Traumatic brain injury is one of the most common causes of morbidity and mortality, especially affecting young adults. Although the majority of patients (85-90%) sustain a mild or moderate head injury (HI), research for several years has been focussed on severe head injury, which affects approximately 10% of patients. Outcome studies have found several factors predictive of outcome in this category of patients. Until recently, mild and moderate HI just were regarded as non-severe HI with relatively good outcome. Although most patients with mild to moderate HI recover within weeks to months after injury, a subgroup of patients continues to have disabling symptoms interfering with outcome and return to work. Studies on the extent of (cognitive) dysfunction have raised inconclusive results due to methodological differences such as heterogeneity of groups and sensitivity of outcome measures used. Also, follow-up of this category of patients often has been limited to a three-month period. Furthermore it has been recognised that the commonly used outcome scales are not sensitive enough as they assess functional disability rather than cognitive deficits which are found to be important for outcome in this category of patients. In recent years, more knowledge of the pathophysiology of head injury has been obtained, in particular regarding the extent of axonal injury which appears to be present not only in severe, but also in mild HI. Nowadays, head injury is regarded as a continuum, with the extent of axonal injury increasing with severity of injury. Evidence is accumulating that even at the milder end of the severity scale, in a subgroup of patients objective residual impairments are present.

Given the tremendous impact HI can have on the victim and the family, it becomes imperative to identify those variables which may have prognostic value. This prospective study was designed to evaluate the effects on outcome of early injury characteristics such as Glasgow Coma Scale (GCS) and posttraumatic amnesia (PTA), behavioural disturbances and lesions detected by imaging procedures with CT and MRI. The extent of cognitive dysfunction was evaluated with event related potentials and a neuropsychological test battery. Follow-up was done at regular intervals until one year after injury, when outcome was determined with the commonly used Glasgow Outcome Scale (GOS) together with a more differentiated outcome scale (DOS) to assess the extent of cognitive and physical sequelae in mild to moderate HI patients.

A review covering the epidemiology and classification of mild to moderate head injury is given in chapter 1. The available information provided by additional diagnostic procedures is summarised and the predictive value for outcome is discussed.
The one-year outcome was described in chapter 2. It appeared that approximately three quarters of patients had resumed previous work or study by then. Consequently, one in four patients was able to resume previous activities only on a significantly lower level. Overall, the time between injury and resumption of previous activities was about three months. However, although patients had resumed work, working on full capacity was possible only several months later, about six months after injury mainly because of the complaints they experienced. Most frequent were complaints of disturbances of memory and concentration, fatigue and headache. It was noted that most patients who resumed previous work or study did have complaints (81%). The outcome as determined with the GOS showed good outcome in 82% although half of these apparently well recovered patients still had minor deficits. With application of a more differentiated outcome scale (DOS) cognitive and behavioural problems interfering with return to work, were observed in approximately half of the patients. Although one in three patients reported physical disabilities, this concerned mainly cranial nerve dysfunction. With multiple regression analysis, duration of PTA was found to be the most important predictor of outcome whereas GCS failed to predict outcome, in contrast to findings in severe HI. The importance of prospective assessment of PTA was underlined. In addition, the application of a more differentiated outcome scale will give more information regarding the factors determining resumption of previous activities.

With imaging studies, it is possible to determine whether focal lesions are present. In chapter 3 the results of serial magnetic resonance imaging (MRI) and computed tomography (CT) studies are presented. It was evaluated whether early and late imaging have additional value in predicting outcome in this category of patients. CT scan on admission was performed together with MRI studies within one to three months (early) and six to 12 months (late) after injury. With CT, intra cranial lesions were seen in 62% of patients compared to 44% with early and 19% with late MRI, located predominantly in the frontal and temporal regions. More than half of the lesions revealed with CT resulted in focal atrophy on MRI. Outcome was found to be worse in patients with oedema and lesions on CT. Likewise, abnormalities detected with MRI were associated with poor outcome scores. It appeared that with MRI lesions less favourable outcome was seen, irrespective of the presence of CT abnormalities on admission. With multiple regression analysis, only lesions in the frontal regions and focal atrophy in the frontotemporal regions were found to be predictive of outcome. This finding suggests that late MRI studies may be more valuable for predicting long-term outcome in patients with mild to moderate HI than CT on admission. Probably
due to increased sensitivity to detect abnormalities at the base of the skull, where damage frequently is located in mild to moderate HI. Furthermore, imaging studies performed one to three months after injury are expected to reflect persistent damage of the white matter which can be detected better with MRI.

As restlessness and agitation are well-known early sequelae of traumatic brain injury in concordance with the PTA, the predictive value of these behavioural disturbances was studied in chapter 4. In more than half of the patients behavioural disturbances were observed in the acute phase after injury. Restlessness was most frequently observed. In all patients restlessness and agitation disappeared before resolution of the PTA. In multiple regression analysis, PTA and restlessness were found to be separate factors in predicting outcome. On imaging studies twice as many lesions were seen in patients with behavioural disturbances, mainly localised in the frontotemporal region. In two third of patients with early behavioural disturbances residual emotional and cognitive disturbances were observed one year after injury. It is suggested that behavioural disturbances are related to frontotemporal lesions and therefore to outcome and that both phenomena predict poor outcome.

Outcome and cognitive impairment after HI are assumed to be related to underlying brain damage. In addition to imaging studies, neurophysiological and neuropsychological tests have been used to provide an objective index of cognitive impairment. In chapter 5 event related potentials (P300) are used as a measure of cognitive dysfunction in an early stage, i.e. target identification. One month after injury, half of the patients did have increased latencies, with decrement of latencies between three and 12 months after injury. One year after injury, still one in four patients had abnormal latencies. When patients were evaluated based on outcome scores, an inverse relation with outcome was observed. Patient with moderate disability had abnormal latencies during the whole follow-up period whereas patients with good recovery had normal latencies. Increased latencies were found to be related to complaints of forgetfulness and mental slowness. The importance of the negative predictive power of event related potentials was emphasized.

As several patients with mild to moderate HI report subjective complaints of memory and concentration interfering with return to work, neuropsychological tests are used to objectify these complaints. Several aspects of memory, attention and speed of information processing were studied in chapter 6. It appeared that lasting cognitive impairments were present in a considerable portion of patients.
Almost half of the patients had impairment of memory or attention whereas one in four patients had impaired speed of information processing. The frequency of deficits on neuropsychological tests was rather high compared to the relatively good outcome, that is good recovery or moderate disability. Consequently, some patients return to work with cognitive impairments. Patients with cognitive impairments had more problems with return to work as only 43% resumed work compared to 83% of patients with normal cognitive tests. Moreover, almost two third of these patients were moderately disabled, compared to 10% of patients with normal tests. To elucidate the relationship of cognitive impairments with outcome, subcategories of outcome were compared regarding the frequency of selective impairments. In particular an increase in attention deficits was seen in patients with less favourable outcome. Patients with cognitive impairments had more complaints of mental slowness, headache and irritability. It was noted that memory complaints were not related to impaired memory tests. The importance to recommend strategies to prevent attention related problems (such as avoiding tasks under distracting conditions, frequent interruptions and time pressure) was underlined. Furthermore it was examined whether outcome could be predicted based on information directly available after admission. In particular patients with prolonged PTA, behavioural disturbances in the acute phase and focal abnormalities in the frontotemporal region diagnosed with imaging studies and EEG are prone to develop cognitive deficits.

In chapter 7 the outcome profile of patients with mild to moderate HI with predominance of mental sequelae over physical disabilities was discussed. This outcome of patients was found to be related to length of PTA, behavioural disturbances short after injury, and local abnormalities on CT, MRI and EEG. The importance of recognising this syndrome of the ‘frontotemporal concussion’ was underlined.

In summary, the present study has been designed to elucidate the outcome of mild to moderate head injury patients and to determine whether prognostic factors are available to predict outcome in this category of patients. First, in this category of patients, knowledge of duration of PTA is important. Information of the presence of behavioural disturbances in the early phase should be obtained. Additional information can be provided by imaging studies. Besides a CT on admission, MRI studies performed several months after injury will have additional value by disclosing persistent abnormalities, that is either focal lesions or atrophy. In those patients with persistent complaints, assessment of event related potentials might be used as a simple and reliable method to detect defi
cits in basic information processing. Definite outcome however, has to be determined with a more detailed outcome scale to measure the more subtle influence of various parameters on outcome. Neuropsychological tests can provide an objective assessment of deficits in memory and attention. Furthermore, these results can provide important information for coaching of patients with regard to resumption of work. Even for those physicians and neurologists who are consulted several months after injury when problems with return to work already are encountered, it is important to obtain additional information to estimate whether present impairments warrant further evaluation and treatment. Mild or moderate head injury is a multifactorial disorder, and outcome of individual patients is determined not only by severity of injury, but also by the patient's premorbid functioning and psychological reaction to the injury. The precise role that each of these factors plays in the recovery process remains to be answered. For now, it is important to recognize that mild head injury is an often underestimated condition, in which careful assessment may reveal objective mental and physical impairments. In case acute injury characteristics are misinterpreted or even missed (such as PTA) the diagnosis post-concussional syndrome will often be made wrongly. Although the majority of patients with mild to moderate head injury recover, those patients with residual impairments interfering with return to work require adequate evaluation and rehabilitation strategies.
Recommendations for management of patients with mild to moderate head injury

At admission:

* **Glasgow Coma Scale (GCS):** determine depth of consciousness and severity of injury by GCS and neurological examination
* **Computed Tomography (CT):** perform CT on admission to reveal oedema or focal (haemorrhagic) lesions
* **PTA (posttraumatic amnesia):** after admission the duration of PTA should be registered on a daily base by a standardised scale
* **Behavioural disturbances:** the presence of behavioural disturbances in the early phase after injury should be recorded in patients. Restlessness and agitation together with inappropriate behaviour are of special importance.

At discharge:

* **Information:** provide information to the patient and family on the kind of complaints patients can experience after head injury, the expected course of recovery and strategies how to resume work. Also additional information for the family is necessary regarding possible changes in personality such as irritability, emotional lability and selfish conduct.

At follow-up:

* **One month after injury:** all patients
  a. When patients are without complaints or have resumed work with little or no disturbances further follow-up is not necessary.
  b. Only when significant complaints are present, interfering with resumption of work or social activities, additional procedures are done: Magnetic Resonance Imaging (MRI), neuropsychological evaluation. Strategies for resumption of work are suggested when possible.
* **Three months after injury:** only patients with persistent complaints interfering with resumption of work or social activities.
  
  **Neuropsychological evaluation** provides information on the extent of impairments in memory, attention and speed of information processing.
  **Magnetic Resonance Imaging (MRI)** provides information on the presence of focal lesions or atrophy in the basal frontotemporal regions.