Resilience and recovery from mild traumatic brain injury

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Contents

Abstract

Despite extensive research, there is considerable diversity and debate concerning the expected recovery course and the etiology of persistent symptoms after mild traumatic brain injury (MTBI). In recent years, resilience, which is defined as an ability to recover from adversity, has emerged as one potential psychological construct associated with outcome from MTBI. The aim of this study was to investigate the psychometric properties of the Finnish version of the Resilience Scale (RS) and its short version (RS-14), their use in MTBI research, and to examine the association between resilience and outcome from MTBI. In addition, this study aimed to thoroughly and prospectively report the recovery from MTBI in previously healthy adults.

The psychometric properties of the Finnish version of the RS were examined with a convenience sample of 243 participants. Working aged participants with MTBI (n=74) without pre-injury neurological or mental health problems and orthopedically injured trauma controls (n=40) were recruited from the Emergency Department of Tampere University Hospital. Participants filled out self-report questionnaires about demographic variables, resilience, post-concussion symptoms, fatigue, insomnia, pain, post-traumatic stress, depressive symptoms, and quality of life at 1, 6, and 12 months following injury. Neuropsychological examination was conducted for the patients with MTBI and for the controls at 1 month after injury and for the MTBI group at 6 months. Data regarding return to work of the MTBI group was also gathered.

The Finnish version of the Resilience Scale (RS) and its short version (RS-14) have good psychometric properties and can be reliably used in MTBI research. Greater resilience was associated with fewer post-concussive symptoms and better quality of life, whereas lower resilience was associated with more symptoms and lower quality of life. Resilience was also a significant predictor of self-reported fatigue following MTBI even when controlling for factors known to be associated with fatigue (depression, sleep disorders, and pain).

In this sample of previously healthy adults, MTBI had a good prognosis. By six months following injury, patients with MTBI did not differ as a group from non-head injury trauma controls on cognition, fatigue, or mental health, and by 12 months their level of post-concussion symptoms and quality of life was similar to that of controls. Almost all (96%) patients with MTBI returned to work/normal activities (RTW) within the follow-up of one year. Patients reporting ongoing mild post-concussion syndrome (PCS) at the 12-month follow-up did not have more severe brain or bodily injuries than those without PCS. A large percentage (62.5%) of those with persistent PCS had a modifiable psychological risk factor (i.e., depression, possible post-traumatic stress disorder, and/or low resilience) at the beginning of recovery.

Tiivistelmä

Laajasta aiheeseen liittyvästä tieteellisestä tutkimuksesta huolimatta tutkimustulokset toipumisennusteesta ja pitkittyneiden oireiden syistä lievän aivovamman jälkeen ovat ristiriitaisia ja kiistanalaisia. Viime vuosina resilienssi on noussut esille psykologisena käsitteenä, joka on mahdollisesti yhteydessä lievästä aivovammasta toipumiseen. Resilienssillä (ei vakiintunutta suomennosta, mutta ilmiöstä voidaan käyttää esim. termejä psyykkinen kuormituskestävyys tai psyykkinen joustavuus) tarkoitetaan ihmisen kykyä selvitä vastoinkäymisistä. Tämän tutkimuksen tavoitteena oli arvioida Resilience Scale-kyselyn (RS) suomenkielisen version sekä sen lyhytversion (RS-14) psykometrisiä ominaisuuksia ja niiden käytettävyyttä lievän aivovamman tutkimuksessa sekä selvittää resilienssin ja lievästä aivovammasta toipumisen välistä yhteyttä. Lisäksi tutkimuksen tavoitteena oli raportoida laajasti pitkittäisasetelmalla aiemmin terveiden aikuisten toipumista lievästä aivovammasta.

Suomenkielisen RS-kyselyn psykometrisiä ominaisuuksia arvioivaan kyselytutkimukseen osallistui 243 henkilöä. Lievien aivovammojen tutkimukseen puolestaan rekrytoitiin Tampereen yliopistollisen sairaalan ensiavusta 74 työikäistä lievän aivovamman saanutta henkilöä, joilla ei ollut aiempia neurologisia tai mielenterveydellisiä ongelmia, sekä 40 ortopedisen vamman saanutta verrokkia. Osallistujat täyttivät itsearviointikyselyt demografisista tekijöistä, resilienssistä, lievän aivovamman oireista, väsyvyydestä, univaikeuksista, kivusta, posttraumaattisesta stressistä, masennusoireista ja elämänlaadusta 1, 6 ja 12 kuukauden kuluttua vammasta. Neuropsykologinen tutkimus tehtiin molemmille tutkimusryhmille 1 kuukauden kuluttua vammasta ja lievän aivovamman saaneille potilaille 6 kuukauden jälkeen. Lisäksi kerättiin tiedot lievän aivovamman saaneiden potilaiden työhön paluusta.

Suomenkielisen RS-kyselyn ja sen lyhytversion (RS-14) psykometriset ominaisuudet ovat hyvät ja niitä voidaan luotettavasti käyttää lievän aivovamman tutkimuksessa. Korkeampi resilienssi oli yhteydessä vähäisempiin lievän aivovamman oireisiin ja parempaan elämänlaatuun, kun taas matalampi resilienssi oli yhteydessä runsaampiin oireisiin ja heikompaan elämänlaatuun. Resilienssi oli myös merkittävä väsyvyyden vähenemisen ennustaja lievän aivovamman jälkeen, vaikka muut väsymykseen liittyvät tekijät (masennus, univaikeudet ja kipu) otettiin huomioon.

Tutkimukseen osallistuneilla, aiemmin terveillä henkilöillä lievän aivovamman ennuste oli hyvä. Kuuden kuukauden kuluttua vammasta lievän aivovamman saaneet potilaat eivät ryhmänä eronneet tiedonkäsittelytoimintojensa, väsyvyytensä tai psyykkisen hyvinvointinsa puolesta verrokkiryhmästä, ja 12 kuukauteen mennessä heidän lievän aivovamman oireidensa ja elämänlaatunsa taso vastasi verrokkeja. Lähes kaikki lievän aivovamman saaneet potilaat (96 %) palasivat töihin/normaaleihin toimintoihinsa vuoden kuluessa vammasta. Potilailla, jotka raportoivat pitkäkestoisia lieviä aivovamman oireita vielä vuoden päästä vammasta, ei todettu olleen vakavampia vammoja kuin niillä, joilla pitkäkestoisia oireita ei ollut. Suurella osalla pitkäkestoisia oireita kokeneista potilaista oli toipumisen alkuvaiheessa psykologisia riskitekijöitä (masennusta, mahdollista posttraumaattista stressiä ja/tai matala resilienssi), joihin voitaisiin vaikuttaa alkuvaiheen hoidolla.

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Tampere, November 2015

Heidi Losoi

List of original publications

This thesis is based on the following original articles, referred to in the text by their Roman numerals I-IV.

I Losoi, H., Turunen, S., Wäljas, M., Helminen, M., Öhman, J., Julkunen, J. & Rosti-Otajärvi, E. Psychometric properties of the Finnish version of the Resilience Scale and its short version. *Psychology, Community & Health*, 2013: 2 (1): 1-10.

II Losoi, H., Wäljas, M., Turunen, S., Brander, A., Helminen, M., Luoto, T.M., Rosti-Otajärvi, E., Julkunen, J., Öhman, J. Resilience is associated with fatigue after mild traumatic brain injury. *Journal of Head Trauma Rehabilitation*, 2015: 30 (3): 24-32.

III Losoi, H., Silverberg, N., Wäljas, M., Turunen, S., Rosti-Otajärvi, E., Helminen, M., Luoto, T.M., Julkunen, J., Öhman, J., Iverson, G.L. Resilience is associated with outcome from mild traumatic brain injury. *Journal of Neurotrauma*, 2015: 32 (13): 942-949.

IV Losoi, H., Silverberg, N., Wäljas, M., Turunen, S., Rosti-Otajärvi, E., Helminen, M., Luoto, T.M., Julkunen, J., Öhman, J., Iverson, G.L. Recovery from mild traumatic brain injury in previously healthy adults. *Journal of Neurotrauma* (in press).

Abbreviations

AGFI	Adjusted Goodness-of-Fit Index
BDI-II	Beck Depression Inventory- Second Edition
BNI-FS	Barrow Neurological Institute Fatigue Scale
CFI	Comparative Fit Index
CT	Computed tomography
DWI	Diffusion weighted imaging
ED	Emergency department
FLAIR	Fluid-attenuated inversion recovery
GCS	Glasgow Coma Scale
GFI	Goodness-of-Fit Index
GOAT	Galveston Orientation and Amnesia Test
GOS-E	The Extended Glasgow Outcome Scale
ISI	Insomnia Severity Index
ISS	Injury Severity Score
LOC	Loss of consciousness
MRI	Magnetic resonance imaging
MTBI	Mild traumatic brain injury
PCL-C	PTSD-Checklist-Civilian Version
PCS	Post-concussion syndrome
PTSD	Post-traumatic stress disorder
QoL	Quality of life
QOLIBRI	Quality of Life after Brain Injury (instrument)
RAVLT	Rey Auditory Verbal Learning Test
RMSEA	Root Mean Square Error of Approximation
RNBI	Ruff Neurobehavioral Inventory
RPCSQ	Rivermead Post-concussion Symptom Questionnaire
RS	Resilience Scale
RS-14	Short (14-item) version of the Resilience Scale
RTW	Return to work
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences

SWI	Susceptibility weighted imaging
SWLS	Satisfaction with Life Scale
TBI	Traumatic brain injury
TMT	Trail Making Test
WAIS-III	Wechsler Adult Intelligence Scale – Third Edition
WHO	World Health Organization

1 Introduction

1.1 Mild traumatic brain injury

1.1.1 Definition and incidence of mild traumatic brain injury

Many different definitions and diagnostic criteria for Mild Traumatic Brain Injury (MTBI) exist in the literature. This has produced significant heterogeneity in patient groups included in the studies on MTBI. Common criteria for defining MTBI have been considered beneficial (Holm et al., 2005). For this purpose the following operational definition of MTBI was created by the World Health Organization's (WHO) Collaborating Centre for Neurotrauma Task Force (Holm et al., 2005): "MTBI is an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) one or more of the following: confusion of disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities, such as focal signs, seizure, and intracranial lesion not requiring surgery; (ii) Glasgow Coma Scale score of 13−15 after 30 minutes post-injury or later upon presentation for health care. These manifestations of MTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries (e.g. systemic injuries, facial injuries or intubation), caused by other problems (psychological trauma, language barrier or coexisting medical conditions) or caused by penetrating craniocerebral injury." Terms such as mild head injury, minor head injury, mild head trauma, mild brain injury, mild closed head injury, and concussion have been commonly used to refer to MTBI (Anderson et al., 2006; Iverson, 2005). In this study we use the term mild traumatic brain injury and define it according to the above mentioned WHO criteria.

It has been estimated that 70−90% of all treated brain injuries are mild with the incidence rate of hospital-treated MTBI about 100-300/100,000 (Cassidy et al., 2004). The average incidence rate of hospitalized TBI in Finland is 101/100,000 (Koskinen & Alaranta, 2008). However, because many patients with MTBI are not hospitalized, the true incidence has been estimated to be above 600/100,000 (Cassidy et al., 2004).

Higher incidence rates of MTBI have been found for males than females (Feigin et al., 2013).

1.1.2 Mechanisms and pathophysiology of mild traumatic brain injury

According to the WHO definition of MTBI (Holm et al., 2005) , the injury is caused by "mechanical energy to the head from external forces". This energy can result from the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, or forces from events such as blast or explosion (Management of Concussion/mTBI Working Group, 2009). The most common causes for MTBI include falls and motor-vehicle accidents (Cassidy et al., 2004).

The pathophysiology of MTBI varies from rapidly resolving cellular changes to macroscopic structural damage of the brain (McCrea et al., 2009). The rates of structural abnormalities vary significantly across studies (Iverson et al., 2012). In the most severe cases of MTBI, the macroscopic damage can include hemorrhagic or non-hemorrhagic contusions, shearing injuries, and cerebral edema (McCrea et al., 2009). However, most MTBIs are not associated with abnormalities on structural neuroimaging (Iverson et al., 2012). It has been suggested that most of the pathophysiology of MTBI produces dysfunction to neurons and neural systems but does not destroy them (Iverson, 2005) and little cell death is generally shown in studies (Giza & Hovda, 2014). The cellular and vascular changes after MTBI are complex and interwoven, including: ionic shifts, abnormal energy metabolism, diminished cerebral blood flow, and impaired neurotransmission (Iverson, 2005). After these immediate physiological changes the affected cells typically recover (Iverson, 2005). Recently, there has been increasing interest in the pathophysiology of repetitive MTBI but the mechanisms underlying traumatic axonal injury, microglial activation, amyloid-beta accumulation, and progressive tau pathology are not yet well understood (Brody et al., 2015). The pathophysiological changes after MTBI have been described in detail in a recent article by Giza and Hovda (2014).

1.2 Outcome from mild traumatic brain injury

Despite extensive research, there is considerable diversity in findings concerning outcome from MTBI. The expected recovery course from MTBI has been a subject of great debate (McCrea et al., 2009) and well-designed confirmatory studies have been called for to better understand its consequences (Carroll et al., 2014). Outcome from MTBI can be conceptualized and assessed in different dimensions, including symptomatic-, cognitive-, mental health-, quality of life-, or psychosocial outcome. Most studies on outcome from MTBI have only reported some aspects of these different outcomes. The current knowledge of different dimensions of outcome from MTBI is presented in the sections below.

1.2.1 Post-concussion symptoms and post-concussion syndrome

In literature symptoms after MTBI have been conceptualized as post-concussion symptoms. In many studies, outcome from MTBI is assessed solely by self-reporting of post-concussion symptoms. These typically include a combination of physical (e.g. headache, fatigue, nausea, balance problems, sensitivity to light/noise, sleep problems, and dizziness), cognitive (e.g. memory and concentration difficulties), and behavioral/emotional (e.g. irritability, depression, anxiety) symptoms. It has consistently been found that post-concussion-like symptoms are also common in the acute stage of other injuries and are thus not specific to MTBI (Cassidy et al., 2014; Meares et al., 2008; Mounce et al., 2013). For example, a high percentage of patients with chronic pain (Iverson & McCracken, 1997) and a non-head traumatic injury (Lange et al., 2012) have been found to report post-concussion-like symptoms.

Self-reported post-concussion symptoms are common after MTBI but there is little consistency of their persistence (Holm et al., 2005). Based on a recent review, post-concussion symptoms continued to persist until 6 months in 14% to 26% of the patients with MTBI (Cassidy et al., 2014). However, none of the studies included in this review included control groups (Cassidy et al., 2014). Studies using appropriate control groups typically report resolution of symptoms within weeks or few months (Holm et al., 2005).

Post-concussion syndrome (PCS) commonly refers to persisting post-concussion symptoms. Based on the diagnostic criteria (ICD10) (World Health Organization, 1992)

used in this study, a diagnostic threshold of three symptoms is required to be present for at least one month. Kraus et al. (2009) reported that about 32% of patients with MTBI had post-concussion syndrome at 3 months after injury compared to 19% in the comparison group of patients with non-head injuries (Kraus et al., 2009). They thus concluded that symptoms were more common in the MTBI group but not specific to MTBI. Prevalence rates for PCS as high as 50% for women and 30% for men have been reported after 3 years from injury (Styrke et al., 2013). Also in other studies a significant proportion (10 to 30%) of patients with MTBI have been reported to experience persistent PCS (Hou et al., 2012; Kraus et al., 2009; Sigurdardottir et al., 2009; Wood, 2004). However, it has been noted, that only a small percentage of cases continue to experience persistent symptoms if the representatives of the sample and the criteria of the syndrome are taken into account (Iverson et al., 2012; McCrea et al., 2009; Rees, 2003).

1.2.1.1 Fatigue

Fatigue is one of the most frequent symptoms after MTBI (Stulemeijer et al., 2006). It is very common especially in the beginning of the recovery, but can also be a persistent problem (Norrie et al., 2010) and limit daily functioning (Stulemeijer et al., 2006). In a study by Stulemeijer et al. (2006), one-third of patients experienced severe fatigue six months after MTBI. It has been found that fatigue after MTBI is not related to injury severity (Borgaro et al., 2005; Stulemeijer et al., 2006) number of days from injury to assessment, or cognitive impairment (Borgaro et al., 2005). The causes of fatigue after MTBI have been considered to be complex, interwoven, and at least partially treatable (Wäljas et al., 2012).

First, fatigue has been associated with psychological factors and depression in several studies (Norrie et al., 2010; Ponsford et al., 2012; Wäljas et al., 2012; Ziino & Ponsford, 2005). However, the nature or direction of the causality between depression and fatigue has not been established (Wäljas et al., 2012). Experiencing fatigue over an extended period may cause depression and anxiety (Ponsford et al., 2012). Patients with TBI are also particularly likely to experience psychosocial stressors, such as inability to return to work or financial difficulties, which can precipitate insomnia (Ouellet et al., 2004) and exacerbate fatigue (Norrie et al., 2010). Also perceived chronic stress has

been found to be a significant explanatory factor of fatigue after mild-to-moderate TBI (Bay & Xie, 2009).

Second, sleep disorders have been linked to fatigue but the causal relationship between them is unclear (Fogelberg et al., 2012). Brain regions and systems regulating alertness, attention, and sleep are known to be vulnerable to the effects of TBI (Ponsford et al., 2012). Thus, sleep disorders are common after TBI (Ouellet et al., 2004). They are reported to be even more common after a mild than a severe TBI (Clinchot et al., 1998). The prevalence of sleep problems after MTBI has been reported to range widely from 21% to 93% (Wallace et al., 2011). Psychological and environmental factors, such as psychosocial stressors related to TBI, may also have a role in explaining the high prevalence of sleep disturbances after TBI (Ouellet et al., 2004). It has also been suggested that mainly the individual's responses (e.g. adaptiveness of sleep habits, dysfunctional beliefs, and attitudes) relating to the initial sleep problem determine whether the sleep disturbance will become chronic (Ouellet et al., 2004).

Third, when studying fatigue, consideration of pain is especially important, because pain is strongly associated with sleep disorders (Beetar et al., 1996; Ouellet et al., 2004). Pain has often been suggested to be taken into account when assessing patients with MTBI (Beetar et al., 1996; Uomoto & Esselman, 1993), and pain is reported more frequently after MTBI than after more severe injuries (Lavigne et al., 2015; Uomoto & Esselman, 1993)—with headache being the most frequent pain type reported in the beginning of recovery (Lavigne et al., 2015). The mechanisms of chronic pain after MTBI are unknown (Lavigne et al., 2015). It has been well acknowledged that post-concussion-like symptoms, such as fatigue, irritability, and cognitive difficulties, are reported frequently by chronic pain patients (Iverson & McCracken, 1997; Stålnacke, 2012).

Thus, according to the literature, fatigue, sleep disorders, pain, and psychological distress are common and strongly intertwined symptoms after MTBI. Additional research on the interactions of these conditions and the contributing factors to fatigue has been considered essential for developing better management strategies and interventions (Bay & Xie, 2009; Bushnik et al., 2008; Fogelberg et al., 2012).

1.2.1.2 Cognitive outcome

Cognitive deficits, such as problems with concentration, memory, and executive functions, have been shown to be present soon after MTBI, but there is less agreement on when they resolve, due to a relatively small number of quality studies (Carroll et al., 2014). However, fairly rapid cognitive resolution is usually found with full recovery expected by 1-3 months (Holm et al., 2005; Karr et al., 2014; McCrea et al., 2009). By comparing the effect sizes from dozens of studies relating to multiple different clinical conditions, Iverson (2005) has shown that after the acute recovery period the effect of MTBI on cognition is very small, and for example considerably smaller than the effects of depression, litigation, or ADHD (see Figure 1). Despite this positive average prognosis, there is evidence of some objectively measured cognitive deficits up to 6 months after injury (Carroll et al., 2014). Thus, it has been suggested that the cognition of a subgroup of patients with MTBI may remain chronically impaired but the size and existence of this subgroup still remains debatable (Bigler et al., 2013; Dikmen et al., 2009; Karr et al., 2014; Rohling et al., 2012; Rohling et al., 2012). More well-conducted longitudinal studies are needed (Carroll et al., 2014).

1.2.1.3 Mental health outcome

There are few studies suggesting that MTBI increases the risk for psychiatric illness (Carroll et al., 2014). Thus, clinical monitoring of mood and psychiatric status may be useful after MTBI (Carroll et al., 2014). Post-injury depression prevalence rates of 7.1% (Bryant et al., 2010) and 10.7% (Meares et al., 2011) have been reported in patients with MTBI. However, it is not clear if the risk for these disorders is higher after MTBI in comparison to a non-head traumatic injury (Bryant et al., 2010; Meares et al., 2011). Post-traumatic stress disorder (PTSD) has recently been widely studied after MTBI (Bahraini et al., 2014). Its prevalence in civilian patients with MTBI has been estimated to range from 12% to 30% (Bahraini et al., 2014). MTBI and PTSD have been considered to have a bidirectional relationship and a potentially additive impact on symptoms (Bahraini et al., 2014). The differential diagnosis of these two conditions is challenging due to the overlap in symptoms, and the lack of objective markers (Bahraini et al., 2014). Besides these psychiatric conditions, MTBI has also been associated with increased irritability (Yang et al., 2013).

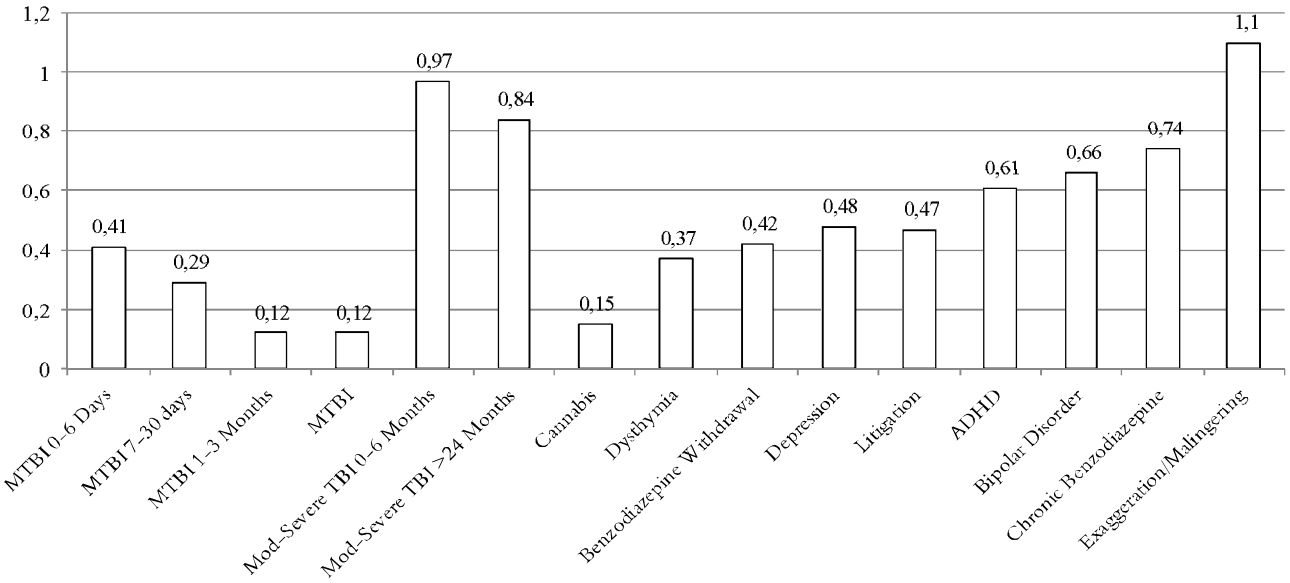

Figure 1. Effect sizes on neuropsychological functioning.

Effect sizes typically are expressed in pooled, weighted standard deviation units. However, across studies, there are some minor variations in the methods of calculation. By convention, effect sizes of .2 are considered small, .5 medium, and .8 large. This is from a statistical, not necessarily clinical, perspective. For this figure, the overall effect on cognitive or neuropsychological functioning is reported. Effect sizes less than.3 should be considered very small and difficult to detect in individual patients because the patient and control groups largely overlap. MTBI 0-6 days, 7-29 days, 30-89 days, moderate-severe TBI 0-6 months, > 24 months, 39 studies, N = 1,716 TBI, N = 1,164 controls; MTBI, 11 studies, N = 314 MTBI, N = 308 controls; Cannabis, long-term regular use, 11 studies, N = 623 users, N = 409 non or minimal users; Dysthymia, Depression, & Bipolar Disorder, 3 comparisons for dysthymia, 97 comparisons for depression, and 15 comparisons for bipolar disorder; Benzodiazepine withdrawal, 10 studies, long-term follow-up, 44 comparisons; Litigation/financial incentives, 17 studies, N = 2,353 total; ADHD, based on Full Scale IQ, 123 studies; Chronic benzodiazepine use, 13 studies, N = 384, 61 comparisons; Exaggeration/malingering, 32 studies published between 1985 and 1998, 41 independent comparisons.

Adapted and reprinted with permission from Iverson, G.L. (2005). Outcome from mild traumatic brain injury. *Current Opinion in Psychiatry, 18*, 301-317.

1.2.2 Quality of life

Quality of life (QoL) has been considered a useful outcome to measure in studies of MTBI (Petchprapai & Winkelman, 2007). However, there is a limited data concerning QoL in patients with MTBI (Beseoglu et al., 2013). For example, none of the 23 studies included in a recent review (Cassidy et al., 2014) of outcome from MTBI reported QoL. Longitudinal studies of QoL after MTBI have been called for (Petchprapai & Winkelman, 2007).

The available studies have suggested that MTBI is associated with lower QoL. Post-concussion symptoms correlate with low levels of life-satisfaction (Emanuelson et al., 2003; Stålnacke, 2007) and QoL (King & Kirwilliam, 2011). Generic QoL has been reported to be significantly lower in patients with MTBI than the normative control group at 3 and 12 months (Emanuelson et al., 2003) and at 3 years after injury (Åhman, et al., 2013). However, it has been suggested that a nonspecific QoL assessment is not sufficient to cover all aspects of MTBI-related impairment (Beseoglu et al., 2013) and according to the recommendations by the TBI Consensus Group (Bullinger et al., 2002), the assessment of QoL after TBI should include both a disease specific and a generic instrument. A disease-specific measure of QoL after TBI has not been available until the development of QOLIBRI (Quality of Life after Brain Injury; (Steinbüchel et al., 2010)). Using QOLIBRI, patients with MTBI have been found to have lower QoL compared to more severe injuries (Siponkoski et al., 2013). The selection of the sample from a residential rehabilitation setting could be one possible explanation for this finding (Siponkoski et al., 2013).

1.2.3 Return to work

Return to work (RTW) is an important domain for evaluating functional outcome after MTBI. The best available evidence suggests 80% to 95% RTW rates for patients within 3 to 6 months after MTBI and that MTBI is not considered a significant risk-factor for delayed RTW (Cancelliere et al., 2014). However, only four studies were accepted in this recent systematic review (Cancelliere et al., 2014) and the authors conclude that making firm conclusions is limited due to varying patient characteristics and MTBI definitions. It is also common for MTBI patients to RTW while still experiencing symptoms (van der Naalt et al., 1999).

Previous studies have shown that anxiety, depression (van der Horn et al., 2013), and PTSD (Friedland & Dawson, 2001) are related to delayed RTW following MTBI. Patients with complicated MTBIs (ie., those with trauma-related intracranial abnormalities on neuroimaging) have been found to be slower to RTW than those with uncomplicated MTBIs (Wäljas et al., 2014). However, standard computed tomography (CT) or magnetic resonance imaging (MRI) techniques have not shown sufficient prognostic value for predicting delayed RTW (Beseoglu et al., 2013; Hughes et al., 2004). Additional bodily injuries and fatigue are strongly associated with delayed RTW after MTBI (Wäljas et al., 2014). The results from studies relating to risk factors (i.e., demographic, background history, injury severity, and clinical outcome variables) for delayed RTW after TBI, however, have been inconsistent (Saltychev et al., 2013). According to a review (Saltychev et al., 2013), no strong evidence has been found that vocational outcomes following TBI could be reliably predicted or improved.

1.3 Factors associated with outcome from mild traumatic brain injury

According to a famous quote from Symonds, "It is not only the kind of injury that matters, but the kind of head" (Symonds, 1937). The cause of persistent symptoms after MTBI is multifactorial (Iverson et al., 2012). Thus, outcome from MTBI should be conceptualized from a biopsychosocial perspective (Iverson et al., 2012; King & Kirwilliam, 2011) which is presented in Figure 2. The known risk-factors associated with poor outcome from MTBI that are essential for this study are discussed in the next sections.

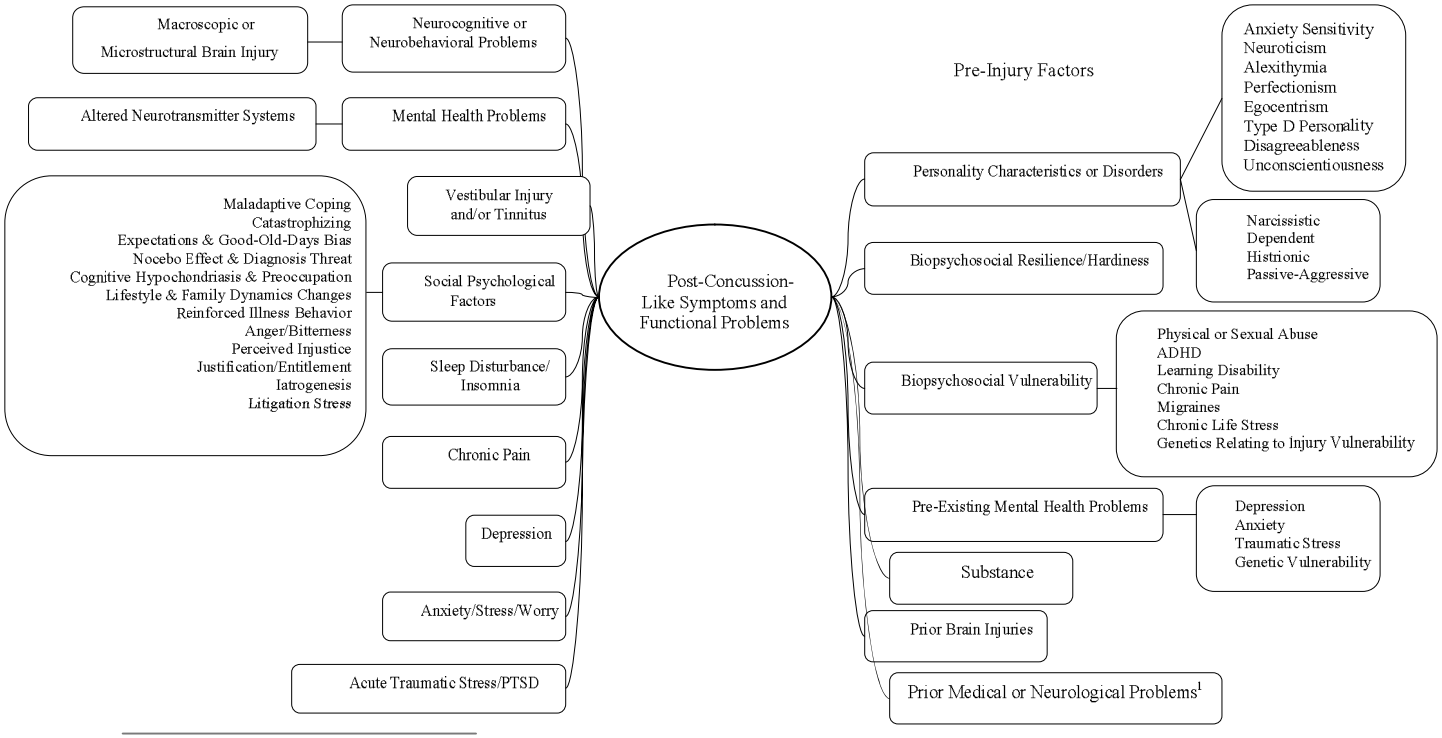

Figure 2. A biopsychosocial conceptualization of poor outcome from MTBI.

[1]For example, hypertension, heart disease, cardiac surgery, diabetes, thyroid problems, and small vessel ischemic disease.

Note: Structural and/or microstructural damage to the brain is not necessary to cause or to maintain the symptoms comprising a post-concussion syndrome. Moreover, structural and/or microstructural damage, if present, is likely insufficient to causally maintain a persistent post-concussion syndrome. Assuming that a constellation of persistent symptoms are present (i.e., not exaggerated), there are many factors that could, singly or in combination, be the underlying cause of these symptoms. Notably, patients with chronic pain frequently report a constellation of symptoms that are post-concussion-like, and patients with depression are virtually guaranteed to report symptoms that mimic a post-concussion syndrome (in the absence of a history of head trauma).

1.3.1 Socio-economic and trauma-related risk factors for poor outcome

Women have usually been found to report more post-concussion symptoms after MTBI than men (Bazarian et al., 2010; Kraus et al., 2009; Mounce et al., 2013; Styrke et al., 2013). However, Bazarian et al. (2010) found that despite reporting more symptoms, women did not return to normal activities or work more slowly than men after MTBI, and there are also findings suggesting women having a better functional outcome from MTBI (Dagher et al., 2013). Greater age (Dagher et al., 2013; King & Kirwilliam, 2011; Zhang et al., 2009) and lower education (Cancelliere et al., 2014; Stulemeijer et al., 2008) have also been found to be risk-factors for poor outcome.

Health status has been associated with clinical outcome from MTBI. For example, McLean et al. (2009) examined patients with a minor injury to the head or elsewhere in the body and found that baseline mental and physical health status were associated with persistent post-concussion syndrome but head injury was not (McLean et al., 2009). In another study, patients who reported having excellent health prior to MTBI were also more likely to report excellent or very good health after injury, regardless of injury severity (Zhang et al., 2009).

Socio-cultural factors may also affect outcome from MTBI. Patients from low- and middle income-countries are less likely to be disabled after a mild or moderate brain injury than patients from high income-countries (De Silva et al., 2009). This might be explained by different social security systems and patterns of social relationships, for example (De Silva et al., 2009). There are also differences between countries and ethnicities in symptom expectations (Ferrari et al., 2001) and perceptions of health (Brown et al., 2004) after a head injury.

Compensation-seeking is associated with increased reporting of post-concussion symptoms (Kashluba et al., 2008) and slower return to work (Reynolds et al., 2003). Involvement in litigation has been considered to influence recovery and to be a major source of stress after MTBI (Iverson et al., 2012). The mechanism and context of MTBI also have to be considered. Motor vehicle accidents, for example, are considered a risk factor for poor outcome (Dagher et al., 2013). This is possibly due to increased frequency of associated musculoskeletal injuries (Dagher et al., 2013), more common psychological traumatization, and access to compensation (Iverson et al., 2012). In contrast, outcome from sport-related injuries is usually better (Iverson et al., 2012).

Findings regarding the association between trauma-related intracranial abnormalities and outcome are inconsistent. Some studies (Lange et al., 2009; van der Naalt et al., 1999; Yuh et al., 2014) have found outcome to be worse for those MTBI patients with findings on brain imaging whereas others have not (Hughes et al., 2004; Lange et al., 2012; Wäljas et al., 2014; Wäljas et al., 2015). A genetic predisposition (such as apolipoprotein E) for poorer outcome after TBI has also been suggested (Han et al., 2007). However, according to a recent review (Davidson et al., 2014), the results on the impact of genetic variation on outcome from TBI have been contradictory due to heterogeneity of studies.

1.3.2 Psychological risk factors for poor outcome

It is well known that pre-injury psychiatric problems are a risk factor for poor outcome from MTBI. Patients with pre-injury psychiatric disorders, such as depression or anxiety, have consistently been shown to have a worse outcome (Dagher et al., 2013; Evered et al., 2003; Kashluba et al., 2008; Meares et al., 2008; Meares et al., 2011; Ponsford et al., 2012). In addition, a history of stressful events (Veldhoven et al., 2011) and certain personality traits, such as dependent, narcissistic, and compulsive, have been found to predispose to having poor outcome from MTBI (Evered et al., 2003; Garden, Sullivan, & Lange, 2010).

There is also compelling evidence that co-occurring psychological variables influence recovery after MTBI. The severity of post-concussion symptoms has been found to correlate with psychological distress more than with MTBI severity or performance on cognitive tests (Silverberg & Iverson, 2011). In one study, post-injury anxiety was associated with PCS at three months after MTBI (Ponsford et al., 2012). Ponsford et al. (2012) suggested that the experienced symptoms can cause anxiety which in turn can exacerbate symptoms. Besides symptom reporting, psychological well-being, depression, and chronic stress have been consistently related to quality of life after TBI (Bay & Xie, 2009; Cicerone & Azulay, 2007; Siponkoski et al., 2013).

Negative expectations about head injuries have been shown to be associated with poorer cognitive test performance (Suhr & Gunstad, 2002; Suhr & Gunstad, 2005) and increased cognitive complaints (Ozen & Fernandes, 2011) in university students with a history of self-reported mild head injury. In these studies students had lower

performance in cognitive tests and reported more cognitive symptoms if their attention was called to a history of a prior head injury ("diagnosis threat") and the potential effects of such injury on cognition than subjects with a similar history of a head injury who did not have their attention called to it. Others have suggested that "diagnosis threat" may have a greater impact on psychological factors, such as academic self-efficacy, than on cognitive performance (Trontel et al., 2013). Illness perceptions have also been shown to affect recovery in patients with documented MTBI (Snell et al., 2011; Whittaker et al., 2007). In a study of Whittaker et al. (2007), symptomatic patients who believed their symptoms to have serious consequences on their lives in the future were at heightened risk for experiencing enduring post-concussion symptoms. Snell et al. (2011) reported that patients with poor outcome had stronger beliefs about the nature and consequences of the injury and less understanding of their condition. In addition, the initial behavioral responses, such as all-or-nothing behavior, are strong predictors of the development of PCS in the early stages (Hou et al. 2012). In the longer term, beliefs about the injury predict outcome from MTBI (Hou et al.2012).

The findings about coping after TBI are somewhat inconsistent. Increased use of unproductive (characterized by passive reactions and avoidance strategies) and decreased use of productive (or problem-solving focused) coping has been found to predict poorer psychosocial outcome at 1-year in a sample of mixed-severity TBI (Gregorio et al., 2014). Moreover, avoidant coping has been shown to be associated with worse emotional functioning and quality of life after MTBI (Maestas et al., 2014). However, in another study, the use of active coping has also been associated with poor outcome from MTBI (Snell et al., 2011). The authors hypothesized that the symptoms might become more stressing if the patients expect themselves to be able to manage recovery (Snell et al., 2011).

Based on previous literature, it can be concluded that various psychological concepts are linked to recovery from MTBI. It has been noted before (Heitger et al., 2007) that patients with mild head injury report significantly more post-concussion symptoms up to one year after injury but the recovery measured by the functional status and quality of life is better and quicker. According to Heitger et al. (2007) this discrepancy between reported post-concussion symptoms and relatively normal functionality and quality of life could suggest that the "good recovery" from MTBI may involve a behavioral

adaptation rather than a complete return to a previous health-status. One possibly useful construct to examine this adaptation after MTBI is resilience, which will be addressed in the next section.

1.4 Resilience

1.4.1 Definition of resilience

In this study resilience is defined as an ability to recover from adversity (Wagnild, 2009b). It is as a positive characteristic that enhances adaptation and moderates the negative effects of stress (Wagnild & Young, 1993). Resilience, as defined here, has been suggested to be comprised of five interrelated components: 1) *equanimity* (a balanced perspective of one's life and experiences); 2) *perseverance* (the act of persistence despite adversity or discouragement); 3) *self-reliance* (a belief in oneself and one's abilities); 4) *meaningfulness* (the realization that life has a purpose); and 5) *existential aloneness* (the realization that each person's life path is unique) (Wagnild & Young, 1993).

Based on the review of dictionary definitions, the consistent theme among the definitions of resilience is "a sense of recovery and rebounding despite adversity or change" (Earvolino-Ramirez, 2007). The defining attributes of resilience that repeatedly appear in the literature also include high expectancy/self-determination, positive relationships/social support, flexibility, sense of humor, and self-esteem/self-efficacy (Earvolino-Ramirez, 2007). The concept of resilience, however, lacks a definitive definition (Neenan, 2009).

Originally, the concept of resilience came from psychiatric literature examining children who were considered to be "invulnerable" to adverse life situations (Earvolino-Ramirez, 2007). Richardson (2002) has presented how the resilience theory has developed in three waves. Historically, the first wave identified resilient qualities, such as adaptability, tolerance, achievement orientation, self-efficacy, planning skills, positive outlook, and self-esteem, by studying different groups of people with a positive outcome though considered to be at high risk due to their environment. The second wave examined the way in which the resilient qualities are acquired through disruptions that can range from minor events (like new information) to life-changing experiences

(like loss of a loved one). Finally, the third wave examined the question about the source of resilience (Richardson, 2002).

Originally resilience was referred to as a personality trait (Earvolino-Ramirez, 2007). However, the term resilience has been also used to refer to a dynamic developmental process (Luthar et al., 2000). It has been considered to be an innate characteristic each person possesses to some degree, but which can also be enhanced or diminished depending on life circumstances (Wagnild, 2003), or be learned (White et al., 2008). Findings about resilience increasing with age (Lundman et al., 2007) support this notion. Thus, resilience is not a fixed attribute someone either has or does not have (Neenan, 2009; White et al., 2008), but instead, something that is continually shaped by interactions with the environment (Luthar & Cicchetti, 2000).

The construct of resilience should thus not be misinterpreted as representing a fixed and longstanding personal attribute of the individual (Luthar & Cicchetti, 2000). This is important to note because this misinterpretation could be used to make the individual inappropriately responsible or to blame for not possessing the characteristics needed to function well (Luthar & Cicchetti, 2000).

1.4.2 The social and neurobiological underpinnings of resilience

Resilience has been considered to result from the operation of basic human adaptational systems (Masten, 2001). The social environment, however, is important for the development of resilience (Helgeson & Lopez, 2012; Neenan, 2009). For example, family and social support systems have been considered to be part of the resilience of the individual (White et al., 2008; Zimmerman & Brenner, 2012). In addition, religiousness is a significant resilience factor for many, because it may provide belief in the meaningfulness of life and be associated with receiving social support (Pargament & Cummings, 2012).

Adverse experiences in early life are known to increase the risk for psychiatric problems (Feder et al., 2012). Recent advances in neuroimaging and genetics have allowed for a closer study of the biological underpinnings of this association and resilience (Lemery-Chalfant, 2012), which has been suggested to depend upon the unique neurological capacity of the individual (McEwen et al., 2015). Early life experiences produce changes to hormonal, neurotransmitter, and central nervous

systems (Feder et al., 2012) and may affect the brain architecture involved in cognitive flexibility (McEwen et al., 2015). The brain controls many of the behaviors involved in adaptation and neural functioning partly determines whether the individual's response (for example autonomic, cortisol, immune/inflammatory, metabolic, and neuromodulators) to stressors is effective (McEwen et al., 2015). For example, the hippocampus and the amygdala affect the response to stressors, and are in turn affected by early development and stress (McEwen et al., 2015). When studying patients with TBI, it should be taken into account, that the neuropathology caused by the injury can affect the functioning of these nervous systems. Also, the neurobiological and developmental underpinnings of resilience should not be considered deterministically, because though this adaptability to stressors has been biologically embedded in early life, brain architecture continues to show plasticity throughout the life (McEwen et al., 2015).

Multiple genes have also been suggested to be involved in the process of resilience (Lemery-Chalfant, 2012). The effect of genes, however, is not deterministic either with positive experiences in the social environment having a potential to protect against the negative effects of genetic risk (Lemery-Chalfant, 2012). Identification of genes that promote resilience in stressful situations has been considered an important area of research in the future (Zautra et al., 2012).

1.4.3 Related concepts and their associations with outcome from TBI

Many related concepts to resilience exist in the psychological literature. *Health locus of control* (HLC) was defined by Rotter as "the degree to which individuals believe their health is controlled by internal (within the person) or external factors (outside the person)" (Rotter, 1966). Internal HLC reflects how strongly the individual believes his health to be determined by his own behavior, whereas examples of external HLC include believing that chance or healthcare professionals control good health (Wielenga-Boiten et al., 2015). Lower than average internal HLC has been found in patients with mixed-severity (with samples of mainly moderate to severe injury) TBI (Izaute et al., 2008; Wielenga-Boiten et al., 2015) with associations to lower health-related quality of life (Wielenga-Boiten et al., 2015).

The concept of *Hardiness* was introduced by Kobasa (1979). According to her, "hardy persons are considered to possess three general characteristics: (a) the belief that they can control or influence the events of their experience, (b) an ability to feel deeply involved in or committed to the activities of their lives, and (c) the anticipation of change as an exciting challenge to further development" (Kobasa, 1979). *Sense of coherence* has been defined by Antonovsky (in (Eriksson & Lindstrom, 2005)) as a "global orientation to view the world and the individual environment as comprehensible, manageable, and meaningful". According to this theory, the way people view their life has an influence on their health (Eriksson & Lindstrom, 2005). Sense of coherence has been found to be strongly associated with life satisfaction in a study of patients with mixed-severity TBI (Jacobsson et al., 2011) and with post-traumatic growth after severe TBI (Powell et al., 2012).

Self-efficacy has been defined by Bandura as "people's beliefs about their capabilities to produce designated levels of performance that exercise influence over events that affect their lives" (Bandura, 1994). Self-efficacy, particularly for the management of cognitive symptoms, has been shown to have a strong association with life satisfaction after TBI (Cicerone & Azulay, 2007). In addition, self-efficacy has been associated with lower anxiety related to discharge from rehabilitation in patients with moderate to severe TBI (Genis et al., 2015) and with long-term QOL in patients with mixed etiology (mainly infarction) acquired brain injury (Brands et al., 2014).

Another related concept is *coping*, which has been defined by Folkman and Lazarus as "the constantly changing cognitive and behavioural efforts to manage the specific external or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984). The findings about the association of coping and recovery from TBI have been presented previously in section 1.3.2.

Concepts similar to resilience have been studied in psychology for a long time and the contents of these related concepts at least partly overlap with resilience. It has been suggested that the ability to recognize the effects of stressful situations and to experience positive outcomes despite adversity sets resilience apart from other similar constructs (Tugade & Fredrickson, 2004). Further concept analysis is beyond the scope of this study. The above mentioned research has shown the association between these related concepts and outcome from TBI, but most studies have been conducted in

patients with moderate to severe or mixed-severity TBI. Thus, there is limited knowledge about the relationship between resilience and recovery from MTBI.

1.4.4 The associations of resilience, behavior, and well-being

Resilient people manifest adaptive behavior in somatic health (Wagnild & Young, 1993) and experience positive emotions even in negative circumstances (Tugade & Fredrickson, 2004). Resilience is, however, not about the lack of (or suppressing) negative emotions but rather about managing those emotions and not getting stuck in them (Neenan, 2009). What differentiates those who are resilient from the non-resilient is the struggle to find some way to a better future, whether it is through support from others and the willingness to receive it, seeking professional help, searching for strengths from within yourself, or the combination of these (Neenan, 2009).

The association of resilience and well-being has been proposed to be mediated by positive views (Mak et al., 2011). However, resilience is not just a psychological phenomenon but reflects to the body as well (Tugade & Fredrickson, 2004). Tugade and Fredrickson (2004) reported that those who rated themselves as more resilient and experienced more positive emotions also demonstrated this quality physiologically by quickly returning to baseline levels of physiological (cardio-vascular) responding after negative emotional arousal. People who are optimistic, hopeful, and engaged in a cause also have higher immune levels than those that perceive themselves as helpless, hopeless, and depressed (Richardson, 2002).

According to previous studies on non-TBI samples, resilience has a positive correlation with life satisfaction, self-esteem, self-rated health, self-actualization, stress management, and social support, and a negative correlation with depressive symptoms and anxiety (Abiola & Udofia, 2011; Heilemann et al., 2003; Humphreys, 2003; Nishi et al., 2010; Wagnild & Young, 1993; Wagnild, 2009b). Results from other health conditions have also suggested that resilience could be associated with fatigue. In cancer patients, resilience was found to be the best predictor of initial fatigue, but not as a predictor of changes in fatigue during radiation therapy (Strauss et al., 2007). In patients with Parkinson´s disease, resilience was found to correlate with fatigue and depression, along with less disability and better health-related quality of life (Robottom et al., 2012). Resilience has also been found to predict the physical health of patients

with diabetes (Yi et al., 2008), and optimal functioning in people aging with disability (Silverman et al., 2015), and to be a possible predictor of psychological distress in chronic spinal cord injury (Shin et al., 2012).

1.4.5 Resilience and outcome from mild traumatic brain injury

It has been suggested that resilience could play an important role in adaptation after TBI (White et al., 2008). The framework of resilience could provide a broader understanding to pre-injury risk for poor outcome from MTBI (Iverson et al., 2012) and a new way for brain injury professionals to develop interventions (Godwin & Kreutzer, 2013).

Despite growing interest during recent years, little research to date has been done on the association between resilience and outcome from MTBI. However, there is preliminary evidence that resilience may contribute to recovery from MTBI. McCauley et al. (2013) asked 46 patients with MTBI to assess their pre-injury resilience using the Connor-Davidson Resilience Scale and found that greater pre-injury resilience was significantly associated with lower post-concussion symptom severity (in Rivermead Post-concussion Symptoms Questionnaire) within the first month after MTBI. However, when controlling for known prognostic factors such as age, gender, and education, greater resilience was paradoxically associated with greater symptom severity. The authors hypothesized that this paradoxical finding could be explained by people with higher resilience not yet having had sufficient time to bounce back during the study period or by unmeasured but important mediator variables (McCauley et al., 2013). Two other studies have found resilience to be clearly associated with outcome from MTBI. In a study of Merrit et al. (2014), the resilience of 196 U.S. military service members with MTBI was assessed with the Response to Stressful Experiences Scale and the outcome with Neurobehavioral Symptom Inventory and PTSD Checklist-Civilian. They found that the low resilience group reported greater symptomatology compared to the moderate and high resilience groups (Merritt et al., 2014). In addition, in a recent study by Sullivan et al. (2015), greater resilience predicted less PCS-like symptomatology, even more than having a history of MTBI or not (Sullivan et al., 2015). In this study resilience was evaluated using The Brief Resilience Scale and symptoms with the Neurobehavioral Symptom Inventory. Finally, another recent study on patients with mild to severe TBI found that patients with TBI had lower resilience than the general

population (Lukow et al., 2015). In this study low resilience was associated with psychological distress and psychosocial maladjustment (Lukow et al., 2015). Thus, based on the four available studies on the subject, there is preliminary evidence that resilience could be associated with outcome from MTBI.

1.4.6 Resilience in rehabilitation

Viewing resilience as a process or an attribute that can develop allows for consideration of possible interventions. There has been a paradigm shift away from a problem-oriented approach toward focusing and nurturing strengths in the field of rehabilitation (Godwin & Kreutzer, 2013; Richardson, 2002; White et al., 2008). Resilience has been considered as a major construct in this positive psychology paradigm (Bertisch et al., 2014; Mak et al., 2011; Richardson, 2002; White et al., 2008), which has created a trend toward building competence instead of correcting weaknesses in treatment (Cui et al., 2010). Resilience is a useful construct in rehabilitation psychology because the goal of rehabilitation usually is to help individuals to learn to cope and adjust with adversity (White et al., 2008).

Considering resilience is important for rehabilitation in various ways. First, knowledge about resilience can help in targeting interventions (White et al., 2008). Second, an understanding and knowledge of resilient characteristics and processes can help health professionals to promote such behaviors (Ahern et al., 2006). Resilience has been improved by an intervention in earlier studies involving groups of employees, soldiers, cancer patients, and college students (Aikens et al., 2014; Lester et al., 2013; Loprinzi et al., 2011; Steinhardt & Dolbier, 2008). Based on a recent systematic review (Macedo et al., 2014), there is evidence of some degree of effectiveness of resilience promotion programs, but more quality research is needed.

1.4.7 Assessment of resilience

1.4.7.1 The Resilience Scale

The Resilience Scale (RS) was developed by Wagnild and Young (1993) to identify the degree of individual resilience (Wagnild & Young, 1993). The RS is a 25-item self-report questionnaire. The Finnish version is presented in Appendix 1. A short version (RS-14) that consists of 14 items (items 2, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 21, and

23) of the original scale was later developed by Wagnild (Wagnild, 2009b). The RS has performed as a reliable and valid tool to measure resilience, and it has been used with a wide range of study populations (Wagnild, 2009a). It has been regarded as the best assessment method to evaluate resilience in the adolescent population due to good psychometric properties and applications in a variety of age groups (Ahern et al., 2006).

The items of the RS were drawn from interviews of persons who characterized the generally accepted definitions of resilience. Thus, the RS has been argued to have a priori content validity (Wagnild & Young, 1993). According to Wagnild and Young (1993), the items of the RS were selected to reflect five interrelated components of resilience: 1) equanimity, 2) perseverance, 3) self-reliance, 4) meaningfulness, and 5) existential aloneness. Thus, one might expect to observe a five-factor structure of RS. However, the factor structure of the RS has not been consistent in previous studies and the expected five factors have only been found in one study (Lundman et al., 2007). The original authors (Wagnild & Young, 1993) found a two-factor solution which explained a total of 44.0% of the variance. Other studies have been ambivalent on the factor structure (Aroian et al., 1997; Heilemann et al., 2003; Nishi et al., 2010).

The internal consistency of the original RS (α = .91) and the RS-14 (α =.93) has been reported to be excellent (Wagnild & Young, 1993; Wagnild, 2009b). The RS has been translated into various languages and the internal consistency of the Russian (Aroian et al., 1997), Spanish (Heilemann et al., 2003), Swedish (Nygren et al., 2005), Japanese (Nishi et al., 2010), and Nigerian (Abiola & Udofia, 2011) versions has also been reported acceptable (α between .83 and .93). The stability of the RS over time (test-retest correlations ranging from 0.67 to 0.84) has been reported in an unpublished study (Wagnild & Young, 1993), and the test-retest reliability of the Swedish version (after one month) was 0.78, but further research about stability is needed (Lundman et al., 2007). The Finnish versions of the RS or the RS-14 have not previously been available.

1.4.7.2 Other assessment methods of resilience

Various questionnaires to evaluate resilience have been introduced in the literature. For example, ten different scales were included in a recent review of resilience measures (Smith-Osborne & Whitehill Bolton, 2013). Four scales were found for use with children and adolescents: 1) *Resilience Scale for Adolescents* (Hjemdal, 2007), 2)

Resilience Scale for Children and Adolescents (Prince-Embury, 2008), 3) *Adolescent Resilience Scale* (Oshio et al., 2003), and 4) *Resilience Skills and Abilities Scale* (Jew et al., 1999). Besides the Resilience Scale (Wagnild & Young, 1993), used in this study, five other adult resilience scales were identified for use with adults (Smith-Osborne & Whitehill Bolton, 2013). These include: 1) *The Connor-Davidson Resilience Scale* (Connor & Davidson, 2003), 2) *The Baruth Protective Factors Inventory* (Baruth & Carroll, 2002), 3) *Resilience in Midlife* (Ryan & Caltabiano, 2009), 4) *Resilience Scale for Adults* (Friborg et al., 2003), and 5) *Brief Resilience Coping Scale* (Sinclair & Wallston, 2004). The review considered the methodological quality of the adult scales as high (Smith-Osborne & Whitehill Bolton, 2013). The more detailed examination of these different scales is beyond the scope of this study. The above mentioned review (Smith-Osborne & Whitehill Bolton, 2013) and two other available reviews (Ahern et al., 2006; Windle et al., 2011) can be referred to for further information on the psychometric properties of the different resilience scales.

2 Aims of the study

The purpose of this study was to examine resilience and recovery after MTBI. The study addressed the measurement of resilience by evaluating the reliability and validity of the Resilience Scale (Wagnild & Young, 1993) and the association of resilience and outcome from MTBI. The five aims, addressed in four studies, are listed below.

1. To investigate the psychometric properties of the Finnish version of the Resilience Scale and its short version (RS-14) (Study I).
2. To assess the reliability and validity of The Resilience Scale in MTBI research (Study III).
3. To examine resilience as a predictor of self-reported fatigue after MTBI (Study II).
4. To examine the association between resilience and outcome from MTBI (Study III).
5. To thoroughly and prospectively report the recovery from MTBI in a sample of previously healthy adults by addressing several limitations in previous MTBI literature (Study IV).

3 Methods

3.1 Study frame and ethical issues

This thesis is part of a larger research program (Tampere Traumatic Head and Brain Injury Study) that aims to identify factors affecting long-term outcome from MTBI. The study group includes researchers from neuropsychology, neurosurgery, neurology, and neuroradiology. The author, Heidi Losoi, has been, as part of the study group, designing the study concept. She has also conducted the majority of the neuropsychological examinations for this study.

Ethics approval for the study was obtained from the Ethics Committee of Pirkanmaa Hospital District, Finland. All subjects gave informed written consent according to the Declaration of Helsinki.

3.2 Subjects

3.2.1 Study I

The data for study 1 was a convenience sample collected by researchers and psychology students mainly from the departments of their workplaces and from the university. The study group consisted of 243 participants [182 (75%) women and 61 (25%) men]. The age of participants ranged from 17 to 92 (mean of 41.0, SD=17.8) with no difference between men and women. The sample was relatively highly educated, with 45% having 17 years of education (range from 8 to 17 years, mean 14.8, SD=2.7).

3.2.2 Studies II, III, and IV

Subjects were enrolled consecutively from the Emergency Department of the Tampere University Hospital, between August 2010 and July 2012. All consecutive patients with head CT due to acute head injury (n=3,023) were screened to obtain a sample of working aged adults without pre-injury medical, psychiatric, or neurological problems who sustained a MTBI, who probably could be reached for an outcome visit, and who were without known communication problems. Criteria for treatment in the emergency department, and indication for acute head CT, were based on the Scandinavian guidelines for initial management of minimal, mild, and moderate head injuries

(Ingebrigtsen et al., 2000). Subjects were included in the study if they: (i) met MTBI criteria of the World Health Organization's Collaborating Centre for Neurotrauma Task Force (Holm et al., 2005), (ii) were aged between 18 and 60 years, and (iii) were residents of the hospital district. Subjects were excluded if they had: (i) premorbid neurological problems, (ii) prior psychiatric problems, (iii) past TBI, (iv) regular psychoactive medication use, (v) neurosurgery, (vi) problems with vision or hearing, (vii) first language was not Finnish, (viii) the time interval between injury and arrival to the emergency department was over 72 hours, and/or (ix) they declined to participate in the study. The major causes of exclusion were: (i) age criteria not met (n=1,552, 51.3%), (ii) MTBI criteria not met (n=942, 31.2%), (iii) psychiatric problems (n=860, 28.4%) and/or (iv) neurological problems (n=744, 24.6%). The cumulative effect of the exclusion criteria on the sample size is presented in Figure 3. Notably, there was major overlap in the causes of exclusion; some patients had multiple reasons. Patient enrolment details are discussed thoroughly in our previous publication (Luoto et al., 2013).

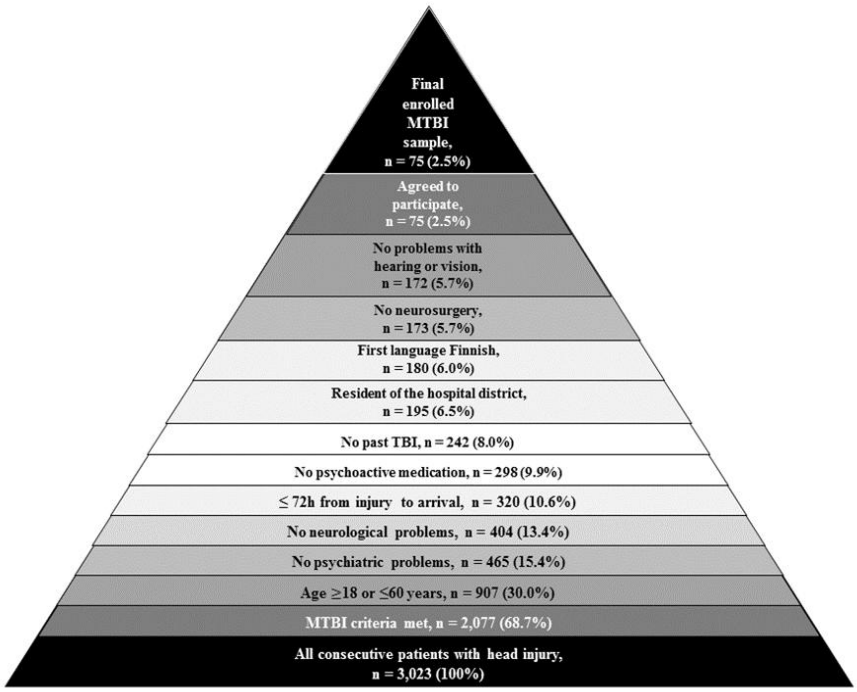

Figure 3. The cumulative effect of the inclusion criteria on the sample size (the number of patients included after each criteria).

Control subjects were orthopedically-injured patients evaluated in the same emergency department as the patients with MTBI. All consecutive patients (n = 609) with ankle injury (bone fracture or distension) were screened for inclusion. The same study criteria used with the MTBI sample were applied in the enrolment of the controls when applicable. Control subjects were enrolled in an age and sex stratified manner, with five men and five women in the following age groups: (i) 18-30 years, (ii) 31-40 years, (iii) 41-50 years and (iv) 51-60 years.

By applying the above mentioned inclusion and exclusion criteria 75 patients with MTBI and 40 trauma controls were recruited from the initial two cohorts [(i) MTBI (n=3,023): CT-imaged head injury patients, and (ii) Controls (n=609): orthopedically-injured patients]. Seventy-four (n=74) patients with MTBI and 40 trauma controls attended follow-up and thus formed the final sample of studies III and IV. The characteristics of the patients with MTBI and the controls are described in Table 1. There were no statistically significant differences between the patients with MTBI and controls in age, education (in years), or gender. None of the controls had loss of consciousness or traumatic findings on MRI. The MTBI group had slightly more physical injuries (ISS) than the controls but the difference did not reach statistical significance. There were no significant differences between the MTBI group and the controls in the time from injury to completing the questionnaires (at 1 and 12 months) or attending to the neuropsychological examination at 1 month after injury. The difference in days to completing the 6 month questionnaires was statistically significant but small (7.7 days). It can be considered clinically irrelevant.

One control subject did not complete the questionnaires used in this study and was excluded from study III. Sixty-seven (n=67) patients with MTBI and 35 trauma controls completed both assessments at 1 and 6 months and thus formed the final sample of study II. Because of a possible confounding effect, one control subject was excluded from the analysis of study III due to untreated severe obstructive sleep apnea.

Table 1. Characteristics of patients with mild traumatic brain injury (MTBI) and orthopedic controls (ankle injury).

Descriptive variables	MTBI (n =74)	Controls (n =40)	p-value*	Cohen's d
Gender Female: n (%)	29 (39.2)	20 (50.0)	0.266	NA
Age (years): Mean (SD)	37.0 (11.8)	40.1 (12.2)	0.186	-0.26
Education (years): Mean (SD)	14.2 (3.1)	14.1 (2.8)	0.891	0.03
Injury Severity Score: Mean (SD)	3.9 (3.2)	2.6 (1.5)	0.056	0.48
Traumatic Findings on MRI: n (%)	15 (20.3)	0	0.001	NA
Loss of Consciousness (LOC): n (%)	27 (36.5)	0	0.000	NA
Duration of LOC (min): Mean (SD)	0.9 (2.2)	NA	NA	NA
Post-Traumatic Amnesia (PTA): n (%)	68 (92.0)	NA	NA	NA
Duration of PTA (h): Mean (SD)	2.6 (3.4)	NA	NA	NA
Neurological Deficit (e.g., the cranial and spinal nerves)	17 (22.7)	NA	NA	NA
Days to 1 month questionnaire: Mean (SD)	25.2 (4.2)	23.9 (3.4)[a]	0.091	0.33
Days to 1 month cognitive testing: Mean (SD)	29.0 (4.9)	30.6 (9.3)	0.832	-0.24
Days to 6 month questionnaires: Mean (SD)	185.5 (11.3)[b]	193.2 (18.4)[b]	0.004	-0.55
Days to 6 month cognitive testing: Mean (SD)	193.5 (47.0)[c]	NA	NA	NA
Days to 12 month questionnaires: Mean (SD)	380.0 (16.0)[d]	393.1 (67.6)[e]	0.854	-0.32

[a] 1 case missing, [b]3 cases missing, [c]9 cases missing, [d]14 cases missing, [e]11 cases missing

3.3 Withdrawal during follow-up

There was some loss of participants during the 12 month follow-up (n=14, 18.9% in patients with MTBI and n=11, 25.6% in controls). The possible effects of attrition were examined using demographic (age, gender, and education) and trauma-related (GCS, and presence of loss of consciousness) variables, self-reported symptoms at 1 month, and return to work. No systematic bias was found due to attrition. However, none of the dropouts had traumatic lesions on MRI (vs. n=15 of non-dropouts, p=0.059).

3.4 Procedure

In study I a standardized procedure was used for translation of the RS into Finnish. The translation and back-translation were accomplished by a professional translator. The aim of translation was not to achieve literal or syntactic equivalence, but to maintain the original denotation and connotation of items. The back-translated version was approved by the original authors. Data for the study was collected with questionnaires by researchers and psychology students. Participants (n=243) completed the RS and questionnaires about demographic variables and evaluated their self-reported health on a visual scale from 1 to 100, as is done in EuroQol 5D (The EuroQol Group, 1990). The procedure for MTBI-studies (II, III, and IV) is presented below.

3.4.1 Acute clinical assessment and neuroimaging

A clinical assessment of the participants was performed by a research physician in the emergency department (ED) or if the patient was discharged before that, in a separate hospital visit as soon as possible (mean time in hours between the injury and acute clinical assessment=48.1, range=2.0-241.0). The assessment included a thorough interview of past health, diagnosed medical conditions, medication use, head injury history, alcohol consumption, and drug and narcotics abuse history. None of the patients in this study had regular psychoactive medication use. Injury-related data consisted of time of injury, mechanism of injury, and alcohol intoxication at the time of injury. The presence and duration of possible loss of consciousness was recorded using information given by eyewitnesses and ambulance personnel where available. The presence and duration of retrograde-and post-traumatic amnesia were evaluated using the Rivermead PTA Protocol and the Galveston Orientation and Amnesia Test (GOAT) (Levin et al., 1979). Glasgow Coma Scale (GCS) scores were collected from the ambulance (if available) and the ED records. A complete neurological examination, including the cranial and spinal nerves, coordination, pronator drift, balance, and diadochokinesis was completed. The overall severity of physical injuries was assessed using the Injury Severity Score (ISS) (Baker et al., 1974). All patients with MTBI and controls underwent 3T MR imaging of the brain (Siemens Trio, Siemens AG Medical Solutions, Erlangen, Germany). The MRI protocol included sagittal T1- weighted 3D IR prepared gradient echo, axial T2 turbo spin echo, conventional axial and high resolution sagittal

FLAIR (fluid-attenuated inversion recovery), axial T2*, axial SWI (susceptibility weighted imaging), and DWI (diffusion weighted imaging) series.

3.4.2 Follow-up

Participants filled out self-report questionnaires about demographic variables, resilience, post-concussion symptoms, fatigue, insomnia, pain, post-traumatic stress, and quality of life on an internet-based platform at 1, 6, and 12 months post-injury. The patients unable to complete the questionnaires online completed them at the follow-up visit (n=9 at 1 month after injury and n=7 at 6 months after injury) or by mail at 12 months after injury (n=4). Depressive symptoms were evaluated at a neuropsychological follow-up visit only at 1 and 6 months post injury. Neuropsychological examination was conducted for the patients with MTBI and for the controls at 1 month after injury and for the MTBI group at 6 months. The assessment methods used at different follow-ups are listed in Table 2.

Table 2. Assessment methods used at different follow-ups for patients with MTBI and controls.

	1 Month		6 Months		12 Months	
	MTBI	**Controls**	**MTBI**	**Controls**	**MTBI**	**Controls**
Self-report questionnaires						
Resilience Scale (RS)	X	X	X	X	X	X
Post-concussion Symptoms (RPCSQ)	X	X	X	X	X	X
Fatigue (BNI-FS)	X	X	X	X	X	X
Insomnia (ISI)	X	X	X	X	X	X
Pain Subscale (RNBI)	X	X	X	X	X	X
Traumatic Stress Symptoms (PCL-C)	X	X	X	X	X	X
Depressive Symptoms (BDI-II)	X	X	X	X		
Quality of Life (QOLIBRI)	X	X	X	X	X	X
The Satisfaction with Life Scale (SWLS)	X	X	X	X	X	X
Neuropsychological examination						
RAVLT	X	X	X			
Stroop	X	X	X			
Verbal Fluency	X	X	X			
Animal Fluency	X	X	X			
TMT A	X	X	X			
TMT B	X	X	X			
Finger Tapping	X	X	X			
WAIS-III Information	X	X				
WAIS-III Digit Span	X	X	X			
WAIS-III Digit-Symbol Coding	X	X	X			
WAIS-III Symbol Search	X	X	X			
General/functional outcome						
The Extended Glasgow Outcome Scale (GOS-E)	X		X			
Return to work	X		X		X	

3.5 Questionnaires and neuropsychological measures

3.5.1 Self-report questionnaires

Resilience was assessed by *The Resilience Scale* (Wagnild & Young, 1993), which has been presented in the previous chapter (please see chapter 1.4.6.1).

Post-concussion symptoms were evaluated with *The Rivermead Post-concussion Symptom Questionnaire* (RPCSQ) (King et al., 1995). It is a 16-item self-report questionnaire measuring the severity of common post-concussion symptoms on a 5-point Likert scale. The patients rate the presence of the symptoms on a scale from 0-4. A total score is a sum of the items. The presence of post-concussion syndrome was defined using ICD-10 diagnostic criteria (Ashley, 1990). Participants were determined to have met the criteria for PCS if they reported symptoms on the RPCSQ in at least three of the following ICD-10 symptoms categories: (i) headaches, dizziness, general malaise, excessive fatigue, or noise intolerance; (ii) irritability, emotional lability, depression, or anxiety; (iii) subjective complaints of concentration or memory difficulty; (iv) insomnia; (v) reduced tolerance to alcohol; (vi) preoccupation with these symptoms and fear of permanent brain damage. The first four of these symptom categories could be assessed by using the RPCSQ. Two thresholds for symptom reporting were considered: mild or greater severity (2-4 points) and moderate or greater severity (3-4 points), and these are referred to as mild PCS or moderate PCS, respectively.

Fatigue was assessed by *The Barrow Neurological Institute Fatigue Scale (BNI-FS)* which is a reliable and valid 11-item self-report questionnaire designed to assess fatigue after TBI (Borgaro et al., 2004; Wäljas et al., 2012). The total BNI-FS score is the sum of the first 10 items (min = 0, max = 70).

The Insomnia Severity Index (ISI) was used to assess the patient`s perception of his or her insomnia. It is a reliable and valid seven-item self-report questionnaire in which the total score ranges from 0 to 28 (Morin et al., 2011).

Pain was evaluated by *the Pain subscale of the Ruff Neurobehavioral Inventory (RNBI)* (Ruff & Hibbard, 2003). The Pain subscale comprises of six items rated on a 4-point scale (1-4), and the total score ranges from 6 to 24.

Symptoms of posttraumatic stress disorder (PTSD) were assessed with *PTSD-Checklist-Civilian Version (PCL-C)* (Weathers et al., 1993). It is a reliable and valid

scale to assess PTSD symptoms in civilians (Ruggiero et al., 2003). The possible scores of the scale range from 17 to 85. The participant was defined as having PTSD if the total score of PCL-C was greater than 50 or the criteria for PTSD in DSM-IV (American Psychological Association, 1994) was fulfilled, and possible PTSD if the total score of PCL-C was greater than 35.

Depressive symptoms were assessed with the *Beck Depression Inventory-Second Edition (BDI-II)* (Beck et al., 1996), a self-report questionnaire in which the total score ranges from 0 to 63. In study II the analysis were conducted with a reduced item set for BDI-II to address the overlap-effect with other questionnaires. In that study three potentially confounding items (15 "loss of energy", 16 "changes in sleeping patterns" and 20 "tiredness or fatigue") were removed from the BDI-II total score. In study IV patients were classified as having depression using selected items of the questionnaire. Ten of the 21 symptoms from the BDI-II, believed to have the least overlap with symptoms of MTBI and being most representative of depression, were selected. These symptoms were: sadness, loss of interest, loss of pleasure, pessimism, past failure, guilt feelings, punishment feelings, self-criticalness, crying, and suicidal thoughts or wishes. The algorithm for defining depression was as follows: (a) Sadness or loss of pleasure must be endorsed, and 3 or more of the 10 core symptoms must be endorsed, and the BDI total score had to be 10 or greater; or (b) 5 or more of the 10 selected symptoms had to be endorsed. Patients meeting either criterion were included in the depression group and the remaining subjects were classified as not depressed.

The disease specific quality of life was evaluated by *The Quality of Life after Brain Injury (QOLIBRI)* which is a reliable and valid health-related quality-of-life instrument specifically developed for TBI (Steinbüchel et al., 2010a; Steinbüchel et al., 2010b). It contains 37 items rated on a 5-point Likert scale, the possible total score thus ranges from 37 to 185. In the present study, controls were asked to rate their quality of life with this questionnaire while considering their orthopedic injury. The generic and global life satisfaction was assessed with *The Satisfaction with Life Scale (SWLS)* which has favourable psychometric properties (Diener et al., 1985). It contains 5 items on a 7-point Likert Scale and the possible total score ranges from 5 to 35.

The general outcome was evaluated with *The Extended Glasgow Outcome Scale (GOS-E)* (Wilson et al., 1998) which is a widely used scale based on a structured

interview. It reports the patients recovery on a scale from 1-8 with scores 1-4 reflecting severe disability, scores 5-6 moderate disability, and 7-8 good recovery.

3.5.2 Neuropsychological examination

The Rey Auditory Verbal Learning Test (RAVLT; total number of words recalled in trials 1-5, recall after interference, and recognition after 30 minutes) (Lezak et al., 2004) was used to assess verbal memory. *The Stroop Test* (Golden version, number of items completed in color-word interference trial) (Lezak et al., 2004), *Trail Making Test* Parts A and B (TMT; time in seconds) (Army Individual Test Battery, 1944), phonemic (P/A/S) and semantic (animals) *verbal fluency* (number of words in one minute) (Strauss et al., 2006) were used to assess executive functions. Motor speed was assessed with the *Finger Tapping Test* (mean number of taps in five consecutive 10 second trials for the dominant and nondominant hand) (Halstead, 1947). The following subtests from *Wechsler Adult Intelligence Scale – Third Edition* (WAIS-III) (Wechsler, 1955) were used: Information to assess verbal intelligence, Digit Span to assess attention and working memory, and Digit-Symbol Coding and Symbol Search to assess processing speed. The participant was defined as having cognitive impairment if four or more of the fourteen primary test scores on the neuropsychological measures were at least one standard deviation below average. This criterion is based on past studies examining the base rates of low scores in healthy adults when multiple scores are considered simultaneously (Binder et al., 2009; Brooks et al., 2009; Mistridis et al., 2015). It is common for healthy adults to obtain some low scores when multiple tests are administered. Adults with above average intelligence obtain fewer low scores than adults with average or below average intelligence. As noted by Iverson and colleagues (Iverson et al., 2012a), it is common for adults of average intelligence to have 20-30% of their test scores $\leq$ 1 SD from the mean, and it is common for adults with above average intelligence to have approximately 15% of their test scores in this range.

3.6 Statistical methods

The statistical analyses were conducted with the supervision and help of a statistician (Mika Helminen) using the Statistical Package for the Social Sciences (SPSS) for Windows, versions 18.0 (Studies I and III), 20.0 (Study II), and 22.0. (Study IV). P-

values less than 0.05 were considered statistically significant. The normality of data was evaluated using the Kolmogorov-Smirnov test of normality.

In studies I and III, the internal consistency (item-total item correlation) for the RS and RS-14 was determined using Cronbach's alpha coefficient. The correlations were calculated using Spearman and Pearson coefficients. Evaluation of the factor structure in study I was done using exploratory and confirmatory factor analysis with LISREL for Windows. The Goodness-of-Fit Index (GFI), the Adjusted Goodness-of-Fit Index (AGFI), the Comparative Fit Index (CFI), and the Root Mean Square Error of Approximation (RMSEA) were used to evaluate the fit of the factor models using the following criteria: GFI > 0.90, AGFI > 0.90, CFI > 0.95 and RMSEA < 0.06 (Kline, 2005). The group comparisons were analyzed using Student´s t-test, Mann-Whitney U-test, and Fisher's Exact test (when cell sizes were less than five). Cohen´s d values were used to illustrate clinical significance. In study II, multiple linear regression analysis was conducted to determine eventual independent predictors of the change in fatigue from 1 to 6 months. In study III, the stability of resilience scores was assessed by the Intraclass correlation coefficient and Spearman's rho coefficient. In study IV, the results from some neuropsychological measures were converted to z-scores using the age-, education-, and gender-corrected meta-norms (Mitrushina et al., 2005).

4 Results

4.1 Assessment of resilience by the Resilience Scale

The use of the Resilience Scale (RS) in the assessment of resilience was examined in two studies (I & III).

4.1.1 Evaluation of the Finnish version of the Resilience Scale (Study I)

The Finnish versions of the RS or the RS-14 have not previously been available. The aim of Study I was to investigate the psychometric properties of the Finnish version of the RS and the RS-14 and the relation of resilience to demographic variables and self-perceived health.

4.1.1.1 The psychometric properties

The mean level of resilience was found to be moderate. The RS total score varied from 67 to 175 (mean 133.8, SD 17.4). The RS-14 total score varied from 35 to 98 (mean 76.3, SD 10.7). The RS and the RS14 total scores were strongly correlated (r=0.95).

Cronbach´s alpha coefficient for the total scale was 0.90, and for the RS-14 0.87. No problematic items were found since removing any of the items did not significantly improve the alpha coefficients.

Confirmatory factor analysis was first conducted to determine how well the RS data from Finnish sample fit the previously presented factor models. Neither the original two-factor solution of RS presented by the original authors (Wagnild & Young, 1993) or the five-factor solution reflecting the five dimensions of resilience (Lundman et al., 2007) were supported by the Finnish data (see Table 3). The one-factor solution for RS-14 presented in the Japanese study (Nishi et al., 2010) was not supported by the Finnish data either. However, a total of 39% of the common variance was explained by this one factor solution and all factor loadings were found to be 0.40 or higher. From exploratory factor analysis five factors emerged for RS and three factors for RS-14 but these were not consistent with previous findings.

Table 3. Summary of test statistics for confirmatory factor analysis for RS and RS-14.

Structure	GFI	AGFI	CFI	RMSEA
RS: 2 factors	0.78	0.74	0.92	0.094
RS: 5 factors	0.79	0.74	0.92	0.092
RS14: 1 factor	0.86	0.82	0.94	0.101

Abbreviations: RS = Resilience Scale, RS14 = Short version of Resilience Scale, GFI = Goodness-of-Fit Index, AGFI = Adjusted Goodness-of-Fit Index, CFI = Comparative Fit Index, RMSEA = Root Mean Square Error of Approximation. Table is reprinted with the kind permission of the copyright holder.

4.1.1.2 The association of resilience and demographic factors

There was no difference in the mean total score of RS between women and men (mean 133.7, SD 18.2 vs. 134.2, SD 14.9, p=0.86, respectively). Education did not significantly correlate with RS or RS-14. Instead, a weak correlation between the RS and the RS-14 with age was found (r=0.16, p=0.015; r=0.12, p=0.06, respectively). The resilience was found to be higher among older people.

The health ratings of the participants ranged from 30 to 100 (mean 82.0, SD 12.3). Both the RS and the RS-14 correlated weakly with self-rated health (r=0.22, p<0.001; r=0.23, p<0.001, respectively). The correlations between the RS and the RS-14 with self-rated health were stronger when age was taken into account in partial correlation (r=0.30, p<0.001; r=0.31, p<0.001, respectively). When gender was taken into account there was a significant correlation between the RS and the RS-14 with self-rated health only in women (r=0.27, p<0.001; r=0.26, p<0.001, respectively) but not in men. When controlled for age the gender difference was even more prominent: for women the correlation between the RS and the RS-14 with self-rated health still strengthened (r=0.38, p<0.001; r=0.39, p<0.001, respectively) but remained insignificant for men.

4.1.2 Assessment of resilience after MTBI (Study III)

The reliability and validity of the RS and RS-14 among patients with MTBI has not been previously studied. Study III examined resilience measured by the RS and RS-14 following MTBI.

Descriptive statistics for the RS and RS-14 scores at follow-ups are presented in Table 4. The majority of the MTBI group reported at least moderate resilience according to the categorization presented by the original test author (68.0% at 1 month, 64.0% at 6 months, and 60.1% at 12 months post-injury). For the controls, at least moderate resilience was reported by 65.0% at 1 month, 76.7% at 6 months, and 47.7% at 12 months post-injury. There were no statistically significant differences in the RS or RS-14 scores between the MTBI and the control groups in any of the follow-ups (p=0.332-0.966).

Table 4. Descriptive statistics and internal consistency reliability for the Resilience Scale and its short version by group and over time.

	Resilience Scale		**Resilience Scale-14**	
1 Month	MTBI	Controls	MTBI	Controls
Sample size	74	39	74	39
Mean	140.0	140.0	80.0	80.0
Median	142.0	143.0	80.5	81.0
Standard deviation	17.5	16.0	10.9	9.1
Quartiles (Q1;Q3)	(128.0;153.3)	(127.0;148.0)	(72.8;88.0)	(74.0;86.0)
Cronbach's Alpha	0.91	0.90	0.91	0.86
6 Months				
Sample size	71	37	71	37
Mean	140.0	144.0	79.6	82.3
Median	143.0	145.0	81.0	82.0
Standard deviation	18.8	14.3	11.5	8.6
Quartiles (Q1;Q3)	(128.8;154.0)	(132.0;145.5)	(72.8;89.0)	(76.0;88.5)
Cronbach's Alpha	0.93	0.88	0.92	0.88
12 Months				
Sample size	60	29	60	29
Mean	143.3	141.5	81.1	81.0
Median	147.0	146.0	82.5	83.0
Standard deviation	18.4	19.2	11.3	11.6
Quartiles (Q1;Q3)	(131.0;156.8)	(126.0;157.0)	(71.8;91.0)	(71.0;90.0)
Cronbach's Alpha	0.93	0.95	0.93	0.94

Cronbach alpha coefficients for the RS at 1, 6, and 12 months after injury ranged from .91 to .93 for the MTBI group and from .88 to .95 for controls (see Table 4). For

the RS-14, the Cronbach alpha coefficients ranged from .88 to .93 for the MTBI group and from .86 to .94 for the controls.

The stability of measured resilience was assessed by comparing resilience scores at 1, 6, and 12 months. The test-retest reliability for the RS and RS-14 ranged from .66 to .80 across groups, versions, and time (see Table 5). The test-retest reliability of the resilience scales was comparable to or better than the stability of the outcome measures (also presented in Table 5 for comparison). The Intraclass correlation coefficient of RS was satisfactory for both MTBI group (.76) and controls (.75).

Table 5. Test-retest reliability of the Resilience Scale compared to outcome measures.

	1-6 Months		**1-12 Months**		**6-12 Months**	
	MTBI	**Controls**	**MTBI**	**Controls**	**MTBI**	**Controls**
	(n=70)	(n=36)	(n=60)	(n=28)	(n=59)	(n=29)
Resilience Scale	0.73	0.70	0.71	0.77	0.80	0.80
Resilience Scale-14	0.74	0.73	0.70	0.76	0.82	0.80
Post-concussion Symptoms (RPCSQ)	0.57	0.39	0.46	0.62	0.61	0.59
Fatigue (BNI-FS)	0.58	0.40	0.52[a]	0.42	0.71	0.75
Insomnia (ISI)	0.61[a]	0.62	0.47[b]	0.59	0.71	0.50
Pain Subscale (RNBI)	0.46	0.69	0.20	0.66	0.34	0.63
Traumatic Stress Symptoms (PCL-C)	0.70	0.61	0.61	0.70	0.66	0.45
Depressive Symptoms (BDI-II)	0.71[c]	0.79[d]	NA	NA	NA	NA
Quality of Life (QOLIBRI)	0.74	0.67	0.67	0.74	0.80	0.78

Test-retest reliability is estimated using Spearman correlations.
[a]1 case missing, [b]2 cases missing, [c] 5 cases missing, [d]7 cases missing
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4.1.3 The association of resilience and outcome from MTBI

4.1.3.1 The association of resilience and fatigue (Study II)

The aim of study III was to examine resilience as a predictor of change in self-reported fatigue after MTBI. Results were compared to those of controls. The group differences between the MTBI and control group on the predictive variables (ISI, RNBI, BDI-II,

and RS) and fatigue variables (BNI-FS) are presented in Table 6. The MTBI group tended to report more symptoms of insomnia than the control group, but the difference between the groups was not statistically significant. The MTBI and control groups did not significantly differ on pain, depressive symptoms, or resilience. The patients with MTBI had a significantly higher level of fatigue at 1- month post injury than the controls. However, there was a decrease in the level of fatigue in the patients with MTBI during follow-up. In the controls, no significant change in fatigue occurred. At 6 months after injury the difference on fatigue between the patients with MTBI and controls was not statistically significant.

Table 6. Group differences in fatigue and predictive variables at 1 month in patients with MTBI and the controls.

	Patients with MTBI (n =67)	**Controls** (n =34)	**Cohen´s d**	**p-value***
Fatigue (BNI-FS) at 1 month: Mean (SD)	14.7 (15.1)	7.2 (6.8)	0.59	0.025
Fatigue (BNI-FS) at 6 months: Mean (SD)	8.9 (12.0)	6.9 (10.1)	0.18	0.641
Change in fatigue (BNI-FS) from 1 to 6 months	-5.8 (12.0)	-0.2 (10.3)	0.49	0.050
Insomnia (ISI)	5.3 (5.3)	3.3 (3.5)	0.41	0.236
Pain subscale (RNBI)	8.2 (2.2)	8.4 (2.6)	0.07	0.943
Depressive symptoms (BDI-II)	3.7 (4.5)	3.4 (4.2)	0.06	0.951
Resilience (RS)	138.9 (17.1)	138.5 (16.1)	0.01	0.733

BNI-FS= The Barrow Neurological Institute Fatigue Scale, ISI= Insomnia Severity Index, RNBI= Ruff Neurobehavioral Inventory, BDI-II= Beck Depression Inventory II, RS= Resilience Scale
* Mann-Whitney p-value

At 1 month, post-injury fatigue correlated significantly with insomnia, pain, and depressive symptoms in both MTBI and control groups. However, significant

correlation between resilience and fatigue was found only in patients with MTBI (see Table 7). At 6 months, fatigue correlated significantly with pain and depressive symptomatology in both groups. In the MTBI group, also resilience and insomnia were significantly correlated with fatigue at 6 months. In patients with MTBI, the correlation between resilience and fatigue was even stronger at follow-up. In the controls, no statistically significant correlation between resilience and fatigue was found.

Table 7. Correlations between the predictive variables (at 1 month) and fatigue (BNI-FS total scores) at 1 and 6 months.

	Patients with MTBI (n = 67)		**Controls** (n = 34)	
Variables	**Fatigue at 1 month (BNI-FS)**	**Fatigue at 6 month (BNI-FS)**	**Fatigue at 1 month (BNI-FS)**	**Fatigue at 6 month (BNI-FS)**
Insomnia (ISI)	0.67**	0.50**	0.42*	0.24
Pain (RNBI)	0.39**	0.54**	0.54**	0.48**
Depressive symptoms (BDI-II)	0.39*	0.39**	0.42*	0.42*
Resilience (RS)	-0.26*	-0.45**	-0.26	-0.27

BNI-FS= The Barrow Neurological Institute Fatigue Scale, ISI= Insomnia Severity Index, RNBI= Ruff Neurobehavioral Inventory, BDI-II= Beck Depression Inventory II, RS= Resilience Scale
*<0.05, **<0.01

Multiple regression analysis was conducted to examine the predictors of the change in fatigue from 1 to 6 months in the MTBI group. The demographic variables (age, gender, and education) and physical injuries (ISS) did not predict change in fatigue (adj. R2 = -0.055, p= 0.968). Adding insomnia, pain, and depressive symptoms simultaneously to the model at the next step produced a significant change (p= 0.033), but the model did not reach statistical significance (adj. R2 = 0.043, p= 0.215). After controlling for the aforementioned variables, resilience added significantly (p= 0.006) to the model. The final step of the regression model (presented in Table 7) significantly (adj. R2 = 0.145, p= 0.026) predicted the change in fatigue from 1 to 6 months after MTBI. In this final

model, insomnia was found to be a significant predictor besides resilience. Depressive symptoms had a trend towards significance but resilience was the strongest predictor. In the regression model, all variance inflation factor values were under 1.8.

Table 8. Results of the final multivariate regression model for the change in fatigue from 1 to 6 months post-injury in patients with MTBI.

Block	**1**		**2**		**3**	
	Standardized β	Sig. (p)	Standardized β	Sig. (p)	Standardized β	Sig. (p)
Gender (males)	-0.011	0.935	-0.080	0.531	-0.142	0.249
Age	-0.073	0.569	-0.094	0.447	-0.134	0.254
Years of education	-0.030	0.814	-0.067	0.606	-0.029	0.812
Injury severity Score (ISS)	-0.043	0.741	-0.011	0.933	0.037	0.764
Insomnia (ISI)			-0.266	0.071	-0.279	0.046
Pain (RNBI)			-0.119	0.427	-0.117	0.409
Depressive symptoms (BDI-II)			-0.072	0.625	-0.257	0.098
Resilience (RS)					-0.380	0.006

ISS= Injury Severity Index, ISI= Insomnia Severity Index, RNBI= Ruff Neurobehavioral Inventory, BDI-II= Beck Depression Inventory II, RS= Resilience Scale. The table is reprinted with the kind permission of the copyright holder.

Figure 4 illustrates the association of resilience and fatigue by presenting the level of fatigue at both measurements (1 and 6 months) in patients groups divided by their resilience scores. Those with lower resilience scores reported more fatigue at both follow-ups.

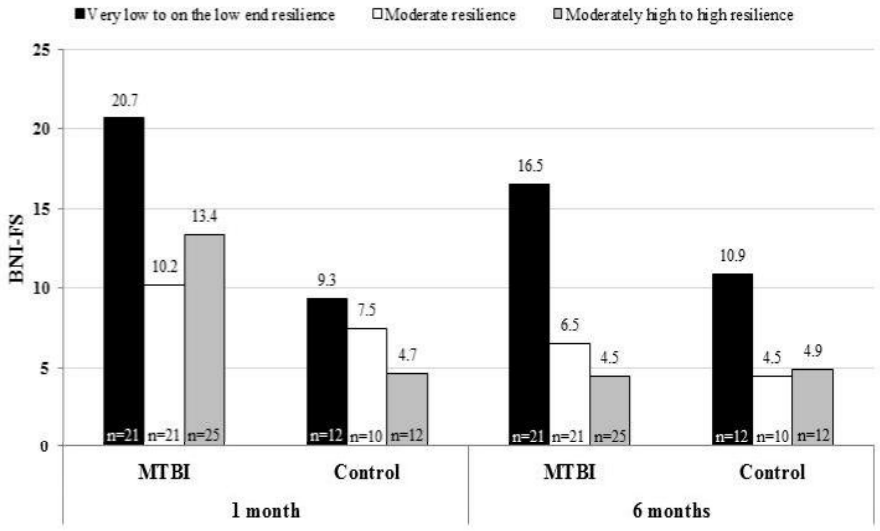

Figure 4. Mean fatigue scores (BNI-FS) of patient groups stratified by different levels of resilience. The figure is reprinted with the kind permission of the copyright holder.

4.1.3.2 The association of resilience and other outcome domains (Study III)

The Spearman correlations between the Resilience Scale (measured at each follow up), its short form, and the outcome measures are presented in Table 9, by group and at each time point. In the MTBI group, greater resilience was associated with: (i) less fatigue and traumatic stress, and better quality of life, at one month; (ii) less fatigue and depression, and better quality of life, at 6 months; and (iii) fewer post-concussion symptoms; less fatigue, insomnia, and traumatic stress; and better quality of life at 12 months following injury. In the control group, greater resilience was associated with: (i) fewer post-concussion-like symptoms, less pain and traumatic stress, and better quality of life at one month; (ii) less depression and better quality of life at 6 months; and (iii) fewer post-concussion-like symptoms; less fatigue, pain, and traumatic stress; and better quality of life at 12 months following injury.

Table 9. Spearman correlations between the Resilience Scale and its short form (measured at each follow up) and the outcome variables.

	Resilience Scale						**Resilience Scale-14**					
	1 Month		6 Months		12 Months		1 Month		6 Months		12 Months	
	MTBI (n=74)	Controls (n=39)	MTBI (n=70)	Controls (n=37)	MTBI (n=60)	Controls (n=29)	MTBI (n=74)	Controls (n=39)	MTBI (n=70)	Controls (n=37)	MTBI (n=60)	Controls (n=29)
Post-concussion symptoms	-0.19	-0.33*	-0.21	-0.24	-0.43**	-0.59**	-0.15	-0.31	-0.21[b]	-0.25	-0.40**	-0.56**
Fatigue	-0.24*[a]	-0.20[a]	-0.31**	-0.24	-0.41**	-0.68**[a]	-0.24*[a]	-0.18[a]	-0.29*	-0.24	-0.37**	-0.69**
Insomnia	-0.18[b]	-0.43	-0.22	-0.24	-0.29*	-0.18	-0.18[b]	-0.15	-0.21	-0.27	-0.25	-0.24
Pain	0.02	-0.34*	-0.05	-0.27	-0.01	-0.45*	0.02	-0.35*	-0.07	-0.34*	-0.03	-0.40*
Traumatic stress symptoms	-0.27*	-0.32*	-0.20[a]	-0.22	-0.49**	-0.78**	-0.28*	-0.32*	-0.21[a]	-0.24	-0.50**	-0.74**
Depressive symptoms	-0.18	-0.06[a]	-0.40**[c]	-0.49**[d]	NA	NA	-0.18	0.03[a]	-0.41**[c]	-0.57**[d]	NA	NA
Quality of life	0.36**	0.57**	0.60**[a]	0.58**	0.75**	0.74**	0.32**	0.55**	0.60**[a]	0.58**	0.76**	0.73**

*<0.05, **<0.01

[a] 1 case missing, [b] 2 cases missing, [c] 6 cases missing, [d] 5 cases missing

The group differences in outcome variables between those with moderate to high resilience and those with low resilience are presented in Table 10. The patients with MTBI and moderate to high resilience (measured one month following injury) reported significantly less post-concussion, fatigue, insomnia, traumatic stress, and depressive symptoms, and their quality of life was rated as better, than the patients with relatively low resilience in both 1- month and 6-month follow ups. The MTBI subgroup with at least moderate resilience continued to report less fatigue and traumatic stress, and better quality of life at 12 months following injury. In controls, the group with better resilience scores (measured at one month following injury) reported significantly less pain and depressive symptoms, and their quality of life was better at 1 and 6 months, compared to the controls with relatively low resilience after injury. The controls with moderate to high resilience also reported less fatigue at 12 months than those with relatively low resilience.

Table 10. Comparison of the outcome variables for subgroups of patients with MTBI and controls according to their resilience measured by the Resilience Scale at 1 month after injury.

	Patients with MTBI				Controls			
Measures	From very low to the low end of resilience (n=23) Mean (SD)	From moderate to high resilience (n=51) Mean (SD)	p-value for group differences	Cohen´s d	From very low to the low end of resilience (n=13) Mean (SD)	From moderate to high resilience (n=26) Mean (SD)	p-value for group differences	Cohen´s d
One Month								
Sample Size	23	51			13	26		
Post-concussion symptoms (RPCSQ)	14.3 (10.6)	8.9 (8.6)	0.026	0.58	8.5 (8.4)	3.1 (5.1)	0.105	0.85
Fatigue (BNI-FS)	19.7 (15.2)	12.5 (15.7) [a]	0.021	0.46	9.3 (7.7) [a]	7.4 (7.6)	0.466	0.25
Insomnia (ISI)	7.6 (5.1)	4.1 (4.8) [b]	0.007	0.37	4.1 (2.8)	4.4 (5.0)	0.489	-0.07
Pain subscale (RNBI)	8.8 (2.6)	8.4 (2.9)	0.369	0.14	9.6 (2.8)	7.6 (2.0)	0.025	0.87
PTSD Symptoms (PCL-C)	28.5 (9.1)	23.8 (8.4)	0.005	0.55	27.3 (9.0)	23.2 (6.3)	0.187	0.56
Depressive symptoms (BDI-II)	9.1 (5.9)	3.8 (4.9)	0.000	1.01	8.1 (6.5)	3.8 (4.1) [a]	0.035	0.86
Quality of life (QOLIBRI)	139.1 (22.9)	157.8 (26.2)	0.000	0.74	144.3 (15.2)	160.7 (17.3)	0.004	0.99
Six Months								
Sample Size	22	48			13	23		
Post-concussion symptoms	12.2 (11.0) [a]	5.2 (7.6)	0.003	0.80	5.3 (6.0)	3.0 (6.5)	0.087	0.36
Fatigue	16.1 (13.7)	6.5 (11.4)	0.000	0.79	10.5 (13.1)	5.7 (8.4)	0.226	0.47
Insomnia	5.9 (4.6)	3.6 (3.6)	0.037	0.58	4.5 (4.0)	3.3 (4.7)	0.131	0.27
Pain subscale	7.8 (2.2)	7.2 (2.4)	0.064	0.26	7.8 (2.2)	6.7 (1.8)	0.093	0.56
PTSD Symptoms	28.3 (12.7)	21.9 (7.1)	0.022	0.70	24.5 (8.2)	22.3 (8.3)	0.281	0.27
Depressive symptoms	7.6 (7.3) [b]	2.8 (5.1) [c]	0.000	0.82	8.3 (7.3) [b]	3.4 (5.3) [c]	0.036	0.81
Quality of life	142.2 (22.0)	164.2 (18.8)	0.000	1.11	156.0 (21.2)	168.0 (23.0)	0.024	0.54
12 Months								
Sample Size	18	42			10	18		
Post-concussion symptoms	9.4 (8.8)	5.9 (8.1)	0.100	0.42	6.9 (7.9)	3.2 (7.8)	0.146	0.47
Fatigue	11.7 (13.7)	6.6 (11.9)	0.028	0.41	16.5 (18.7)	4.6 (6.7)	0.018	0.97
Insomnia	5.0 (3.6)	4.1 (4.3)	0.196	0.22	4.5 (4.7)	3.7 (3.8)	0.869	0.19
Pain subscale	7.4 (2.7)	7.2 (2.5)	0.985	0.08	8.0 (3.5)	6.8 (1.4)	0.724	0.51
PTSD Symptoms	26.0 (6.7)	22.1 (6.5)	0.004	0.60	25.8 (11.4)	21.2 (6.1)	0.245	0.55
Quality of life	143.9 (18.7)	164.6 (19.6)	0.000	1.07	142.6 (32.6)	162.1 (20.6)	0.109	0.77

[a] 1 case missing, [b] 2 cases missing, [c] 3 cases missing. Abbreviations: RPCSQ=The Rivermead Post-concussion Symptom Questionnaire, BNI-FS=The Barrow Neurological Institute Fatigue Scale, ISI=The Insomnia Severity Index, RNBI=The Ruff Neurobehavioral Inventory, PCL-C= PTSD-Checklist-Civilian Version, BDI-II=Beck Depression Inventory- Second Edition, QOLIBRI=Quality of life after Brain Injury. The table is reprinted with the kind permission of the copyright holder.

The time to return to work (RTW) for the total MTBI sample (N=73) ranged from 0 to 1,174 days (mean=50.7, median=15.0, IQR = 5-43, SD=147.6). One patient retired due to his multiple bodily injuries and was excluded from the RTW analyses. Resilience measured at 1 month did not significantly correlate with RTW in the total sample of patients with MTBI (Spearman r=.094 and .115 for the total score and the short form, respectively). After removing two outliers (one with RTW greater than one year in each group), there was no significant difference (Mann Whitney U = 573.5, p=.54) in days to RTW between those with moderate to high resilience (n=50, M=30.2, SD=45.6) and those with low resilience (n=21, M=28.0, SD=38.6). Removing two outliers and those patients from the analyses whose primary reason for the sick leave was assessed to be only bodily injuries did not change the above results.

4.1.4 Recovery from MTBI in previously healthy adults (Study IV)

4.1.4.1 Post-concussion symptoms and syndrome

At 1 and 6 months after the injury, patients with MTBI reported significantly (p=0.001, Cohen's d=0.64; p=0.029, Cohen's d=0.43, respectively) more post-concussion symptoms than the controls (see Table 11). At 12 months (p=0.07, Cohen's d=0.30) the clinical significance of the difference in post-concussion-symptom reporting was small.

Based on their self-reported symptoms, 31.1% of the patients with MTBI were determined to have mild PCS at 1 month after injury, 24.6% at 6 months after injury, and 26.7% at one year after injury (see Table 12). However, mild PCS was also found in a fairly large proportion of the controls as well in the follow-ups, 20.5%, 13.5%, and 17.2%, respectively. Using the reporting of at least moderate symptoms as a criteria, the prevalence of PCS at the follow-ups was much smaller: 5.4%, 4.3%, and 5.0% for the patients with MTBI and 2.6%, 0%, and 3.4% for the controls. Patients with MTBI did not meet criteria for PCS (mild or moderate) statistically significantly more often than controls at any follow-up (see Table 12).

Table 11. Comparison of outcome variables of patients with MTBI and controls.

	MTBI	**Controls**	p-value	Cohen´s d
1 Month	Mean (SD)	Mean (SD)		
Sample size	74	40		
Post-Concussion Symptoms (RPCSQ)	10.5 (9.6)	4.9 (6.8)[1]	0.001	0.64
Fatigue (BNI-FS)	14.6 (15.8)[1]	8.0 (7.6)[2]	0.060	0.49
Insomnia (ISI)	5.2 (5.2)[2]	4.3 (4.3)[1]	0.520	0.18
Pain Subscale (RNBI)	8.5 (2.8)	8.3 (2.5)[1]	0.654	0.07
PTSD Symptoms (PCL-C)	25.3 (8.9)	24.4 (7.4)	0.719	0.11
Depressive Symptoms (BDI-II)	5.4 (5.8)	5.1 (5.4)[1]	0.597	0.05
Resilience (RS)	139.5 (17.5)	139.5 (16.0)[1]	0.821	0.00
Quality of Life (QOLIBRI)	152.0 (27.0)	155.8 (18.3)	0.833	-0.16
Life Satisfaction (SWLS)	27.0 (6.0)	26.8 (4.8)[1]	0.964	0.04
6 Month				
Sample size	71	37		
Post-Concussion Symptoms (RPCSQ)	7.3 (9.3)[2]	3.7 (6.3)	0.029	0.43
Fatigue (BNI-FS)	9.4 (13.0)	10.4 (7.8)	0.774	-0.09
Insomnia (ISI)	4.3 (4.0)	4.4 (3.8)	0.267	-0.03
Pain subscale (RNBI)	7.4 (2.3)	7.1 (2.0)	0.406	0.14
PTSD Symptoms (PCL-C)	24.0 (9.6)[1]	23.0 (8.1)	0.384	0.11
Depressive symptoms (BDI-II)	4.3 (6.2)[3]	5.0 (6.4)[4]	0.779	-0.11
Resilience (RS)	139.7 (18.8)[1]	143.3 (14.4)[1]	0.475	-0.21
Quality of Life (QOLIBRI)	157.3 (22.2)[1]	163.7 (22.5)	0.035	-0.29
Life Satisfaction (SWLS)	26.4 (5.5)	26.8 (5.2)	0.601	-0.07
12 Month				
Sample size	60	29		
Post-Concussion Symptoms (RPCSQ)	6.9 (8.4)	4.4 (7.8)	0.070	0.30
Fatigue (BNI-FS)	8.1 (12.6)	8.7 (13.4)[1]	0.912	-0.05
Insomnia (ISI)	4.3 (4.1)	4.0 (4.0)	0.784	0.07
Pain Subscale (RNBI)	7.3 (2.6)	7.2 (2.3)	0.915	0.04
PTSD Symptoms (PCL-C)	23.3 (6.8)	22.7 (8.4)	0.142	0.08
Resilience (RS)	143.3 (18.4)	141.2 (19.5)[1]	0.674	0.11
Quality of Life (QOLIBRI)	158.4 (21.4)	155.7 (26.4)	0.916	0.12
Life Satisfaction (SWLS)	27.0 (5.3)	26.5 (5.7)	0.752	0.09

[1]1 case missing, [2]2 cases missing, [3]6 cases missing, [4]5 cases missing
Abbreviations: RPCSQ=The Rivermead Post-concussion Symptom Questionnaire, BNI-FS=The Barrow Neurological Institute Fatigue Scale, ISI=The Insomnia Severity Index, RNBI=The Ruff Neurobehavioral Inventory, PCL-C= PTSD-Checklist-Civilian Version, BDI-II=Beck Depression Inventory- Second Edition, RS = Resilience Scale, QOLIBRI=Quality of life after Brain Injury, SWLS=Satisfaction with Life Scale. The group comparisons were conducted with Mann Whitney- or t-tests. The table is reprinted with the kind permission of the copyright holder.

Table 12. Outcome from Mild TBI and Ankle Injury.

	1 Month		p-value	6 Months		p-value	12 Months		p-value
	MTBI	Controls		MTBI	Controls		MTBI	Controls	
Sample Size	74	40	--	69	37	--	60	29	--
Good Recovery on GOS-E N (%)	50 (67.6)	NA	--	56 (88.9)[6]	NA	--	NA	NA	--
Post-Concussion Syndrome Mild N (%)	23 (31.1)	8 (20.5)[1]	0.273	17 (24.6)	5 (13.5)	0.312	16 (26.7)	5 (17.2)	0.431
Post-Concussion Syndrome Moderate N (%)	4 (5.4)	1 (2.6)[1]	0.658	3 (4.3)	0	0.549	3 (5.0)	1 (3.4)	1.000
Cognitive Impairment N (%)	14 (19.4)[2]	4 (10.5)[2]	0.290	6 (9.2)[4]	NA	NA	NA	NA	--
Depression N (%)	12 (16.4)[1]	6 (15.8)[2]	1.000	5 (7.7)[4]	6 (18.8)[5]	0.167	NA	NA	--
Possible PTSD N (%)	12 (16.2)	5 (12.5)	0.784	7 (10.0)	5 (13.5)	0.536	4 (6.7)	3 (10.3)	0.675
Probable PTSD N (%)	3 (4.1)	1 (2.5)	1.000	3 (4.3)	2 (5.4)	1.000	2 (3.3)	0	1.000
Psychiatric Disorder (Depression or Probable PTSD) N (%)	12 (16.4)[1]	6 (15.8)[2]	1.000	6 (8.0)	6 (15.0)	0.193	NA	NA	--
Return to Work (RTW) %	68.0	NA	--	93.3	NA	--	96.0	NA	--

The numbers represent the percentages of subjects in each group who meet criteria for the specific outcome. NA = Not available.
[1]1 case missing, [2]2 cases missing, [3]3 cases missing, [4]4 cases missing, [5]5 cases missing, [6]6 cases missing. The table is reprinted with the kind permission of the copyright holder.

4.1.4.2 Fatigue, insomnia, and pain

There were no statistically significant differences between the study groups in reporting of fatigue, insomnia, and pain at any of the follow-ups (See Table 11). At 1 month after the injury there was a trend towards significance ($p=0.06$, Cohen´s $d=0.49$) in patients with MTBI reporting more fatigue symptoms than the controls (see Table 11) but at the 6- and 12-month follow-ups there was no difference in the level of fatigue between the groups.

4.1.4.3 Cognition

At 1 month after the injury, 14 (19.4%) of the patients with MTBI and 4 (10.5%) of the controls met criteria for mild cognitive impairment (See Table 12). At the 6 month follow-up, however, the rate of cognitive impairment in the MTBI group was 9.2% (n=6). At the group level, at one month after the injury there were no statistically significant differences in neuropsychological test performance between the patients with MTBI and controls (See Table 13). At the 6 month follow-up, the memory (RAVLT total and post-interference recall, $p<.01$), and processing speed (Stroop, $p=0.01$; TMT A, $p<.01$; WAIS-III Symbol Search, $p<.01$; WAIS-III Digit symbol Coding, $p<.01$) performance of patients with MTBI was significantly better than at one month after injury, likely reflecting a combination of practice effects and improvement in cognition in some people.

Table 13. Comparison of neuropsychological variables (z-scores) of patients with MTBI and controls.

	MTBI 1 months (N=74)	MTBI 6 months (N=65)	MTBI 1 month vs. MTBI 6 months		Controls (N=40)	MTBI 1 month vs. Controls		MTBI 6 months vs. Controls	
Neuropsychological Test	M (SD)	M (SD)	p	d	M (SD)	p	d	p	d
RAVLT total recall	.18 (.98)	.74 (.93)	.00	-.60	.34 (.93)	.37	-.17	.04	.43
RAVLT post-interference recall	-.03 (.96)	.38 (.97)	.00	-.40	.20 (.85)	.22	-.25	.11	.19
RAVLT recognition	.04 (1.16)	.30 (.75)	.51	-.10	.26 (1.04)	.32	-.20	.65	.05
Stroop Color-Word	-.04 (1.48)	.17 (1.26)	.01	-.19	.29 (1.14)	.22	-.24	.84	-.10
Verbal Fluency total	-.12 (1.17)	.13 (1.31)	.02	-.17	.32 (1.25)	.07	-.37	.54	-.15
Animal Fluency total	.69 (1.47)	.80 (1.62)	.56	-.05	1.18 (1.20)	.07	-.36	.07	-.26
TMT A (seconds)	.03 (1.10)	.37 (.87)	.00	-.37	-.06 (1.04)	.66	-.03	.02	.46
TMT B (seconds)	-.31 (1.73)	-.03 (1.04)	.11	-.23	-.04 (.72)[1]	.35	-.18	.69	.01
Finger Tapping (dominant)	.24 (1.18)	.32 (1.26)	.62	-.04	.51 (1.51)	.30	-.21	.51	-.14
Finger Tapping (non-dominant)	.22 (1.19)[2]	.29 (1.17)	.76	-.02	.42 (1.27)	.42	-.16	.34	-.11
WAIS-III Information	.48 (.49)[1]	NA	NA	NA	.62 (.67)	.51	-.25	NA	NA
WAIS-III Digit Span	.52 (1.54)	.75 (.87)	.43	-.12	.53 (.90)	.95	-.01	.17	.25
WAIS-III Digit-Symbol Coding	.51 (.98)	.84 (.93)	.00	-.32	.39 (1.06)[1]	.55	.12	.05	.46
WAIS-III Symbol Search	.23 (1.00)	.63 (.95)	.00	-.44	.51 (.96)	.16	-.28	.54	.13

[1]1 case missing, [2]2 cases missing
Abbreviations: RAVLT=Rey Auditory Verbal Learning Test, TMT= Trail Making Test, WAIS-III= Wechsler Adult Intelligence Scale, Third edition.
The comparisons were conducted using independent samples t-test and paired samples t-test. The table is reprinted with the kind permission of the copyright holder.

4.1.4.4 Mental health outcome

There were no significant differences in reporting of traumatic stress or depressive symptoms between patients with MTBI and controls (see Table 11) at any of the follow-ups. At 1 month after the injury, 16.0% of the MTBI group and 15.0% of the controls, and at 6 months 8.0% of the patients with MTBI and by 15.0% of the controls, were defined as having a mental health problem (depression or traumatic stress) (See Table 12). At 12 months, depressive symptoms were not assessed and 3.3% of the patients with MTBI and no control met criteria for probable PTSD.

4.1.4.5 Quality of life

At one and 12 months after the injury there were no statistically significant differences in quality of life (QOLIBRI) between the patients with MTBI and controls, and at 6 months after the injury the controls reported better (p=.04) quality of life than the patients with MTBI (See Table 11). In generic satisfaction with life (SWLS) there were no significant differences between the groups in any of the follow-ups. At 1 month after injury GOS-E ranged from 4 to 8 and at 6 months from 5 to 8. At one month 67.7% and at 6 months 88.9% of the patients with MTBI were classified as having a good recovery (see Table 12).

4.1.4.6 Return to work

Almost all (71 out of 74, 96%) of the patients with MTBI returned to work or normal activities (RTW) within the follow-up period of one year. The median time to RTW was 16.0 days, with most people (n=61, 82.4%) returning to work within two months following injury (IQR=5.0-42.0 days). The cumulative rates for RTW at each follow-up are presented in Table 12. There were 10 patients (13.3%) who did not have any sick leave after their injury. Out of the 64 patients with sick leave, the primary reason for it was a brain injury for 41 (64.1%), bodily injury for 14 (18.8%), and the combination of them for 11 (17.2%) patients. For all 3 patients who remained on sick leave at 12 months, the primary reason for initial sick leave was brain injury. All three were successfully followed up after the study period. One of these patients returned to work at 1 year and 2 months after the injury, one 3 years and 2.5 months after the injury, and

one patient retired, not because of problems relating to MTBI, but due to problems relating to physical injuries sustained at the time of the accident.

There were 50 MTBI subjects who returned to work within 1 month, and some of these individuals had problems identified during the one month follow-up. For example, 6% had mild cognitive impairment, 26% had mild PCS, 2% had moderate PCS, 14% met criteria for depression, and 2% met criteria for PTSD and 10% for possible PTSD. A large number had at least one of these problems (36%).

4.1.4.7 Recovery trajectories during a 12-month follow-up

The self-reported outcome measures are plotted over time in Figure 5. Several observations are noteworthy. The MTBI and trauma control group trajectories track closely together for most measures, except for post-concussion symptoms (RPCSQ) and fatigue (BNI), which are initially more elevated in the MTBI group. The slope changes at 6 months for most outcomes, reflecting that recovery is more rapid prior to this point. Slight ongoing recovery beyond 6 months is evident for some measures (fatigue, post-traumatic stress), whereas others appear to plateau by 6 months (e.g., sleep, pain). Quality of life and satisfaction with life appear relatively stable over time.

The rate of symptomatic, cognitive, and vocational outcome for patients with MTBI and controls are shown in Table 12. The rate of PCS is relatively stable across follow-ups, while the proportion who RTW steadily increases after MTBI. Cognitive impairment in the MTBI group also appeared to steadily decrease. RTW often occurred while patients with MTBI continued to meet criteria for mild PCS.

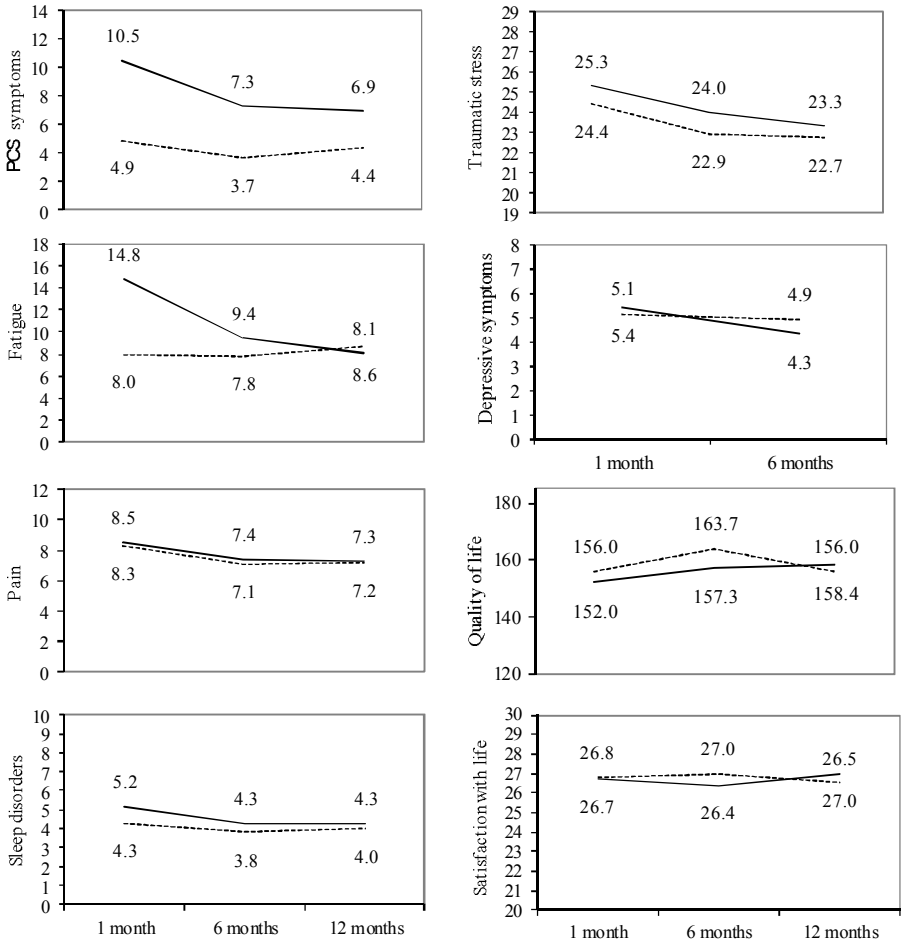

Figure 5. Recovery trajectories of self-reported outcomes for patients with MTBI and controls.

Note: Solid lines are for those with MTBIs and dotted lines are for the control subjects. Data about depressive symptoms not available at 12 months. The figure is reprinted with the kind permission of the copyright holder.

4.1.4.8 Multidimensional recovery

PCS, cognitive impairment (at 1 and 6 months), and RTW outcomes of patients with MTBI were combined to examine the multidimensional recovery of these core domains. PCS was defined here by at least moderate symptoms, because mild symptom endorsement was commonly found in controls as well. The patients who did not have moderate PCS, did not have cognitive impairment, and had returned to work were defined as being favorably recovered. Of patients with MTBI, recovery was achieved by 62.2% at 1 month, 84.4% at 6 months, and 93.3% at 12 months (see Table 12). In contrast, the patients who had moderate PCS, had cognitive impairment, and did not return to work were defined as being definitely impaired. Only one patient filled this criteria at all follow-ups (1.4-1.7%). The rest of the patients (36.4% at 1 month, 14.5% at 6 months, and 5% at 12 months) had different combinations of PCS, cognitive impairment, and RTW and can be classified as having a partial recovery.

At one month after injury, 51.4% of those with MTBI (38/74) and 34.2% of control subjects (13/38) met criteria for having at least *mild* PCS, depression, possible PTSD, or cognitive impairment. At six months, 32.8% of those with MTBI (21/64) and 25.0% of controls (8/32) met criteria for having at least mild PCS, depression, or possible PTSD. At 12 months, 30.0% of those with MTBI (18/60) and 21.4% of controls (6/28) met criteria for having at least mild PCS or possible PTSD (as previously noted, the depression measure was not administered at 12 months). These differences in mental health and mild post-concussion symptom reporting between the groups were not statistically significant.

4.1.4.9 Factors associated with persistent mild PCS and delayed return to work

Further exploratory analyses were conducted with subgroups who had PCS or remained on sick leave at the one year follow-up. The aim of these analyses was to thoroughly characterize patients with incomplete recovery and explore possible reasons for chronic PCS and delayed return to work. Of the 3 patients with MTBI who had moderate PCS at 12 months, none had trauma-related abnormalities on MRI and 1 had cognitive impairment at 1 month post injury (but no longer at 6 months post injury). Of these

same 3 patients, 2 reported elevated symptoms of depression and/or traumatic stress at some point.

As displayed in Table 14, patients with mild PCS at 12 months (n=16, 26.7%) did not have more severe original injuries than those without PCS at 12 months (n=44, 77.3%), and there were no differences in age, education, or gender between these two groups. Patients with mild PCS at 12 months were more likely to have cognitive impairment at one month, but neuropsychological differences disappeared by 6 months. Patients with mild PCS at 12 months also reported greater symptoms of PCS and fatigue, and there was a trend toward them reporting greater traumatic stress, at one month following injury. Those who had mild PCS at 12 months, reported significantly greater symptoms of PCS, fatigue, insomnia, traumatic stress, and depression, and worse quality of life, at six months following injury. At 12 months, those who met criteria for mild PCS also reported greater fatigue, insomnia, and traumatic stress, lower resilience, and lower quality of life and life satisfaction, than those who did not meet criteria for mild PCS.

For the 16 people with MTBIs who met criteria for mild PCS at 12 months, 10 (62.5%) met criteria for Mild PCS at one month and 12 (75%) met criteria for mild PCS at six months. Six (37.5%) met criteria for possible PTSD at one month and 3 (18.8%) met this criteria at six months. Six (37.5%) met criteria for low resilience at one month. Four (25%) met criteria for depression at one month, but only one (6.3%) met criteria for depression at six months. Ten (62.5%) met criteria for a modifiable mental health risk factor (i.e., low resilience, depression, or possible PTSD) at one month. There were five control subjects who met criteria for mild PCS at 12 months, and all five met criteria for possible PTSD or depression at one month.

Of the three patients with MTBI not returning to work within 12 months, one had trauma-related abnormalities on MRI, and two had cognitive impairment at 1 and 6 months post injury, and two reported elevated symptoms of depression and/or PTSD at some point. One of these patients had mild PCS and one moderate PCS at 12 months; one did not answer questionnaires at 12 months.

Table 14. Comparison of patients with MTBI with and without mild post-concussion syndrome at 12 months after injury.

	Mild PCS at 12 months	**No Mild PCS at 12 months**	p-value	Cohen´s d
Sample size	16	44		
Injury Severity Score: Mean (SD)	4.1 (3.1)	3.9 (3.3)	0.652	0.062
Loss of Consciousness (LOC): n (%)	5 (31.3)	17 (38.6)	0.587	
Age: Mean (SD)	40.5 (13.4)	37.4 (12.1)	0.442	0.249
Education: Mean (SD)	13.6 (3.5)	14.5 (2.9)	0.258	-0.293
Gender: Female: n (%)	8 (50.0)	18 (40.9)	0.568	
Traumatic Lesion on MRI: n (%)	4 (25.0)	11 (25.0)	1.00	
1 month variables				
Mild PCS+: n (%)	10 (62.5)	9 (20.5)	0.002	
Moderate PCS+: n (%)	4 (25.0)	0	0.001	
Cognitive Impairment at 1 months: n (%)	6 (40.0)[1]	5 (11.6)[1]	0.025	
Fatigue (BNI-FS): Mean (SD)	26.7 (20.4)	10.9 (10.9)[1]	0.003	1.126
Insomnia (ISI): Mean (SD)	7.4 (6.8)	4.4 (4.2)[1]	0.178	0.598
Pain Subscale (RNBI): Mean (SD)	9.8 (4.2)	7.8 (1.8)	0.093	0.758
Post-Traumatic Stress Symptoms: Mean (SD)	31.1 (12.6)	23.6 (6.5)	0.054	0.882
Depressive Symptoms: Mean (SD)	7.0 (6.2)	4.7 (5.4)	0.130	0.409
Quality of Life (QOLIBRI): Mean (SD)	140.1 (34.3)	155.8 (20.2)	0.128	-0.637
Life Satisfaction (SWLS): Mean (SD)	25.4 (4.1)	26.9 (6.5)	0.183	-0.251
Resilience (RS): Mean (SD)	137.7 (15.4)	141.4 (14.5)	0.328	-0.251
6 month variables				
Mild PCS+: n (%)	12 (75.0)	2 (4.7)	0.000	
Moderate PCS+: n (%)	2 (12.5)	0	0.070	
Cognitive Impairment at 6 months: n (%)	3 (7.5)[1]	1 (6.7)[4]	1.00	
Fatigue (BNI-FS): Mean (SD)	18.3 (17.0)	5.1 (6.8)	0.002	1.264
Insomnia (ISI): Mean (SD)	6.0 (4.2)	3.1 (2.8)	0.006	0.900
Pain Subscale (RNBI): Mean (SD)	7.8 (3.4)	7.1 (1.7)	0.675	0.309
Post-Traumatic Stress Symptoms: Mean (SD)	29.2 (11.5)[1]	21.5 (6.0)	0.001	0.997
Depressive Symptoms: Mean (SD)	6.5 (7.3)[1]	3.2 (5.3)[2]	0.007	0.560
Quality of Life (QOLIBRI): Mean (SD)	147.1 (25.5)	162.5 (15.7)	0.016	-0.822
Life Satisfaction (SWLS): Mean (SD)	24.7 (5.4)	26.9 (5.7)	0.092	-0.391
Resilience (RS): Mean (SD)	135.6 (23.2)	143.0 (16.9)[1]	0.375	-0.394
12 month variables				
Fatigue (BNI-FS): Mean (SD)	22.1 (15.9)	3.0 (5.4)	0.000	2.048
Insomnia (ISI): Mean (SD)	7.8 (4.3)	3.1 (3.2)	0.000	1.336
Pain Subscale (RNBI) : Mean (SD)	8.6 (4.0)	6.7 (1.7)	0.341	0.758
Post-Traumatic Stress Symptoms: Mean (SD)	27.3 (8.5)	21.8 (5.4)	0.003	0.866
Quality of Life (QOLIBRI): Mean (SD)	146.4 (22.6)	162.8 (19.5)	0.003	-0.806
Life Satisfaction (SWLS): Mean (SD)	24.9 (4.4)	27.7 (5.5)	0.038	-0.535
Resilience (RS): Mean (SD)	135.3 (17.6)	146.2 (18.0)	0.040	-0.609
Functional outcome				
Not returned to work: n (%)	2 (12.5)	0	0.068	
Return to work in days: Mean (SD)	146.4 (295.2)	26.1 (40.0)	0.014	0.883

[1]1 case missing, [2]4 cases missing. The table is reprinted with the kind permission of the copyright holder.

5 Discussion

5.1 The properties of the Resilience Scale

Based on the results of this study, the Finnish version of the Resilience Scale (RS) and its short version (RS-14) seem to have good psychometric properties. In addition, it was shown that both RS and RS-14 can be reliably used in MTBI research.

The internal consistency reliability was high for the Finnish version of the RS and RS-14 in the Finnish convenience sample (Study I), in patients with MTBI, and in trauma-controls (Study III). This is consistent with several previous studies showing good internal consistency for different language versions of the RS (Aroian et al., 1997; Heilemann et al., 2003; Lundman et al., 2007; Nishi et al., 2010; Wagnild & Young, 1993).

No clear factor structure of the RS was found in this study. Neither the original two-factor solution of RS (Wagnild & Young, 1993) or the five-factor solution reflecting the five dimensions of resilience (Lundman et al., 2007) were supported by the Finnish data. The factor structure of RS has also been inconsistent in previous studies (Aroian et al., 1997; Nishi et al., 2010). Due to the inconsistent factor structure found in this study and in prior studies, it could be suggested that the total score of the Finnish version of the scale should be used instead of separate dimensions.

Cultural differences could be expected in the RS scores. There are many ways to be resilient in different cultures; the Western views focus on choice and mastery over the environment, whereas the Eastern philosophies emphasize full awareness and acceptance of even painful experiences to sustain well-being (Zautra et al., 2012). The mean RS and RS-14 scores for the Finnish population were consistent with "moderate resilience" according to the original author (Wagnild, 2009b). This suggests that no significant cultural difference seems to exist between the RS scores of the original measure and the Finnish version. Cultural issues might, however, explain different findings about the association of resilience and gender. In this study there was no significant difference in resilience between genders. This concurs with previous findings from Sweden (Lundman et al., 2007). However, a significant difference in resilience between genders has been reported in other studies. In a Nigerian study, men

were found to report significantly greater resilience than women (Abiola & Udofia, 2011). In the Finnish population, again similar to findings from Sweden (Nygren et al., 2005), a significant correlation between the RS and self-rated health was only found in women. This was found in the study of the Finnish convenience sample (Study I). In our studies of patients with MTBI, our sample size did not allow for separate gender analyses. The relation between gender and resilience has not been widely reported in literature. Differences in brain responses to stress between men and women have, however, been found and determining how the processes of resilience differ between genders has been considered to be an important challenge for future research (McEwen et al., 2015).

The results of this study suggest that resilience is relatively stable during a follow-up of one year following MTBI, but also support the view of resilience as a dynamic process. Originally, resilience was conceptualized as a personality trait (Earvolino-Ramirez, 2007), meaning that it should be a fairly stable construct. In this study, resilience was relatively stable from 1 to 6 and 12 months post-injury in patients with MTBI and controls. This finding suggests that resilience can be used in prognostic research of MTBI. However, the follow-up of one year is too limited to make firm conclusions about the long-term stability of resilience. Further research on the stability of resilience over time is needed (Zautra et al., 2012). Current resilience research widely suggests that resilience is dynamic and malleable (Lundman et al., 2007; Luthar et al., 2000; Wagnild, 2003). Our, and others (Lundman et al., 2007), results of resilience being positively correlated with age also support this notion. It has been suggested that resilience can be enhanced or diminished depending on life circumstances (Wagnild, 2003), or learned (White et al., 2008). The extent to which resilience is modifiable was not examined in this study.

Greater resilience correlated in this study with less traumatic stress, less severe depressive symptoms, and better quality of life and self-reported health. These correlations are consistent with prior research with other health conditions (Abiola & Udofia, 2011; Heilemann et al., 2003; Humphreys, 2003; Nishi et al., 2010; Wagnild & Young, 1993; Wagnild, 2009b) and support the validity of the scale.

The results of this study also suggest that the Finnish short version (RS-14) of the RS can be reliably used to examine resilience. RS-14 correlated highly with RS and the

reliability and validity coefficients were similar for the RS and the RS-14. In addition, the Finnish version of RS-14 fitted the previously proposed one factor solution (Nishi et al., 2010) acceptably.

Scales, such as the RS, to evaluate resilience are needed especially in scientific studies. In clinical practice however, an interview can also be used to assess resilience. Resilience could, for example, be assessed by asking the clients how they have dealt successfully with previous problems or what qualities they like about themselves to uncover their strengths (Neenan, 2009).

5.2 The association of resilience and outcome from MTBI

To date, there have been few studies on the association between resilience and outcome following MTBI. According to the results of this study, resilience is associated with outcome from MTBI. First, resilience was found to be a significant predictor of less self-reported fatigue following MTBI, even when controlled for the factors known to be associated with fatigue (depression, sleep disorders, and pain). Second, greater resilience was associated with fewer post-concussive symptoms and better quality of life, whereas lower resilience was associated with more symptoms and lower quality of life.

Resilience has previously been shown to be associated with fatigue in cancer patients (Strauss et al., 2007) and patients with Parkinson's disease (Robottom et al., 2012). This was the first study to report the association of resilience and fatigue in patients with MTBI, although in many previous studies it has been shown that psychological factors such as depression or stress are associated with fatigue. This study showed that also in a healthy population, with no previous psychiatric problems, resilience is associated with fatigue. In patients with MTBI, the correlation between resilience and fatigue was greater during follow-up. In controls, significant associations between resilience and fatigue were not found. In addition, insomnia, pain, and depressive symptoms were significantly correlated with fatigue. The MTBI and control groups did not significantly differ on these symptoms, which might partly be explained by the symptoms induced by the physical injuries of the controls.

Besides fatigue, resilience was also found to be associated with broader symptomatic outcome from MTBI. By comparing MTBI patients with low versus moderate to high

resilience it was found that resilience at 1 month not only was associated with symptoms measured at the same time (i.e., at one month) but also with outcome at follow-up (i.e., at six and 12 months). Participants with moderate to high resilience reported significantly less post-concussion, fatigue, insomnia, traumatic stress, and depressive symptoms, and better quality of life, than the patients with relatively low resilience concurrently (at 1 month post injury) and at 6-month follow-up. At 12 months after injury, those MTBI patients with at least moderate resilience reported less fatigue and traumatic stress and better quality of life than those with relatively low resilience.

The association between resilience and outcome from MTBI has previously not been widely studied. Only in recent years, the topic has begun to attract increasing scientific interest. The results of this study about the association of resilience and outcome from MTBI are consistent with the recent available studies about resilience contributing to recovery from MTBI (McCauley et al., 2013; Merritt et al., 2014; Sullivan et al., 2015). All these studies have, however, used different measures of resilience and also defined outcomes differently. Thus, more research is needed before making firm conclusions.

Despite significant associations with resilience and symptomatology, no significant association between resilience and time to return to work was found in this study. This might be due to social, cultural, and compensational issues that can affect return to work (Cancelliere et al., 2014). The literature on RTW after MTBI is limited (Cancelliere et al., 2014) and to the best of our knowledge, no previous reports on the association between resilience and RTW have been published. More research is thus needed.

It is noteworthy that the significant association with resilience and symptoms was found when resilience scores were examined as categorical or dichotomic variables (Studies II and III). When resilience was examined as a continuous variable (Study IV), it was significantly associated with chronic mild PCS only at 12 months. This suggests that the association of resilience and outcome may not be linear. Simply put, those with less than moderate resilience may be more at risk for poor outcome.

In the literature, there has been longstanding controversy between the psychological and organic etiologies of chronic post-concussion symptoms. However, this debate has been considered simplistic and non-productive and a focus on developing interventions instead has been called for (Iverson et al., 2012; Ruff, 2005; Shenton et al., 2012). Similarly, resilience should be considered a modifiable psychological construct that can

be enhanced to help patients recover instead of conceptualizing it as a stable personal attribute of the individual (Luthar & Cicchetti, 2000). Resilience is developed through our life experiences (McEwen et al., 2015), it is not something one chooses to have or not to have. Thus, the results of resilience being associated with outcome from MTBI should not be used to hold patients accountable for their delayed recovery.

5.3 Recovery from MTBI in previously healthy adults

In this study recovery from MTBI was examined across multiple domains (symptomatic, quality of life, mental health, and cognitive outcome, and RTW) in a sample with no pre-existing health conditions. Because fatigue is one of the most frequent symptoms after MTBI (Stulemeijer et al., 2006) with complex and interwoven underlying causes (Wäljas et al., 2012) it was examined in more detail.

The results of this study supported the established knowledge about fatigue being an prominent symptom after MTBI. The comparison to the control group illustrated that the course of fatigue was different after MTBI than after an orthopedic injury. Fatigue was found to be significantly greater in patients with MTBI than the controls at 1 month after the injury. This concurs with previous findings (Wäljas et al., 2012). Previously, up to one-third of patients with MTBI have been found to experience severe fatigue six months after injury (Stulemeijer et al., 2006). In this study, however, there was a significant decrease in fatigue in patients with MTBI during follow-up. At 6 months after injury, there was no significant difference between patients with MTBI and controls regarding self-reported fatigue.

In this study, patients with MTBI did not differ as a group from non-head injury trauma controls on cognition, fatigue, or mental health by six months following injury, and by 12 months their level of post-concussion symptoms and quality of life was similar to that of controls. In addition, examining individual patient outcomes, more than 90% achieved favorable recovery from MTBI by one year following injury and almost all (96%) returned to work or normal activities. These findings support that MTBI has a good prognosis, at least in patients who were healthy prior to injury (Cassidy et al., 2014).

In the literature, the expected recovery course from MTBI has been debated (McCrea et al., 2009) and the findings about the persistence of symptoms have not been

consistent (Holm et al., 2005). Many previous studies have found persistent PCS prevalence rates from 10% to 30% (Hou et al., 2012; Kraus et al., 2009; Sigurdardottir et al., 2009; Wood, 2004). It is well acknowledged that post-concussion symptoms are not specific to MTBI (Iverson & McCracken, 1997; Lange et al., 2012; Meares et al., 2008; Mounce et al., 2013), and studies using appropriate control groups typically report resolution of symptoms within weeks or few months (Holm et al., 2005). In this study the prevalence of self-reported PCS (i.e., 27%) was consistent with those rates if mild symptoms were used as the criterion. However, our multidimensional assessment battery and trauma control group help provide context for this finding; mild PCS was also found in a fairly large proportion (17%) of the controls. If at least moderate symptoms were used as the criterion, the prevalence of PCS at the follow-ups was much smaller (from 4.3% to 5.4% in the follow-ups). It is also noteworthy, that there was no significant difference in the rate of mild or moderate PCS between patients with MTBI and controls at any of the follow-ups. The recovery from MTBI in this study was more rapid than in some previous studies (Thornhill et al., 2000; Sigurdardottir et al., 2009; Cassidy et al., 2014). Our results, however, are in accordance with arguments that if issues relating to representatives of the sample and criteria of the syndrome are taken into account, a relatively small percentage of patients with MTBI continue to experience persistent symptoms (Iverson et al., 2012b; McCrea et al., 2009; Rees, 2003).

There are other possible reasons for finding a favorable recovery after MTBI in this study. First, a highly selected sample of previously healthy adults was used to minimize confounding factors. Second, cultural issues, such as symptom expectations after a head injury, have been shown to differ between countries and possibly contribute to development of persistent symptoms (Ferrari et al., 2001). For example, it has been found that there is a significantly lower rate of any chronic sequelae from a head injury in Lithuania than in Canada (Ferrari et al., 2001). To the best of our knowledge, there are no studies of symptom expectations after MTBI in Finland. This study did not include an intervention and the patients were treated according to the normal protocol after their assessments. However, all the patients received information about their injury at the visit with the physician and neuropsychologist, and it could be hypothesized that this could have affected their symptom expectations. Third, compensational issues can affect the results because litigation, for example, has been considered to influence

recovery from MTBI (Iverson et al., 2012b). Exact data about subjects' litigation status was not available. However, it can be hypothesized that compensation seeking was rare because in the Finnish system injured patients receive government compensation for their time off work and during the first year after injury personal litigation is uncommon. Fourth, the mechanism and context of MTBI have to be considered as possible factors associated with outcome. After car accidents, for example, bodily injuries, psychological traumatization, and access to compensation are more common than in other injury mechanisms, whereas outcome from sport-related injuries is usually better (Iverson et al., 2012b). In this study there was a similar number of sport-related injuries and car accidents. Fifth, it has been suggested that the patients who do not attend follow-ups have a more favorable outcome than those who do (Vikane et al., 2014). Thus, it can be hypothesized that the low drop-out rate in this study resulted in more recovered patients included the follow-ups.

The multidimensional outcome battery and longitudinal design of this study also allowed an examination of the trajectories of different domains of recovery. It was found that recovery was not uniform across the outcome domains. The quality of life and satisfaction with life were found to be stable during the follow-up of one year and similar between groups, suggesting that these domains are relatively unaffected by minor traumatic injury. Most other outcome measures showed recovery and plateau by 6 months post injury and RTW often preceded recovery in other domains. It was also found that a large proportion of patients who had returned to work within one month had PCS, cognitive impairment, or psychiatric problems at the 1 month assessment. Simply put, it was common for people to return to work while still symptomatic. RTW despite having complaints was common for MTBI patients in another study (van der Naalt et al., 1999). It has been noted before that recovery from mild head injury is better and faster when evaluated by functional status and quality of life than by post-concussion symptoms (Heitger et al., 2007). This discrepancy between post-concussion symptoms and relatively normal functionality and quality of life could suggest that the "good recovery" from MTBI may involve a behavioral adaptation rather than a complete return to a previous health status (Heitger et al., 2007). This view is in accordance with our findings about resilience being associated with outcome.

Patients reporting ongoing mild PCS at the 12-month follow-up were compared to those without PCS to examine associations of the syndrome with injury related factors and other symptoms. Patients reporting ongoing mild PCS at the 12-month follow-up did not have more severe brain injuries than those without PCS (as reflected by LOC or MRI findings). They also did not have more severe bodily injuries or chronic pain. They were much slower to return to work but virtually all were able to return within one year. They had higher rates of cognitive impairment at 1 month but no longer at 6 months post injury. A large percentage (62.5%) had a modifiable psychological risk factor at one month (i.e., depression, possible PTSD, and/or low resilience), and at six months they had greater PCS, fatigue, insomnia, traumatic stress, and depression, and worse quality of life. In summary, patients with chronic mild PCS in our cohort achieved cognitive and functional recovery but continued to be psychologically distressed and dissatisfied. Similarly, all five of the control subjects who had mild PCS at 12 months also had a mental health problem (i.e., depression, traumatic stress, or both). Thus, it can be hypothesized that interventions targeting these variables could be beneficial for recovery. These findings concur with previous findings that patients with persisting post-concussion symptoms have a high prevalence of comorbid psychiatric problems (King & Kirwilliam, 2011), even though we excluded patients with pre-morbid psychiatric problems. Unlike the majority of prior studies (King, 2014; Silverberg et al., 2015), for reasons that are unclear, gender was not associated with chronic PCS in this study.

Our study design did not allow to us to make conclusions about the cause(s) of chronic PCS. Although chronic mild PCS, depression, and traumatic stress were associated, it is not clear if emotional problems are responsible for chronic PCS, PCS results in emotional consequences, or whether the associations between post-concussion symptom and psychiatric symptom reporting are due to shared method variance (i.e., self-report) or etiology (i.e., brain injury). The finding that depression, traumatic stress, and PCS did not differ between patients with head vs. ankle injuries at 12 months following injury makes it somewhat less likely that underlying brain injury accounts for these outcomes.

5.4 Possibilities for enhancing resilience and improving outcome from MTBI

It was beyond the scope of this study to examine the mechanisms of the association of resilience and outcome from MTBI or to address interventions for resilience. However, conceptualizing resilience as an attribute that is modifiable, together with the findings about resilience being associated with outcome from MTBI, call for attention to the possibilities for its enhancement to improve recovery.

Results from resilience research could be used to identify individuals who may benefit from interventions early after injury (White et al., 2008). In this study, the patients with relatively low resilience had poorer outcome, suggesting that these patients could benefit from closer follow-up and interventions. This has been suggested by other researchers as well (Sullivan et al., 2015). In addition, the assessment of resilience has been considered useful in defining more individualized rehabilitation programs and in considering patients expectations of neurorehabilitation (Bertisch et al., 2014; Tonks et al., 2011).

Resilience could also be targeted by interventions to improve outcomes from MTBI. Resilience in rehabilitation can be conceptualized as part of the broader positive psychology paradigm that focuses on nurturing strengths instead of correcting weaknesses (Bertisch et al., 2014; Cui et al., 2010; Godwin & Kreutzer, 2013; Mak et al., 2011; Richardson, 2002). There are few interventions that have focused on resilience per se (Zautra et al., 2012), but based on a recent systematic review (Macedo et al., 2014) there is evidence of some degree of effectiveness of resilience promotion programs. Resilience enhancement or training has been considered useful in stress-management and stress-prevention programs for college students (Steinhardt & Dolbier, 2008), and for improving stress, anxiety, fatigue, and quality of life in cancer patients (Loprinzi et al., 2011). Mindfulness-based interventions might be useful for promoting resilience (McEwen et al., 2015; Neenan, 2009), and these approaches to managing stress have shown effectiveness in enhancing resilience in the workplace (Aikens et al., 2014) and for reducing anxiety (Feder et al., 2012).

An interesting and well-described example of a resilience training program is the one developed for use in the U.S. Army (Reivich et al., 2011). This program includes: (i) learning about resilience; (ii) building resilience competencies with techniques from

cognitive behavioral therapy (CBT), such as challenging negative thoughts, learning about explanatory styles and thinking traps (like over-generalizing), identifying deeply held beliefs and values, energy management (such as breathing and relaxation), problem solving skills, minimizing catastrophic thinking, and cultivating gratitude; (iii) identifying strengths; and (iv) strengthening relationships (Reivich et al., 2011). This training has been shown to improve the resilience and psychological health of soldiers (Lester et al., 2013). In addition, the positive psychotherapy developed by Seligman et al. (2006) focuses on targeting personal strengths and building positive emotions and meaning, and positive psychology exercises have been delivered successfully via the internet (Seligman et al., 2006). Others have considered the promotion of positive appraisal styles essential for developing resilience (Tugade & Fredrickson, 2004).

In addition to psychological interventions, social support and physical activity could enhance resilience (McEwen et al., 2015). In the context of MTBI, it is noteworthy, that physical activity and exercise has been shown to improve cerebral blood flow and executive function, increase hippocampal volume, and to be an effective antidepressant (McEwen et al., 2015). There is some evidence for both direct and indirect benefits of exercise after MTBI as well (Tan et al., 2014). It has also been suggested that as the understanding of the neurobiological underpinnings of resilience progresses, the pharmacological treatment options also will broaden (Feder et al., 2012).

A broader approach to enhancing resilience following MTBI encompasses related psychological constructs. For example, a belief in oneself and one's abilities, positive views, and high expectancy have been considered to be part of resilience (Mak et al., 2011). After MTBI, there is consistent evidence that expectations about injury/illness perceptions are associated with outcome (Pargament & Cummings, 2012; Snell et al., 2011; Suhr & Gunstad, 2002; Suhr & Gunstad, 2005; Trontel et al., 2013; Whittaker et al., 2007). These expectations could be targeted by patient education and reassurance of expected full recovery early after injury (Kraus et al., 2009; Management of Concussion/mTBI Working Group, 2009). It has also been suggested that in clinical work with patients with MTBI, words such as brain injury and brain damage should be avoided in favor of more neutral terms to lessen the distress of patients (Management of Concussion/mTBI Working Group, 2009; McLean et al., 2009). This literature suggests that patients who have stronger negative beliefs about the nature and consequences of

the injury are more at risk for poor outcome. Thus, the resilience perspective together with these findings about recovery expectations and illness perceptions supports the view of giving patients with MTBI realistic but hopeful information about the good prognosis of their injury. This could be delivered in person, by phone or mail, or via email or a web site (Kraus et al., 2009).

However, only providing information or education does not seem to be enough for some patients who are at risk for chronic symptoms (Silverberg et al., 2013). Adaptive health behavior is also part of resilience (Wagnild & Young, 1993), and maladaptive behavior, like all-or-nothing coping, is associated with risk for the post-concussion syndrome after MTBI (Hou et al., 2012). Thus, early interventions targeting coping skills have been widely suggested for patients with MTBI to improve outcome (Gregorio et al., 2014; Hou et al., 2012; Ponsford et al., 2012). Interventions may be especially beneficial for patients at risk for persistent symptoms (Cassidy et al., 2004) and a closer follow-up is recommended for those with pre-injury psychiatric disorders (Dagher et al., 2013). As mentioned above, one potential intervention is CBT. In patients with chronic fatigue syndrome, CBT has been shown to improve health, physical activity, and cognitive performance, and effective CBT was also associated with increased grey matter volume in the lateral prefrontal cortex (de Lange et al., 2008). CBT delivered soon after injury could be beneficial for supporting recovery from MTBI (Hou et al., 2012; Silverberg et al., 2013), especially for those with previous stressful life events (Veldhoven et al., 2011).

In summary, early interventions to enhance resilience and recovery from MTBI are both important and feasible. It has been noted however, that as the applications of positive psychology continue to grow, there is a need to develop clearer definitions and instruments to evaluate these constructs and the way they apply to patients with brain injury (Bertisch et al., 2014). More quality research is also needed on the associations between resilience and related concepts such as coping and illness perceptions in recovery from MTBI, and about the effectiveness of resilience promotion programs (Macedo et al., 2014).

5.4 Methodological considerations

Some methodological considerations should be addressed when evaluating the results of this study and drawing clinical conclusions. First, the selection of the samples should be considered. In Study I, the psychometric properties of the RS were examined using a convenience sample that was not randomly selected. The participants were relatively highly educated. However, the findings of our and previous studies (Wagnild & Young, 1993) suggest that education is not significantly associated with the RS or RS-14. Additionally, age-wise our sample could be considered representative. The MTBI sample (Studies II, III, and IV) was carefully screened to exclude patients with pre-existing psychiatric or neurological disorders, substance abuse, or brain injuries. By applying strict exclusion criteria, we enrolled only 2.5% of all consecutively screened patients with head CT due to an acute head injury. Thus, the MTBI group was highly selected, which limits the generalizability of the results into everyday clinical practice. By excluding patients with prior psychiatric problems, the sample likely had an inadequate representation of individuals with low resilience. In this study, we aimed to avoid possible bias due to a heterogeneous sample by obtaining a homogenous MTBI group with all the patients meeting the criteria for MTBI proposed by World Health Organization's Collaborating Centre for Neurotrauma Task Force (Holm et al., 2005). In addition, examining a previously healthy group minimizes pre-injury confounding factors. We have discussed the implications of the sample selection to drawing clinical interpretations in detail in a previous publication of our study group (Luoto et al., 2013). The sample size of this study was also relatively small and like in most longitudinal MTBI studies, follow-up was incomplete. However, the drop-out rate can be considered relatively low and participants with missing follow-up data did not differ from those who completed all assessments with respect to demographic or trauma-related (GCS, LOC) variables, symptoms at 1 month, or RTW. This suggests minimal systematic bias due to attrition.

The inclusion of an orthopedic control group enrolled with the same exclusion criteria was a strength of this study and helped avoid over-estimating the significance of mild nonspecific symptoms. However, the controls only completed the neuropsychological examination once, whereas in patients with MTBI possible practice effects could have affected the results in the second examination. In addition, this study

did not include a healthy control group. In future studies of MTBI, it would be beneficial to have healthy controls in addition to trauma controls, for whom pain, for example, can affect symptom reporting and test performance.

The assessment methods used in this study also need to be considered. Both resilience and the symptomatic outcomes were assessed by self-report questionnaires. In using self-report measures, over-reporting of symptoms is seen in some patients following MTBI (Management of Concussion/mTBI Working Group, 2009). In addition, due to using self-report variables, the associations can be influenced by common method variance because there is considerable overlap in the evaluated constructs. When studying fatigue (Study II), we aimed to reduce the overlap-effect of the questionnaires (BDI-II, BNI, and ISI) by conducting the analysis with a reduced item set for BDI-II (with three potentially confounding items removed). Also, we carefully evaluated the outcome broadly including not only symptoms, but also cognitive and mental health outcome, quality of life, and RTW. Resilience was assessed in this study using the RS, and certain aspects of resilience (such as social support) were thus not evaluated. Future studies could incorporate a broader assessment of resilience and also compare the RS to other questionnaires of resilience.

Another limitation of this study is a lack of a three month follow-up which has been considered important because the symptoms lasting at least three months are part of the diagnostic criteria for post-concussion syndrome in Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (Cassidy et al., 2014). In addition, exact data about litigation in this study sample was not available and symptom validity/effort testing was not used. However, injured patients receive government compensation for their time off work in the Finnish system. Thus, personal litigation is uncommon during the first year after injury. Despite the above mentioned limitations, we have been able to overcome many of the challenges of previous studies by using a longitudinal study design with a 12 month follow-up, low drop-out rates, and minimal confounding factors.

5.5 Clinical implications

This study provides information about the use of the Resilience Scale. Due to its good psychometric properties, the Finnish version of the RS can be recommended for use in clinical and scientific settings to assess resilience. Gender is recommended to be taken into account in further research on resilience. The short version of the scale (RS-14) was found to have similar good psychometric properties and associations with outcome. Thus, it can also be recommended to assess resilience, especially in situations when burden to the participants and time taken to complete the questionnaires need to be decreased.

According to the results of this study, resilience is a potential construct to be taken into consideration when examining and treating patients with MTBI. Assessment of resilience could, for example, be used to identify patients who may benefit from follow-up and treatment. This could be done by using the RS or other structured methods to assess resilience. Alternatively, a resilience framework could be applied in the clinical interview by emphasizing not only the subjective symptoms but also the strengths of the patient. In addition, resilience could be targeted in interventions to improve outcome from MTBI. Those patients with persistent mild long-term symptoms after MTBI had modifiable psychological problems throughout the first year (e.g., traumatic stress, depression, and low resilience). Thus, the results of this study also illustrate the potential importance of providing treatment and rehabilitation services early in the recovery period. Moreover, in management of fatigue, patients with MTBI might benefit from early post-injury guidance along with treatment of sleep disorders, pain, and depressive symptoms.

The findings of this study support that MTBI has a favorable prognosis, at least in patients who were healthy prior to injury. Because there is consistent evidence that expectations about injury and illness perceptions are associated with outcome, this information about good prognosis could be used in patient education and reassurance to support recovery.

5.6 Main findings and conclusions

1. The Finnish version of the Resilience Scale (RS) and its short version (RS-14) have good psychometric properties.

2. The RS and RS-14 can be reliably used in MTBI research.

3. Resilience was found to be a significant predictor of less self-reported fatigue following MTBI, even when controlling for factors known to be associated with fatigue (depression, sleep disorders, and pain).

4. Greater resilience was associated with fewer post-concussive symptoms and better quality of life, whereas lower resilience was associated with more symptoms and lower quality of life.

5. MTBI had a good prognosis in this sample of patients who were healthy prior to injury. By six months following injury, patients with MTBI did not differ as a group from non-head injury trauma controls on cognition, fatigue, or mental health, and by 12 months their level of post-concussion symptoms and quality of life was similar to that of controls. Almost all (96%) patients with MTBI returned to work or normal activities within the follow-up of one year.

6. A subgroup of patients with MTBI (27%) reported mild post-concussion-like symptoms at one year. However, 17% of the trauma controls also reported mild post-concussion-like symptoms at one year which helped provide context for this finding.

7. A large percentage (62.5%) of those with persistent post-concussion symptoms had a modifiable psychological risk factor during the one-month follow-up assessment (i.e., depression, possible PTSD, and/or low resilience). This illustrates the importance of providing evidence-supported treatment and rehabilitation services early in the recovery period.

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Appendix: The Finnish version of the Resilience Scale (RS)

Ole hyvä ja ympyröi kunkin väittämän yhteydessä se vaihtoehto, joka parhaiten ilmaisee, missä määrin olet väittämän kanssa samaa tai eri mieltä.

		Eri mieltä						Samaa mieltä
1.	Kun olen suunnitellut jotain, myös toteutan suunnitelmani.	1	2	3	4	5	6	7
2.	**Yleensä kyllä selviydyn asioista tavalla tai toisella.**	1	2	3	4	5	6	7
3.	Luotan itseeni enemmän kuin kehenkään muuhun.	1	2	3	4	5	6	7
4.	Minulle on tärkeää olla kiinnostunut erilaisista asioista.	1	2	3	4	5	6	7
5.	Voin olla yksin, jos on pakko.	1	2	3	4	5	6	7
6.	**Olen ylpeä siitä, että olen saanut jotain aikaan elämässäni.**	1	2	3	4	5	6	7
7.	**En tavallisesti hermostu tai järkyty vastoinkäymisistä tai yllätyksistä.**	1	2	3	4	5	6	7
8.	**Olen sinut itseni kanssa.**	1	2	3	4	5	6	7
9.	**Mielestäni pystyn käsittelemään monta asiaa yhtä aikaa.**	1	2	3	4	5	6	7
10.	**Olen määrätietoinen.**	1	2	3	4	5	6	7
11.	Mietin harvoin, mitä järkeä tässä kaikessa on.	1	2	3	4	5	6	7
12.	Elän elämääni päivä kerrallaan.	1	2	3	4	5	6	7
13.	**Kestän vaikeat ajat, koska olen kokenut niitä aikaisemminkin.**	1	2	3	4	5	6	7
14.	**Minulla on itsekuria.**	1	2	3	4	5	6	7
15.	**Pidän yllä kiinnostusta asioihin.**	1	2	3	4	5	6	7
16.	**Minun on yleensä helppo keksiä naurun aihetta.**	1	2	3	4	5	6	7
17.	**Selviydyn vaikeista ajoista, koska uskon itseeni.**	1	2	3	4	5	6	7
18.	**Hätätilanteissa minä olen yleensä se, johon ihmiset voivat luottaa.**	1	2	3	4	5	6	7
19.	Yleensä pystyn tarkastelemaan tilanteita monelta kannalta.	1	2	3	4	5	6	7
20.	Joskus pakotan itseni tekemään jotain riippumatta siitä, haluanko vai en.	1	2	3	4	5	6	7
21.	**Elämälläni on jokin tarkoitus.**	1	2	3	4	5	6	7
22.	En jää hautomaan asioita, joille en mahda mitään.	1	2	3	4	5	6	7
23.	**Jos joudun kiperään tilanteeseen, keksin yleensä jonkin ulospääsytien.**	1	2	3	4	5	6	7
24.	Minulla on riittävästi energiaa siihen, mitä minun pitää tehdä.	1	2	3	4	5	6	7
25.	Ei haittaa, vaikka jotkut eivät pidäkään minusta.	1	2	3	4	5	6	7

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