head injury severity, but was the only available over 30 years ago.

In their recent review of factors related to employment outcome following TBI Ownsworth and McKenna (Ownsworth & McKenna, 2004) found the prognostic
value of brain scan results to be inconsistent. Levin et al. (Levin et al., 1993) found that in childhood brain injury, MRI revealed areas of abnormal signal predominantly in the frontal lobes in 40% of the patients. Interestingly, there was also a relationship between left frontal injury and cognitive flexibility. Mathias et al. (Mathias et al., 2004) found that mean corpus callosum measures were 5% to 19% smaller in the patients compared to those of a normative control group. White matter atrophy was moderately related to visual and tactile RT performance and hippocampal volume to memory performance.

As all study patients had suffered at least moderate, mostly severe TBI, brain scan findings were not considered essential in studying their very long-term cognitive outcome. In Study II we found that slight cortical or central atrophy on CT had no prognostic significance but moderate cortical atrophy was always associated with poor functional and vocational outcome, as was the presence of cavities within the brain tissue. This is in accordance with other studies (Grosowski et al., 2002; Wallesch et al., 2001). EEG had no prognostic value and length of unconsciousness was of limited predictive value of long-term outcome which is in accordance with the findings of Klonoff et al. (Klonoff et al., 1993).

Since a component of DAI is believed to be present in all motor vehicle crashes where the patient has lost consciousness (Meythaler et al., 2001) all our patients probably also had DAI. In a study of 450 non-selected human brains DAI was detected in 12% of the samples, but only one third had a history of TBI (Niess et al., 2002). The authors suggested that various causes may produce DAI and that TBI is not the only and perhaps not even the main cause of DAI.

The relationship of DAI to neuropsychological complications is not clear, either. There is some evidence that traumatic DAI would result in mainly transient neuropsychological deficits in mild-to-moderate TBI (Wallesch et al., 2001) and as Meythaler et al. (Meythaler et al., 2001) point out DAI rarely occurs in isolation, there are often accompanying focal lesions that could contribute to the deficits.

Ichise et al. (Ichise et al., 1994) investigated the correlations of functional (Technetium-99m-HMPAO SPECT) and structural neuroimaging measurements of TBI patients with neuropsychological performance. They suggested that HMPAO SPECT, as a complement to CT and MRI, may play a useful role by demonstrating brain dysfunction in morphologically intact brain regions and thus providing objective evidence of some of the impaired cognitive performance (memory, attention and executive function), especially in mild TBI. However, they conclude that the correlation between neuroimaging and neuropsychological performance is not simple. Further investigation is needed especially concerning the relationship between neuropsychological deficits and DAI.
6.2. The effect of age

The ‘Kennard principle’ (Kennard, 1936) modified by Teuber to a frequently quoted statement “It is better to have your brain lesion early in life” (Schneider, 1979) is in contrast to many more recent follow-up studies of preschool TBI (Asikainen et al., 1996; Ewing-Cobbs et al., 1997; Max et al., 1999). However, the follow-up time has usually been from two to six years (Bigler et al., 1997; Taylor et al., 2002; Verger et al., 2000). Asikainen et al. (Asikainen et al., 1996) showed that patients with severe TBI sustained early in life (childhood and early teens) coupled with poor educational attainment had a relatively poor social and vocational outcome. Better outcomes were observed in those who were injured in their late teens or early adulthood. The data in Study I support these previous observations. The young patients in the poor outcome groups of the GOS and incapacity for work had equally poor test results on speed performance as the older ones. This finding suggests that young age does not result in a more favourable recovery. Despite of the considerable scientific evidence that damage to the developing brain can be even more harmful than equivalent damage to the adult brain, the health-care professionals tend to expect greater recovery from brain damage in children than in adults (Webb et al., 1996).

As the frontal lobes develop rapidly during the first five years of life and continue to mature till late adolescence (Hudspeth & Pribram, 1992), the executive defects caused by these injuries may be subtle and overlooked in children and adolescents. Thus, there is the possibility of psychosocial changes becoming apparent later, when more demands are placed on the individual (Oddy, 1993) and when everyday life situations become more unstructured, like in working life in general. There is also evidence that frontal lobe injury early in life leads to poor performance in adulthood on all tests sensitive to frontal lobe injury (Kolb, 1989). In a recent 2-year follow-up study on executive skills following paediatric TBI (Anderson & Catroppa, 2005) greatest deficits were found in cognitive flexibility and abstract thought domains. For planning, goal setting and problem solving the group with severe TBI demonstrated to some extent recovery over time. Due to multi-dimensional nature of executive functions the importance of long-term follow-up was expressed by the authors. In Studies III and IV inflexibility was associated with poor employment outcome in young adulthood and midlife.

Heiskanen and Sipponen (Heiskanen & Sipponen, 1970) suggested that less than 30% of severe brain injury patients were able to return to work whereas more than 70% of patients under 20 years were able to return to work or go to school. In Study III 64 % of the patients had attended normal school. In 1990, 593/1000 people in Finland had at least comprehensive school education (Statistics, 2003), which is in accordance with the TBI cohort. However, in Finland the general employment rate
DISCUSSION

in 2001 was 67.7% (Statistics, 2003), twofold compared with the TBI patients in Study IV. In addition, vocational education rate of the same age (37-49 years) population was 80% (Statistics, 2003), 1.65 times higher compared with 48% of the TBI patients in Study IV.

Brooks et al. (Brooks et al., 1987) found that those with technical or managerial jobs and under 45 years of age were more likely to return to work than patients over 45 years. Klein et al. (Klein et al., 1996) found the cognitive performance of middle-aged (mean age 49 years) TBI patients to be similar to that of old (mean age 70 years) controls. It has also been suggested that the greater neuropsychological impairment noted in older individuals with TBI may be related to normal ageing (Johnstone et al., 1998). However, there were only 5 patients in the 60+ age group in this study. Further studies with larger number of older individuals are thus needed to study the effects of ageing in TBI patients.

6.3. Performance speed and long-term functional and vocational outcome after TBI

The aim of Study I was to provide information about the clinical usefulness of neuropsychological tests in estimating long-term functional and vocational outcome of patients with moderate and severe TBI. The study was focused on performance speed as it affects several aspects of cognitive performance in different types of work tasks. We excluded the patients with mild TBI because they were so few of them in the two youngest age groups. In addition, mild TBI patients are not systematically referred to a rehabilitation programme because of their better recovery, and therefore this group is more biased. Another study is needed to evaluate the significance of speed performance to outcome in patients with mild TBI.

In the Stroop test which can be considered as a measure for processing speed, performance speed of the patients was the slowest in the poor outcome group with a GOS score of 3. The Purdue Pegboard test has been reported to be sensitive to brain damage (Clifton et al., 1993; Hoofien et al., 2001; Lezak et al., 2004). An association between the PB type of test and the GOS has also been previously reported (Clifton et al., 1993). A significant difference in performance speed was also detected in both tests between the patients incapable of work and those capable of independent or subsidized employment with those unable to work being the slowest. Leskelä et al. (Leskela et al., 1999) also found the frontal lesion stroke patients to be slower in the tasks (including the Stroop test) measuring speed of mental processing. The Stroop test contains a stimulus-response incompatibility, and can be interpreted as a measure of divided attention (Lezak et al., 2004) which is relevant for many types of work tasks. It is thus understandable that this finding correlates with working capacity.
DISCUSSION

Associations between simple visual and auditory reaction times and the outcome variables were not significant. This may be due to the tests used, which probably are not sensitive enough to subtle changes in the speed of information processing, e.g. due to attention problems. In earlier studies it has also been suggested that simple reaction times normalize during long follow-up (Van Zomeren & Deelman, 1978).

6.4. Cognitive indicators of long-term outcome after TBI

After normal school performance, 8 of 21 patients in Study III were able to work independently, 9 were not. It has been suggested already in the 40’s (Hebb, 1942) that brain injury in early childhood may have a more generalised effect on the brain than injury at a later age, as high level problem solving and insight into social relations develop during adolescence. Children suffering moderate to severe head injuries prior to age 7 have been shown to be less likely to exhibit recovery with performance IQ scores (Anderson & Bigler, 1995) suggesting that head injury has more impact on “fluid” intelligence skills. In our study we also found a trend for better results in the full-time working group for the performance tests of the WAIS in Study III when the patients were in young adulthood. Study V suggested a significantly better performance in all intelligence tests measured with WAIS-R in middle-age for the patients working full-time. One plausible explanation may be associated with the activating/rehabilitative effect of work life on cognitive performance.

In Study III we found that the Wisconsin Card Sorting Test (WCST) (Heaton, 1981) was associated with vocational outcome in young adulthood after childhood TBI. We replicated this result almost two decades later in Study IV with a computerized WCST-like test (the Extradimensional/Intradimensional test from Cantab) showing that inflexibility was significantly correlated with not being at work and also with not having a family. Defective executive functions are known to have a negative effect on working capacity and psychosocial outcome (Vilkki et al., 1994). Earlier studies have also found significant relationships between long-term functional outcome and objective indicators of social adaptation after TBI, including employment status and relations with family members (Klonoff et al., 1993; Taylor et al., 2002; Vilkki et al., 1994). Impaired performance in executive tests has also been found with age-associated memory impairment suggesting a central role for frontal dysfunction in age-related memory loss in elderly people (Hanninen et al., 1997).

All patients in Study V performed poorly in the Associative Learning Task, in spite of their vocational status. Thus, a decline in learning performance in the neuropsychological assessment seems not to be associated with late vocational outcome of TBI. Rather, it seems to be more of a permanent, possibly brain injury
related deficit. In a study of Finnish War Veterans (Jarho, 1973) investigating Korsakoff-like amnesic syndrome in penetrating brain injury the amnesic patients did not show significant learning effect between the first and second learning stages unlike the controls.

It is also interesting that neither group experienced subjective memory difficulties in the Profile of Mood States (POMS) questionnaire. In our cohort of childhood TBI patients, lack of subjective experience of memory difficulties in adulthood may be due to developmental adaptation and adjustment rather than merely poor insight. It has also been suggested (Levine et al., 2002) that TBI patients in general perform memory tasks using altered and more widespread neuroanatomical frontal networks as compared with controls. This may allow the use of compensation strategies in real life situations which was also suggested as an explanation by Klein et al. (Klein et al., 1996) to the finding that TBI patients did not perceive deficit memory test performance as a limiting factor in everyday life. In a recent study (Schmitter-Edgecombe & Woo, 2004) metamemory was suggested to be better preserved than actual memory performance in severe head injury patients. An interesting finding with normal elderly people is that subjective memory complaints are more closely associated with personality traits than with actual memory performance (Hanninen et al., 1994).

On the other hand, the Logical Memory-Delayed test discriminated between the FTW and NGW groups in Study V. In a recent study on the relationship between neuropsychological test performance and productivity following TBI Logical Memory was strongly associated with productivity (Atchison et al., 2004). Deficit delayed memory for a story has been found in children with TBI (Donders, 1993). Levin et al. (Levin et al., 1988) found the selective reminding test of verbal memory to be less sensitive to the effects of head injury in children, which may reflect the relative immaturity of memorisation strategies compared with that of adolescents. However, the follow-up periods are short in both studies and the need for longer follow-up periods is expressed.

Attention problems are common sequelae following TBI (Lezak et al., 2004) but little is known of their pattern of recovery or in cases of childhood head injuries, their interaction with ongoing brain development. Impairments in sustained attention have been reported (Catroppa et al., 1999; Kaufmann et al., 1993) in children with severe head injury. The colour-word discrepancy part of the Stroop test can be considered as a test of divided attention, where in Study III the not working patients made significantly more mistakes than the patients at work. In Study IV, no significant difference was found in the Stroop test between the groups, although the FWT group showed a trend for better performance. Future research on the recovery of attention over time after TBI is needed because of the increasing need for different components of attention in many work tasks.
DISCUSSION

Neuropsychological assessment is useful with TBI patients where it can aid in the detection of subtle deficits, provide information on cognitive outcome and prognosis, contribute to construction of directed rehabilitation strategies, and facilitate rehabilitation that leads to more functional independence (American Academy of Neurology, 1996). In predicting outcome after TBI it has been suggested that inability to complete neuropsychological tests at 1 year postinjury is associated with non-productive outcome (Atchison et al., 2004) and that early neuropsychological assessment is related to and predicts employment outcome (Sherer et al., 2002). However, it is important to consider many factors (e.g. age, injury severity, cognitive status) when predicting vocational outcome.

6.5. Behavioural and psychosocial factors associated with vocational outcome

An interesting finding in Study III was that a strong sense of identity was highly significantly associated with final outcome from TBI, i.e. all the patients working full-time had a strong identity. The sense of identity was assessed before the evaluation of employment status. We defined identity as the integrated whole of different parts of the individual’s self image and its compatibility with reality. Behavioural dysfunction following paediatric brain injuries has been reported in several studies (Fletcher & Ewing-Cobbs, 1991; Klonoff et al., 1993; Max et al., 1999; Prasad et al., 2002; Yeates et al., 2004). In the 23-year follow-up study of children with head injuries (Klonoff et al., 1993) it was found that the presence of long-term subjective sequelae is consistent with objective indicators of social adaptation, one measure of which was employment status. On the other hand, in a recent study (Max et al., 1999) it has been shown that cognitive decline after severe TBI in childhood was significantly related to neuropsychiatric and psychosocial disadvantage factors. In our study, the sense of identity was not related to test performance and could be considered as an indicator of social adjustment, which seems to be a very important predictor of final outcome following childhood TBI. Realistic therapeutic and educational efforts enable the development of a firm identity, which could be expressed as “I’m intelligent enough but because I have memory problems and difficulties in planning my activities, it restricts my educational and vocational choices”.

Study III suggested that the full-time working patients had a realistic view of one self as young adults and were able to cope with the environment with sufficiently preserved cognitive and social skills. Studies IV and V implicated that almost two decades later in middle-age all the full-time working patients lived in a marital relationship, of who four out of seven were the same individuals as in the first follow-up. The full-time working patients also had less neurobehavioral symp-
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toms in middle-age than the patients not working. In a recent population-based study, family relations were found to be an important factor influencing outcome after TBI (Engberg & Teasdale, 2004), which is in accordance with our results.

In middle-age, having a driving licence was significantly associated with full-time work (Studies IV and V). On the other hand, there were as many patients driving a car in the not-at-work group. A recent study on road traffic accident rate after severe brain injury suggested that the relative risk in severe brain injured patients (coma lasting at least 48 hours) was significantly higher compared with uninjured individuals (Formisano et al., 2005). In Britain, Brooks and Hawley (Brooks & Hawley, 2005) performed a large multi-centre study of 563 adults with TBI, of whom 68% had suffered a severe TBI. 381 were drivers before the injury and 139 had returned to driving 3-9 months post-injury, of which more than a half (56.2%) had received a severe head injury. Only 61/563 (16%) TBI patients had been formally advised not to drive following the injury, leaving the decision of whether or not to return to driving to the patient. However, in predicting safe driving after severe TBI the patients’ pre-morbid histories should also be carefully considered as they were found to explain 72.5% of the variance with years post-injury regarding driving safety (Pietrapiana et al., 2005).

Although psychiatric disability was not studied per se, two patients reported depressive symptoms in the interview. The depression scale of the POMS was one of the four variables in Study V that correctly classified all but one of the cases although the scores did not reveal depression above cut-off level in the full-time working and not working groups. Several studies have shown that unemployed subjects present more frequently depressive symptoms than those who are working (Franulic et al., 2004; Hoofien et al., 2001). However, at least 6 months post-injury, no association has been found between depression status and performance on neuropsychological measures although depressive symptoms increased the patients’ complaints of cognitive decline (Satz et al., 1998). On the other hand, patients with depression-dysexecutive syndrome had worse psychosocial functioning compared with patients who had only depression (Vataja et al., 2005). There is also evidence for strong association between TBI and mood disorders (van Reekum et al., 2000). TBI may also cause decades lasting vulnerability to depressive episodes, delusional disorder, and personality disturbances in some individuals (Koponen et al., 2002).

In Study IV, alcohol consumption did not differ at group level between patients working full-time and patients not at work. In the Finnish birth cohort study (Ti- monen et al., 2002), childhood TBI was not significantly associated with later alcohol usage. The main finding of the study was that childhood TBI increased the risk of developing mental disorders up to two-fold.

In Study V, the Neurobehavioral Rating Scale (NRS) also revealed more neurobehavioral symptoms in the patients not working as compared with patients at work. The differences between the groups were detected using sum scores of all
the 27 questions included in the NRS (Levin et al., 1987) as in the present study. Cifu et al. (Cifu et al., 1997) have demonstrated the validity of the NRS in predicting a patient’s successful return to work. Franulic et al. (Franulic et al., 2004) found the significant differences in the cognitive, emotional and metacognitive factors of the scale among employed and unemployed patients. They suggest that the NRS could be a useful instrument in evaluating the patients before return to work and could aid in directed work rehabilitation to decrease the incidence of job reinsertion failure.

In their summary report of evidence for the effectiveness of rehabilitation for TBI patients Chesnut et al. (Chesnut et al., 1999) found that the studies (although very few) of early intervention, compensatory cognitive rehabilitation, and supported employment suggest positive effects. The model where supervisors and co-workers are trained to act as ‘job-coaches’ was found to be a potentially effective and low-cost model of providing supported employment. Access to appropriate post-acute rehabilitation services is of crucial importance, eg. early formalized rehabilitation after severe TBI has been shown to increase the frequency of return to work to 43% as compared with 0% in the group of patients with no formalized rehabilitation (Sörbo et al., 2005). More rehabilitation effectiveness studies are needed to evaluate the generalization of treatment effects to everyday situations and the long-term maintenance of improvements produced by rehabilitation (Cicerone et al., 2000).

6.6. Limitations of the present study and implications for the future

It is acknowledged that the small sample size in Studies II-V restricts the power of conclusions. In addition, the sample is unrepresentative of the TBI population in general because all head injuries have been sustained in traffic-related accidents ensuring the best possible rehabilitation arrangements according to Finnish legislation. However, at the time of the injuries (between 1959 and 1969) the overall supply of rehabilitation services was very limited compared to modern times. Despite of the limitations of the study sample, the drop-outs during the almost four decade follow-up period were mainly the most severely injured patients, who probably in the first place never had entered work life. Corrigan et al. (Corrigan et al., 2003) have suggested that in follow-up studies of patients with TBI severe enough to warrant hospital admission, 3 categories of patients tended to be missing from samples available for evaluation 1 to 2 years post-injury: 1) persons from socio-economically disadvantaged groups (eg. those with little education, those unemployed, those dependent on public funding), 2) persons with pre-injury history of alcohol or drug abuse and 3) persons injured with violence. A systematic bias because of the loss of
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patients may be at least partly avoided with a small, well-documented sample such as that of the present study.

To the author’s knowledge, there are no previously published studies with preschool TBI patients followed-up until midlife. The present study brings new information of the multiple factors related to late TBI outcome, but a prospective long-term study is needed in order to find out the predictive value of different cognitive factors.

In the future, the cohort is valuable for studying the effects of aging on TBI patients’ cognitive performance and outcome. With modern brain imaging techniques the impact of the frontal lobes on outcome can also be studied in more detail in relation to the different components of executive functions. Interest in the influence of genetic factors especially the apolipoprotein E genotype on the prognosis of TBI is a new era of research. There is some evidence that after severe TBI later cognitive decline may occur (Jellinger, 2004; Millar et al., 2003) but the relation between dementia after TBI and apolipoprotein E status is still ambiguous.

The role of environmental factors such as the presence of a support network (including family support and supported employment services) and willingness of employers to make accommodations may become increasingly important factors in predicting employment outcome as years go by after the TBI. In Finland, clinical neuropsychological assessment and rehabilitation services are well-established and of high standard but insufficient considering the amount of patients. At least for a subgroup of TBI patients, a successful vocational outcome is possible to achieve. A system of a supported employment network with multi-professional competence is needed to facilitate work-entry and improve vocational outcomes among TBI patients.
CONCLUSIONS

7. CONCLUSIONS

The main findings of the study were:

1. TBI severity at the acute stage estimated by GCS (Study I) or LOC (Studies II-V) was not unambiguously related to either cognitive or vocational outcome in case of moderate to severe injuries.

2. Complex performance speed was associated with functional and vocational outcome. Of executive functions, flexibility in young adulthood and middle-age was related to employment outcome, whereas planning ability was not. School performance did not directly predict vocational outcome. Intellectual capacity and memory performance were only partly related to employment status.

3. Strong sense of identity (self-awareness) was associated with full-time work in young adulthood.

4. The full-time working patients had less neuropsychiatric symptoms than the patients not at work. Alcohol consumption was not related to vocational outcome.

5. Between young adulthood and middle-age, no significant change in vocational outcome was detected. The clinical neurological examination revealed no overall change in the posttraumatic state.

6. In the neuropsychological assessment, there was no change in general cognitive performance in any of the patients between young adulthood and middle-age.
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