ENERGY CRISIS: PREVALENCE, SEVERITY, TREATMENT AND PERSISTENCE OF FATIGUE AFTER MILD TRAUMATIC BRAIN INJURY

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ABSTRACT

The objectives of this research were to investigate the prevalence and severity of post-mild traumatic brain injury (MTBI) fatigue in a non-litigant New Zealand sample and to evaluate the effectiveness of a treatment programme. Subsequently, a third objective evolved – the investigation of the natural history of post-MTBI fatigue and the degree to which reliable clinically significant change occurred over time regardless of intervention type. The research took the form of two studies where analysis was based on group data followed by analysis of the Study Two data at an individual participant level.

Study One, a longitudinal prospective study examined fatigue prevalence, severity, predictors and co-variates over six months post mild traumatic brain injury (MTBI). Participants completed the Fatigue Severity Scale (FSS), Rivermead Postconcussion Symptoms Questionnaire (RPSQ), Hospital Anxiety and Depression Scale (HADS) and the Short Form 36 Health Survey-Version 2 (SF-36v2). Complete data were available for 159 participants. Key measures; prevalence - RPSQ Item 6: severity - FSS. The effect of time on fatigue prevalence and severity was examined using ANOVA. Multiple regression analysis identified statistically significant covariates. The study found post-MTBI fatigue prevalence was 68%, 38% and 34% at 1 week, 3 and 6 months respectively. There was a strong effect for time over the first three months and moderate to high correlations between fatigue prevalence and severity. Early fatigue strongly predicted later fatigue. Depression, but not anxiety, was a predictor. Fatigue was seen as laziness by family or friends in 30% of cases. Conclusions for Study 1 were that post-MTBI fatigue is a persistent postconcussion

symptom, exacerbated by depression but not anxiety. It diminishes in the first three months and then becomes relatively stable, suggesting the optimum intervention placement is at three months or more post-MTBI.

Study Two was a quasi-experimental longitudinal prospective controlled study which had a two by three, treatment by time, repeated measures research design. Participants with a history of MTBI were recruited from three Concussion Clinics. Post-MTBI fatigue was identified through Item 6 of the Rivermead Postconcussion Symptoms Questionnaire (RPSQ) and the outcome measures were the FSS, Fatigue Assessment Scale, RPSQ, Hospital Anxiety and Depression Scale and Sydney Psychosocial Re-integration Scale. All treatment group participants (N = 18) came from the same Concussion Clinic as the principal researcher, and control participants (N = 23) came from other Concussion Clinics. The question of whether the participants thought their significant others perceived them as lazy was also explored in Study Two. A 12 week manualised programme (PERT) was developed specifically for Study Two and was delivered by either a clinical psychologist or occupational therapist through a combination of personal and phone sessions. No significant time by group effect was found for any of the outcome measures. A time effect was found for all of the outcome measures. During the search for explanations for these findings it was discovered that the two conditions were more similar than expected. The majority (85.7%) of the control group had, in accordance with current rehabilitation practice, engaged in exercise and/or received interventions similar to the treatment group which presented a confound to the study. The data from the two groups was combined and analysed for information regarding reliable clinically significant change RCSC in individual participants. No significant correlations with demographic variables such as time since

injury, age, gender, level of education, work type and injury type were found. Female gender was related to positive RCSC at three months post-baseline but not at six months post-baseline. Fatigue severity was significantly positively related to participants' belief that relatives perceived them as lazy. Study Two provided no evidence to support this treatment for post-MTBI fatigue. Prevalence and severity of post-MTBI fatigue reduced over the six months of Study Two, however on examination of individual data the majority of the participants showed no reliable clinically significant change, supporting the need for further research into finding an effective post-MTBI fatigue treatment. The small sample size and the similarity of the treatment and control group conditions were major factors in confounding the findings of the study.

There is a comparatively large percentage of individuals reporting prevalence and severity of post-MTBI fatigue in New Zealand samples and, although the combined psychoeducation and aerobic exercise approach could not be evaluated, the postconcussion and general literature suggests there is merit in continuing research into its effectiveness in treating post-MTBI fatigue.

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THESIS RESEARCH OUTPUTS

Parts of this thesis research have been published in refereed journal literature and presented at national and international conferences.

Norrie, J. (2005, August). *"Hitting the wall": Fatigue and traumatic brain injury.* Paper presented at the TBI Functional Rehabilitation Conference: 'Get Real' Top Ten Challenges in TBI Rehabilitation.

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ABBREVIATIONS

5HT	5-Hydroxytryptamine or Serotonin
ANOVA	Analysis of Variance
APOE	Apolipoprotein E
CBT	Cognitive Behaviour Therapy
CDC	Centres for Disease Control and Prevention
CFS	Chronic Fatigue Syndrome
CMRO2	Cerebral Metabolic Rate of Oxygen
CT	Computed Tomography
DAI	Diffuse Axonal Injury
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DTI	Diffusion Tensor Imaging
FAS	Fatigue Assessment Scale
FSS	Fatigue Severity Scale
DWI	Diffusion Weighted Imaging
GCS	Glasgow Coma Scale

HADS	Hospital Anxiety and Depression Scale
ICD	International Classification of Diseases
IQ	Intelligence Quotient
LOC	Loss of Consciousness
MCID	Minimum Clinically Important Difference
MS	Multiple Sclerosis
MTBI	Mild Traumatic Brain Injury
NIH	National Institutes of Health
OEF	Oxygen Extraction Fraction
PCS	PostConcussion Syndrome
PET	Positron Emission Tomography
PMRS	Proton Magnetic Resonance Spectroscopy
PPCS	Persistent PostConcussion Syndrome
POMS	Profile of Mood States
PERT	Postconcussion Energy Recovery Training
PTA	PostTraumatic Amnesia
PTSD	PostTraumatic Stress Disorder

QOL	Quality Of Life
rCBF	regional Cerebral Blood Flow
RCI	Reliable Change Index
RCT	Randomised Controlled Trial
RPSQ	Rivermead Postconcussion Symptoms Questionnaire
SPECT	Single Photon Emission Computed Tomography
SPRS	Sydney Psychosocial Reintegration Scale
TBI	Traumatic Brain Injury
WAIS-R	Wechsler Adult Intelligence Scale – Revised
WHO	World Health Organisation

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Chapter 1

OVERVIEW

Persistent fatigue is a common problem for all who sustain traumatic brain injury (TBI) (Elovic, Dobrovic, & Fellus, 2005). Unlike other common problems after TBI where severity of TBI predicts severity of outcome, fatigue appears to result from TBI across the severity spectrum and can be enduring. Most TBI (70% - 90%) are mild in severity (McCrea, 2008; New Zealand Guidelines Group, 2006; Uzzell, 1999) with approximately 689/100,000 New Zealanders presenting to hospital with a mild traumatic brain injury each year (New Zealand Guidelines Group, 2006), a rate that increases when those who presented to their General Practitioner or who did not seek medical attention at all are added (Wrightson & Gronwall, 1998). Post-MTBI fatigue is reported to persist for months or years after the initial injury with rates of 22% to 47% reported at three months (Dijkers & Bushnik, 2008; Mittenberg, Tremont, Zielinski, Fichera, & Rayls, 1996; Ouellet & Morin, 2006; Rao, Rollings, & Spiro, 2005), and 20% at one year. Given these figures, it is clear that post-MTBI fatigue is a major problem affecting multiple facets of life.

Wrightson & Gronwall (1999) described post-MTBI fatigue as the most important single factor that patients must deal with when returning to work after MTBI. Others (e.g., Cantor, 2008) suggest that post-TBI fatigue could interfere with the quality of participation in work, home and recreational activities. When post-MTBI fatigue exceeds a critical level, function deteriorates, stress accumulates and symptoms such as headache, dizziness and irritability reappear. While this process of deterioration is characteristic of normal fatigue, the experience of post-MTBI fatigue is distinguished

by its sudden onset occurring, particularly, after a period of comparatively 'normal' (i.e., pre-injury level) mental effort, usually manifesting in the early afternoon (Wrightson & Gronwall, 1999).

In spite of the frequency of post-MTBI fatigue and its impact, research in the area is sparse. During the current literature review the frequency with which "fatigue" was listed in the index of books purporting to discuss MTBI was minimal. Rao et al. (2005) wrote of post-TBI fatigue as did Elovic (2005) but it was rare to find more than a small section in other books about MTBI and even rarer to find specific treatment approaches explored. This may have been partly due to the views held, until recently, that there was no actual neurological disruption associated with post-MTBI fatigue and other postconcussion symptoms, and that the aetiology lay in pre and post injury psychosocial factors. However, early in the twenty-first century, the neurometabolic cascade occurring after TBI was described (Giza & Hovda, 2001) and functional Magnetic Resonance Imaging (fMRI) raised the scientific world's awareness of the way the brain reacts to even quite minimal trauma (Anderson, Taber, & Hurley, 2005; Bigler, 2005; McCrea, 2008). Given new information that there are changes to brain functioning, even with MTBI, it is important to distinguish between severity groups when researching fatigue. Previous studies of fatigue following TBI (Cantor et al., 2008; Ziino & Ponsford, 2005a, 2005b) have listed the percentage of participants with mild, moderate and severe TBI in their samples, but have not reported the fatigue results by TBI severity. This leaves the reader wondering if there was a difference in post-TBI fatigue across the TBI severity levels. Fortunately, figures supplied by Ouellet & Morin (2006) made it possible to calculate the percentage reporting significant fatigue within each TBI severity category. Unfortunately, they divided

those with the least severe TBI into two groups, *minor* and *mild*, making their results more difficult to understand in the context of other post-TBI studies where all those with a Glasgow Coma Scale (GCS) score of 13-15 are usually classified as having a *mild* TBI. Nevertheless, Ouellet & Morin went on to state that there was no significant difference in fatigue severity across the four TBI severity categories; minor, mild, moderate and severe. One wonders if their result would have been different if there had only been three TBI severity categories, mild, moderate and severe.

The need to conduct research in the area of post MTBI fatigue became apparent to the current researcher during her clinical experience in a New Zealand Concussion Clinic. Discussion with fellow psychologists and other rehabilitation professionals heightened awareness of the way post-MTBI fatigue interferes with recovery, participation and quality of life for long periods of time post-injury. Given then that post-MTBI fatigue presents a major barrier to returning to full pre-injury participation for so many people, and that there is so very little in the scientific literature to guide intervention, further investigation was clearly warranted.

The first opportunity to respond to that need arose through the development of a study to investigate the prevalence of post-MTBI fatigue in a New Zealand population. This opportunity presented itself when the principal researcher became aware that a large study looking at oculomotor movement following closed head injury as a predictor of persistent postconcussion symptoms was being carried out in Christchurch, New Zealand. Marcus Heitger, PhD, the principal researcher of that study kindly agreed to add a fatigue questionnaire to his study protocol, enabling the gathering of data regarding post-MTBI fatigue and the investigation of a number of possible correlates

such as depression and anxiety. The prevalence study combined with a literature review led to the development of a model of post-MTBI fatigue which, in turn, led to the third stage involving the development, trial, and evaluation of an intervention for post-MTBI fatigue.

Chapter 2 presents a review of the literature related to MTBI, concussion, postconcussion syndrome (PCS) and persistent postconcussion syndrome (PPCS) with a particular focus on fatigue, its prevalence, persistence and impact on rehabilitation post MTBI. Given the lack of consensus across professions, e.g., medical and psychological, on the overlap between the various terms there is a need to clarify the MTBI terminology.

Chapter 3 examines the concept of fatigue in general and draws a distinction between normal and pathological fatigue. Brief discussions of fatigue versus energy, fatigue versus sleepiness and fatigability are followed by an examination of the base rate of fatigue in the general population. The remainder of the chapter focuses on post-MTBI fatigue. The current knowledge of biological and psychological factors associated with, or predicting, post-MTBI fatigue is discussed. Finally, a preliminary ecological model of post-MTBI fatigue is proposed.

Chapter 4 outlines the lead up to Study One, an investigation of post-MTBI fatigue in a New Zealand sample. It also contains the paper[1] published in *Brain Injury* which

[1] Norrie, J., Heitger, M., Leathem, J., Anderson, T., Jones, R., & Flett, R. (2010). Mild traumatic brain injury and fatigue: A prospective longitudinal study. *Brain Injury*, *24*(13-14), 1528-1538. doi:10.3109/02699052.2010.531687

describes the study and its findings. These findings added support to the development of the intervention programme which was evaluated in Study Two.

A review of the fatigue treatment literature is presented in Chapter 5 with a focus on the use of psychoeducation and exercise in this context.

Chapter 6 contains a description of the development of the Postconcussion Energy Recovery Training programme. Each module of the programme was chosen for its contribution to fatigue management as demonstrated in fatigue literature from other illnesses such as MS and CFS as well general postconcussion literature.

Chapter 7 introduces Study Two, a longitudinal investigation of the effectiveness of a post-MTBI fatigue treatment the Postconcussion Energy Recovery Training (PERT) programme. Initial analysis found no significant time by group effect. Subsequent investigation identified the similarities between the groups. The results of analysis of the combined group and the individual participant data are also presented in this chapter.

Finally, Chapter 8 draws together a discussion of the literature review, the findings and the limitations of the studies and, any revisions suggested by the research findings. This chapter also contains suggestions for further research in the area of post-MTBI fatigue.

Chapter 2

MILD TRAUMATIC BRAIN INJURY

This chapter reviews the literature on MTBI and postconcussion syndrome (PCS), including its natural history, aetiology, epidemiology, assessment and treatment of postconcussion symptoms in the acute (≤ 48 hours) and chronic (>2 days) stages post MTBI. The purpose of this review is to examine the context within which post-MTBI fatigue arises. MTBI is caused by external mechanical force to the head and results in comparatively minor signs and symptoms. Recovery is rapid (7 days to 3 months) but a small percentage of MTBI patients exhibit symptoms for months or years. Postconcussion syndrome (PCS), a contentious concept, refers to the cluster of chronic or persistent symptoms of MTBI which can involve as few as one or two postconcussion symptoms (e.g., headache, fatigue or dizziness) and which remain for three months or more. Post-MTBI fatigue is one of the three most common persistent symptoms (Belmont, Agar, Hugeron, Gallais, & Azouvi, 2006; Kashluba et al., 2004b; Mittenberg, Canyock, Condit, & Patton, 2001; Stulemeijer et al., 2006). The review will explore neurogenic, psychogenic and biopsychosocial models of PCS in order to develop a model of post-MTBI fatigue upon which to base the development of a therapy programme for post-MTBI fatigue. Although the literature is sparse in the area of post-MTBI fatigue therapy, a wide range of PCS treatments have been evaluated and a review of the postconcussion symptoms treatment literature contributed to the development of a post-MTBI fatigue therapy programme.

MTBI Definition

Traumatic brain injury (TBI) is sustained through application of an external mechanical energy force to the head either accidentally or purposefully (assault) resulting in temporary or permanent neurophysiological change. The continuum of TBI severity ranges from mild to severe and MTBI, or concussion, refers to the mild end comprising the majority (70-90%) of TBI (McCrea, 2008; New Zealand Guidelines Group, 2006; Uzzell, 1999). This research deals entirely with the population falling at the mild end of the TBI continuum.

One of the most important difficulties facing those who do research with, or provide a clinical service to individuals with a comparatively minor brain injury is the lack of consensus on a definition of MTBI, concussion or PCS. For instance professionals, (medical and psychological) disagree, at least in New Zealand, on whether MTBI and concussion are the same or different conditions. The various internationally published systems of MTBI criteria have significant overlap. However, most include criteria such as a brief period of loss of consciousness, retrograde and anterograde amnesia, degree of coma and exclusion criteria such as substance intoxication.

To date there is no internationally accepted "gold standard" definition of MTBI. After a systematic review of explicit case definitions, the World Health Organisation (WHO) produced an operational definition of MTBI which was later adopted by the New Zealand Guidelines Group (NZGG) to "delineate the lower threshold of 'definite TBI'" (New Zealand Guidelines Group, 2006, p.21).

The Operational Definition of MTBI developed by the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury is as follows: -

> MTBI is an acute brain injury resulting from mechanical energy to the head from external forces. Operational criteria for clinical identification include: (i) 1 or more of the following: confusion or 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 healthcare. 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 (e.g., psychological trauma, language barrier, or co-existing medical conditions) or caused by penetrating craniocerebral injury. (Carroll, Cassidy, Holm, Kraus & Coronado, 2004, p115).

One area of neuroscience – biomarkers, still in its infancy, holds potential for more accurate diagnosis of TBI, and its severity. These internal indicators of tissue damage could facilitate more accurate diagnosis and guide treatment of TBI by enabling measurement of changes in the cellular, biochemical and molecular events during the TBI injury (Larner, 2008). Ongoing expansion of our understanding of the internal workings of the brain under pathological conditions brings us closer to the gold standard for diagnosing and treating TBI.

Postconcussion Syndrome

Postconcussion Symptoms, Postconcussion Disorder (PCD), Postconcussion Syndrome (PCS) and/or Persistent Postconcussion Syndrome (PPCS) are terms for a controversial concept that refers to a cluster of symptoms observed following a MTBI. The cluster includes some or all of the following: - headache, dizziness, nausea and/or vomiting, fatigue, sleep disturbance, irritability, hypersensitivity to noise, photophobia, reduced frustration tolerance, irritability, anxiety, depression and/or emotional lability, attention deficit, memory impairment, diminished concentration, slowed information processing, hypochondria, and blurred and/or double vision (Elgmark Andersson, Emanuelson, Bjorklund, & Stalhammar, 2007; Emanuelson, 2003; Katz & DeLuca, 1992; Middleboe, Andersen, Birketsmith, & Friis, 1992; Olver, Ponsford, & Curran, 1996; Wade, King, Wendon, Crawford, & Caldwell, 1998).

There is no one standard set of symptoms agreed as necessary for the label. Two of the most cited sources of information about the criteria for MTBI are the International Statistical Classification of Diseases and Related Health Problems, Tenth Edition (ICD-10) (World Health Organisation, 1992a) and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 1994) which set out criteria for Postconcussional Syndrome and Postconcussional Disorder respectively. Both sets of criteria require comparatively early onset after head trauma and stipulate loss of consciousness, not just a period of confusion, as a necessary criterion, That would essentially exclude 90% of MTBI patients from meeting a diagnosis of PCS (McCrea, 2008) as many who present with problems did not lose consciousness at the time of their accident. Problems with the other symptoms (listed above) arise from their subjective nature and their non-

specificity to MTBI and high incidence in many other illness conditions. The debate about whether the cluster of MTBI sequelae constitutes a "syndrome" per se, will not be examined here. The primary focus of this research is on just one post-MTBI symptom - fatigue.

Challenges to the existence of PCS as a separate phenomenon are frequently based on the proposition that there is no evidence-based link between the observed persisting symptoms and the MTBI. However, studies using modern neuroimaging techniques are revealing the likely neuropathology underlying at least some PCS symptoms (Chen, Johnston, Petrides, & Ptito, 2008; Leddy, Kozlowski, Fung, Pendergast, & Willer, 2007). Additionally, many MTBIs are accompanied by other injuries such as musculo-skeletal or whiplash-associated disorders which may either mask or mimic postconcussion symptoms (Paniak, Toller-Lobe, Durand, & Nagy, 1998).

PCS Base Rates in General Population

Another argument against the existence of PCS is the high base rate of the definitive symptoms in the general population as can be seen from the studies reported in Table 2.1 where percentages of PCS symptoms in non-head injured samples are listed. The three most common PCS symptoms are headache, dizziness and fatigue but, as the studies in Table 2.1 show, those symptoms are common within the non-head injured population. Nonetheless, two PCS symptoms, fatiguing quickly and dizziness, were found to differentiate a MTBI group from the normal control group at three months post injury (Kashluba, Casey, & Paniak, 2006). Another study (Smith-Seemiller, Fow, Kant, & Franzen, 2003) found significant differences between the MTBI and chronic pain groups at one year post injury on 9 of the 16 Rivermead Postconcussion

Symptoms Questionnaire (King, Crawford, Wenden, Moss, & Wade, 1995) items. However, of those nine symptoms, six were significantly more prevalent within the MTBI than the chronic pain group and were more likely following MTBI – noise and light sensitivity, memory, concentration, slowed information processing speed and double vision.

Suhr & Gunsted (2002) found no significant difference in PCS symptoms between college student controls (base rate) and those with MTBI without depression. However, if both MTBI and depression or depression alone was present the PCS score was significantly higher than the control group. The reason for the apparent lack of specificity in PCS base rate studies lies in the tendency to gather frequency ratings of symptoms and to neglect to measure their severity (Kay, Newman, Cavallo, Ezrachi, & Resnick, 1992). Citing findings from "unpublished data" (p.374) Kay et al. stated that it was severity ratings which distinguished "normal subjects" from those who had an MTBI. Dikmen, Machamer and Temkin (2001) in a brief review of the literature listed several other methodological problems which confound studies of PCS symptoms in both MTBI and general population samples. Methodological factors which make a difference to the meaningfulness of PCS study results include 1. the type of samples used - prospective, clinic-based, retrospective, file audits; 2. the type of controls used - trauma, non-trauma, general practice patients, students; 3. the criteria used to define mild head/brain injury; 4. neuropsychological confounds - practice effects masking brain injury effects, the sensitivity of neuropsychological measures; 5. co-morbidities being mistaken for brain injury; and 6. attrition leading to biased samples, particularly in longitudinal studies.

Table 2.1

Base Rates of Common PCS Symptoms in Non-MTBI Samples

First Author	Sample Type	Headache %	Dizziness %	Fatigue %	Irritability %	Memory %	Concentration %
Gouvier 1988	College students *N* = 98	x	x	28	31	20	6**
Lees-Haley Brown (1993)	Litigants no head injury *N* = 170	88	44	79	77	53	78
Dunn et al (1995)	Non-TBI PI claimants *N* = 156	77	41	71	63	46	71
Sawchyn et al. (2000)	College students *N* = 326	36	18	53	36	17	42
Trahan et al. (2001)	Normal *N* = 496	13	4	16	9	12	18
Chan (2001)	General population *N* = 85	40	31.8	53.5	43.6	58.9	58.9
Smith-Seemiller et al (2003)	Chronic pain *N* = 63	71	40	90	86	67	78
Kashluba et al. (2004)	General population *N* = 118	58	27	59	56	50	42
Kashluba et al. (2006)	General population *N* = 118	59	16	36	47	48	37
Lundin et al. (2006)	Controls good health *N* = 35	11	6	11	14	6	14
Garden et al. (2010)	Healthy participants *N* = 96	28	7	24	22	22	21

PCS = Postconcussion Syndrome; PI = Personal Injury complainants, x = no results for headaches or dizziness reported by Gouvier (1988).

Natural History of MTBI

Acute post MTBI symptoms resolve quickly in 85% to 99% of MTBI patients; 7-10 days for simple, uncomplicated sports concussion and 3 and 12 months in complex, complicated (space occupying lesions or multiple MTBI) sports concussion (Carroll, Cassidy, Peloso, et al., 2004; Iverson, 2005; Katz & DeLuca, 1992; McCrea, 2008; Ruff, 2005). The comparatively large discrepancy in the percentages arises partly because the definition of MTBI or concussion is very broad (Iverson, 2005) and there are discrepancies in the definition of recovery. Iverson (2005) and later McCrea (2008) in their reviews of the literature argued for a minimal percentage (1% – 5%) of persistence of postconcussion symptoms. McCrea traced the origin of the much cited "15%" back to the original papers written by McClean, Temkin, Dikmen & Wyler (1983) and Rutherford, Merrett & McDonald (1979). He found that Rutherford et al., for instance, reported just one or two persistent symptoms in 16 of the 19 participants still symptomatic at one year. Dismissing these findings on the basis that there are only one or two persistent symptoms does not take into account the negative impact these symptoms, e.g., fatigue, could have on postconcussion psychosocial and occupational adjustment.

Table 2.2 brings together several reviews and meta-analyses which look at the natural history of postconcussion symptoms. The general picture that emerges from the studies listed in Table 2.2 is that PCS symptoms continue to be reported by at least a small percentage of individuals, months or years post MTBI. The somewhat confusing aspect is the wide range in size of the groups who are reporting postconcussion symptoms well after their injury date. For instance, Binder's (1997) review of 17 studies involving 5414 participants found between 3% and 16% of participants were

reporting persistent PCS symptoms at 6 months. However, within their review they also found within one study that the incidence of PCS at one year post injury was just 1%, a reduction of 87% from one month after the injury. On the other hand Kay et al.'s (1992) study found headaches, dizziness, memory problems, unemployment and decreased socialisation were reported by 11% to 23% of the sample. A review by the World Health Organisation (Carroll, Cassidy, Peloso, et al., 2004) found the prognosis for children after an MTBI was better than for adults and there were persistent symptoms one to five years after the injury.

Besides identifying the long term nature of PCS, many of the studies in Table 2.2 examined prognostic factors which might indicate whether the outcome was likely to be good or bad. Part two of Binder's (1997) review of mild head trauma (MHT) cautions that "the association between MHT and cognitive deficits, symptoms, and disability may not be causal: data suggest that MHT patients have more psychosocial problems prior to injury than do non-injured persons" (p.432). In Binder's summary of risk factors for lingering symptoms, higher levels of education, occupational status, younger age, and pre-accident psychosocial health were protective, while female gender, older age, previous head injury and fat embolism were associated with a slower recovery. Many other studies (Carroll, Cassidy, Peloso, et al., 2004; Ryan & Warden, 2003; van Veldhoven et al., 2011) support the concept that pre-existing conditions, including a history of MTBI, are predictive of poorer prognosis following MTBI. Characteristics of the injury such as whether it is a simple or complicated (space occupying lesion) MTBI

Table 2.2

Summary of Studies Reporting MTBI Prognosis

First Author	Research Design	Prognosis
Levin et al. (1989)	Review	Simple versus complicated MTBI affects length of recovery
Kay et al. (1992)	Longitudinal prospective study *N* = 808	Symptoms decreased over the 12 months post injury but a substantial minority remained symptomatic: 23% headache, 11% dizziness, 13% memory problems, and 8% decreased socialization. Most common persistent symptoms were headache, fatigue, forgetfulness and sleep disturbance. 11% had not returned to work at 12 months post injury.
Binder (1997)	Review Part 1: 17 studies, *N* = 5414; Recovery Criteria – Persistent postconcussion syndrome Part 1: 17 studies, *N* = 2660, 8 countries; Recovery Criteria – Return to work	PCS incidence across the studies ranged from 88% at 1 month to 1% at 1 year. After 6 months, 3% of uncomplicated and 16% of complicated MTBI had moderate disability. *Poor prognosis factors* - advanced age, pre-morbid psychological problems, occupational status, low educational level, female, previous head injury and fat embolism. Multiple MTBI were complicated by confounding factors – deficient judgement or skills, sports like football and boxing not relevant because of multitude of blows to head. Alcohol and adverse life circumstances were associated with occurrence of MTBI. *Better prognosis factors* – higher level education and occupational status, younger age and pre-accident psychosocial health. Return to work – varied across studies e.g., at 6 months 63%, 12 months 80% of participants with GCS 13-15 and 88% of participants with PTA < 24 hrs; but orthopaedic injuries confound as prevented many with MTBI from returning to work. Few studies controlled for orthopaedic injuries. Range of chronicity 1 month to 5 years post MTBI.

(continued)

First Author	Research Design	Prognosis
Bazarian et al. (1999)	Prospective, longitudinal controlled study 1, 3, 6 months MTBI *N* = 70, Orthopaedic Controls *N* = 60	Incidence of PCS decreased to 25% at 6 months. Sports injury less predictive of PCS at 1 month than other injury mechanisms, female gender predictive of PCS but fewer females in sports injury category so is confusing as a global predictor of PCS. Neuropsychological factors do not predict prognosis of PCS beyond 3 months.
Van der Naalt et al. (1999)	Prospective, longitudinal 1, 3, 6, 12 months postinjury, TBI *N* = 67 (43 Mild, 24 Moderate)	At 12 months, 73% had resumed previous work but 84% reported complaints - headache 32%, irritability 34%, poor concentration 42% and fatigue 45%. Cognitive (40%) and behavioural problems (48%) interfered with return to work. Younger age (31 vs. 41) predicted full resumption of pre-injury activities. No gender or education differences. Mixed TBI severity sample– outcome correlated with PTA but not GCS.
Ponsford et al. (2000)	Longitudinal prospective controlled, MTBI *N* = 84; Controls minor non-head injuries *N* = 53.	At 3 months 24% of the MTBI sample reported significant ongoing problems. Only significant pre-morbid factor was single marital status.
Dikmen et al. (2001)	Longitudinal prospective controlled, MTBI *N* = 157 Controls (other trauma) *N* = 109	MTBI: 37% had pre-existing conditions including alcohol problem, prior head injury, other central nervous system disorder, psychiatric condition or learning disability. Trauma controls 44% pre-existing condition. MTBI not significantly different from controls, neuropsychologically or symptomatically at 1 month or 12 months, only MTBI had mild memory difficulties at 12 months. Pre-existing conditions significant at 12 months across all neuropsychological tests for MTBI; age and education significant across many neuropsychological tests. Major sequelae of mild head injury were headache, dizziness, and memory impairment
Hawley (2003)	Retrospective, longitudinal, paediatric; MTBI *N* = 411, ModTBI *N* = 61, STBI *N* = 49; Controlled (healthy) *N* = 31	Only MTBI results summarised here. At first interview 6 months to 5 years post-injury, significant differences between MTBI and controls for behaviour, school problems, temper, vision, headaches, speech and schoolwork. At second interview 1 year later 66.3% MTBI and 58.5% controls still symptomatic, but no statistically significant differences between the groups.

(Continued)

First Author	Research Design	Prognosis
Carroll et al (2004)	Review by WHO Collaborating Centre Task Force on MTBI; *N* = 121 studies	Children: prognosis good, quick resolution and little evidence of residual cognitive, behavioural or academic deficits. Adults: cognitive deficits and symptoms are common in the acute stage but pain and distress could be confounds. Resolution of cognitive deficits within 3 months; range of symptom reports from resolution within 3 weeks to persistent symptoms after 1 – 5 years. Complicated MTBI, focal lesions or skull fracture predictive of poorer cognitive function within first 3 months. Sports concussions prognosis – resolution within 15 minutes to 2 weeks. Prognostic factors for persistent postconcussion symptoms: litigation and/or compensation., married, off work due to injury, not at fault for accident, post-injury nausea and memory problems, other injuries including pain, history of concussion delayed return to play but the mechanism unknown e.g., medical caution or longer symptom resolution. Pre-morbid personality or psychological problems, female gender both supported and discounted. Acute stress disorder predicted posttraumatic stress disorder and greater number of self-reported symptoms and delays in functional measures of recovery. Disability prognostic factors: Lower GCS increases likelihood of poor outcome but GCS 13 had 76% good outcome and attribution to MTBI is in doubt. Age over 40, pre-existing physical limitations and history of brain illness (e.g., stroke), alcohol/drug use and, criminal convictions. However, these cannot be attributed to MTBI as are also predictors of MTBI events. Malingering or incomplete effort have been proposed as predictors of poor outcome.
Belanger et al. (2005)	Meta-analysis, *N* = 39 studies	Effect size of MTBI on neuropsychological status .01 – 2.35. Overall effect size 0.54. Clinic-based samples and litigation–based samples exhibited greater cognitive MTBI sequelae; secondary gain, implicit beliefs or self-expectation, poor coping styles, emotional reactions to an adverse event or other factors. Persistent symptoms 7% - 33% across studies.

(Continued)

First Author	Research Design	Prognosis
Iverson (2005)	Literature review	Athletes' recovery 2 – 14 days; trauma lengthens recovery. Pre-existing or co-morbid problems – poor prognosis, psychiatric or substance abuse problems, poor general health, concurrent orthopaedic injuries.
Collins et al (2007)	Review, sport concussion *N* = 2141	Majority (≅98%) recovered within 2 – 4 weeks across studies reviewed. Three or more concussions are associated with small but measurable cumulative effects and increased risk for future concussions.
Iverson (2007)	Review of meta-analyses and reviews	Neuropsychological recovery usually 2–21 days, but trauma patients after 1–3 months, or up to a year in prospective group studies. Individuals with less severe MTBI (GCS = 15, no LOC) have higher return to work rate. Very wide range of return to work rates across studies from (a) 25% to 100% within the first month post-injury (b) 38% to 83% 6-9 months post injury (c) 47% to 83% 1-2 years post-injury, and (d) 62% to 88% 3 or more years post-injury.
Jakola et al (2007)	Longitudinal, prospective, clinic-based, *N* = 23	5–7 years post MTBI, patients reported significantly more PCS symptoms than controls; self report of somatic and cognitive symptoms, but not affective symptoms.
Vanderploeg (2007)	Cross-sectional, retrospective, male Army veterans; Controls (no injury or accident), *N* = 3214 Accident no MTBI, *N* = 539 MTBI *N* = 254	MTBI - depression, PCS, vision, impaired gait, poorer psychosocial outcomes. Significantly higher sequelae than accident/no MTBI or normal controls

PCS = postconcussion syndrome, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, ICD-10 = International Statistical Classification of Disease and Related Health problems 10th Edition, TFC = Time to follow commands, LOC = Loss of consciousness, MTBI = Mild traumatic brain injury, ModTBI = Moderate traumatic brain injury, STBI = Severe traumatic brain injury; PTA = posttraumatic brain injury, PCS = Postconcussion syndrome, GCS = Glasgow Coma Scale

were predictive of longer time to recovery and persistent postconcussion symptoms (Bohnen, Twijnstra, & Jolles, 1993; Borgaro, Prigatano, Kwasnica, & Rexer, 2003; R. Lange, Iverson, & Franzen, 2009).

Factors such as previous MTBI are predictive of poorer prognosis following MTBI. Characteristics of the injury such as whether it is a simple or complicated (space occupying lesion) MTBI as well as litigation, factitious disorder and/or malingering can inflate the frequency of reported persistent postconcussion symptoms (McCrea, 2008). New Zealand's no fault government sponsored accident insurance provides an environment in which to study MTBI without the confounding effect of litigation.

Aetiology of PCS

Historically, debate about the aetiology of PCS has tended to be polarised. Some attribute PCS to neurogenic factors (Bigler, 2001, 2003b; Leddy et al., 2007) while others prefer to see PCS as of psychogenic aetiology (Gunstad & Suhr, 2001; Lees-Haley, Green, Rohling, Fox, & Allen, 2003; Ruff, 1996; Whittaker, Kemp, & House, 2007). Given the prevalence of postconcussion-type symptoms among non-head-injured samples, the absence of evidence from commonly used neuroimaging methods (CT scans) and the relatively rapid recovery of neuropsychological function following MTBI, there has been a tendency among many researchers and clinicians to attribute the aetiology of persistent postconcussion symptoms to psychogenic factors rather than pathophysiological or neurogenic ones (Bigler, 2003b; Lees-Haley et al., 2003). Recently a multifactorial perspective is gaining ground and current theories about the aetiology of PCS integrate biological, social, cognitive, affective and behavioural factors (Kay, 1999; Ruff, 2005; Wood, 2008). The next section of this chapter will

examine the characteristics of, and the evidence for, the many factors which contribute to the holistic multifactorial perspective of PCS.

Biological factors

MTBIs are frequently categorised as simple or complicated. Complicated MTBI refers to injuries where there is evidence of space occupying lesions (contusions, haemorrhage or haematoma) on CT or MRI scans (Borgaro et al., 2003) or skull fracture, and/or delayed neurological deterioration or a history of multiple concussive episodes (Alves, Macciocchi, & Barth, 1993; Bohnen, Jolles, & Twijnstra, 1992; Borgaro et al., 2003). Uncomplicated or simple MTBI refers to a single instance with no space occupying lesions. Recent literature reviews (Carroll, Cassidy, Peloso, et al., 2004; McCrea, 2008) reported that a simple MTBI is usually associated with rapid recovery, but the picture is not that simple. In some instances, an apparently uncomplicated MTBI is followed by long lasting symptoms which interfere with resumption of pre-accident levels of activity (Bigler, 2003a; Lezak, Howieson, & Loring, 2004; McCrea, 2008; Wright & Telford, 1996). Complicated MTBI increases the risk for slow or incomplete recovery. For instance, complications such as intracranial lesions and early clinical symptoms (headache, dizziness and fatigue) were strongly associated with persistent postconcussion symptoms at eight weeks post injury (Yang, Hua, Tu, & Huang, 2009). However, eight weeks is relatively soon after a MTBI for identification of PPCS especially as approximately 42% of Yang et al.'s sample were ≥40 years old so expected to take longer to recover even without complications such as intracranial lesions (Zasler & Martelli, 2003).

Neurogenic factors

Neuroscience is currently expanding knowledge of the brain and brain-behaviour relationships at a very fast rate, providing hard evidence to support the role of pathophysiology in the aetiology of PCS. In the majority of patients with MTBI, neuropsychological deficits are largely undetectable by formal testing within days or months of the MTBI (Dikmen, Machamer, & Temkin, 2001; Dikmen, Machamer, Winn, & Temkin, 1995; McAllister, 2005; McCrea, 2008; Potter & Barrett, 1999; Schretlen & Shapiro, 2003). However, neuroimaging such as functional magnetic resonance imaging (fMRI), single photon emission computed tomography (SPECT) and magnetoencephalography (MEG) have demonstrated that while the individual's cognitive function may be similar to pre-injury or non-injured controls, the neural mechanisms by which the performance is achieved are not (Bigler, 2001; Chen et al., 2004). fMRI studies have revealed more widespread brain activation occurs during the performance of mental tasks by the injured brain than by the uninjured brain (Marushi, Miyantani, Nakao, & Muranaka, 2006; Mendez, Hurley, Lassonde, Zhang, & Taber, 2005). It is argued that increased brain activation post brain injury places a greater drain on the brain's energy resources which then results in the experience of post-MTBI fatigue.

My clinical impression in a Concussion Clinic has been that there is a small percentage of people who have a "sense" that they are not functioning with the same effectiveness as they did prior to their MTBI. They report this "sense" long after the expected (weeks to three month) recovery period.

In another study, De Beaumont et al. (2007) found electrophysiological changes in athletes with a history of multiple concussions who were asymptomatic (self report on PCS checklist) when the electrophysiological recording was made a minimum of nine months after their last concussion. Neuropsychological test performance did not differentiate the three groups; controls, single concussion and multiple concussions. De Beaumont and colleagues hypothesized that multiple concussions increased the vulnerability to diffuse axonal injury which explained the electrophysiological changes observed.

A Japanese study of chronic MTBI (Kabasawa, Ogawa, Iida, & Matsubara, 2002) investigated the relationship between higher brain function and regional cerebral blood flow (rCBF), oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen (CMRO2) in the bilateral frontal, parietal, temporal, and occipital lobes. The Positron Emission Tomography (PET) findings showed significant differences in CMRO2, but not for rCBF and OEF between the chronic MTBI group and a control group. Additionally, within the chronic MTBI group they found, after 9.3 months, a significant increase in higher brain dysfunction (full scale IQ, WAIS-R) as well as in CMRO2. They concluded that higher brain dysfunction following MTBI was significantly related to a generalised decrease of brain oxygen metabolism. This decrease in brain oxygen use could be seen as a possible mechanism for post-MTBI fatigue.

A range of imaging techniques such as CT scans, magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), diffusion-weighted and perfusion-weighted magnetic resonance imaging (PMRS),

single photon emission computed tomography (SPECT) and PMRS are used by clinicians and/or researchers to investigate neurological damage after brain injury (Bigler, 2001, 2003b; Gallagher, Hutchinson, & Pickard, 2007; Hattori et al., 2009; McAllister, 2005). Both depression and fatigue in concussed individuals were found to be associated with different patterns of neuronal activation than was observed in concussed individuals without depression or fatigue (Chen et al., 2008; Hattori et al., 2009).

As the discussion moves on to the role of psychosocial factors in PCS it should be remembered that there is significant overlap between psychological factors, such as depression, and anxiety, and neurogenic factors. For instance, depression and anxiety, whether secondary to TBI or idiopathic, involve lateralized activation particularly of the right-anterior fronto-temporal and right parietal-temporal regions respectively and "should be understood as behaviourally similar syndromes with overlapping pathophysiological findings" (Moldover, Goldberg, & Prout, 2004). The similarity between psychiatric disorders and PCS is not surprising given similar neuropathology - frontal and temporal region dysfunction; disruption of neurotransmitter (dopamine and serotonin) functions and/or pathways.

Psychosocial factors

Wood's (2008) multifactorial model of PCS maintained that the prognosis for MTBI recovery is also influenced by demographic, psychogenic (coping style, expectation, depression and anxiety), medical, motivational and environmental factors. A range of risk factors have been identified as having a role in the aetiology of PCS. Zasler and Martelli (2003) identified factors such as the context of the injury including both the

circumstances of the trauma and other non-cerebral injuries sustained, previous brain injury, age >40 years, pre and post psychosocial variables (lower intelligence, history of alcohol or substance abuse, psychiatric history, poor school achievement, not being married, deficient social support systems, and poor family support). Pre-existing psychopathology, maladaptive belief systems, helpless attributional style, external locus of control, depressogenic beliefs and automatic thoughts have been proposed as PCS risk factors. Additionally, post-injury psychological factors (anxiety, depression and stress) have also been proposed as PCS risk factors (Fann et al., 2004; King, 2003; King, Crawford, Wenden, Caldwell, & Wade, 1999). Female gender, it was argued, made the individual more susceptible to depression and anxiety while litigation, factitious disorder and/or malingering have also been implicated in the aetiology of PCS (King, 2003; King et al., 1999; Larrabee, 2004).

The perceived comorbidity of psychological problems, depression and anxiety, and PCS is also attributed to greater awareness or insight that MTBI patients are believed to have, compared with those with moderate or severe TBI. That awareness can lead to adjustment difficulties including grief, anxiety, depression and failure on the part of others to recognize the reason for reduced functionality. Also some people who have had a MTBI report PCS symptoms because they mistakenly attribute actual or perceived difficulties to the MTBI because they are misremembering their pre-morbid functioning as better than it actually was (Uomoto & Fann, 2004) .

Illness perceptions early after head injury play a part in the persistence of PCS expectations among symptomatic patients. A recent study found MTBI patients, who believed, early after their injury, that their symptoms have serious negative

consequences on their lives, continue to do so at three months, and are at heightened risk of experiencing significant enduring postconcussion symptoms (Whitaker & Marsh, 1997). This finding confirms the role of pre-morbid psychological or personality factors such as illness perception which is more likely to be a pre-existing belief than to be precipitated by the brain injury. Whittaker et al. (2007) found adding measures of severity of injury, post-traumatic stress symptoms, anxiety and depression to their regression model did not improve prediction of outcome. Those with a history of anxiety, whether at clinical or sub-clinical level, could be more likely to be prone to noticing mild functioning changes, or perceived changes, worrying about them and thereby contributing to continued reporting of perceived postconcussion symptoms. Additionally, recall of pre-morbid functioning has been shown not to be reliable in many instances (Davis, 2002; McCullagh & Feinstein, 2003) and distress at perceived loss of function leads to, or fuels, psychological difficulties.

The holistic multifactorial perspective of PCS is gaining ground over the neurogenic and psychogenic approaches to the theorising about the aetiology of PCS. Theories and knowledge about PCS aetiology are built around research in that area, however, research design characteristics, such as retrospective versus prospective design, trauma versus non-trauma control groups, clinic-based versus community samples (Dikmen et al., 2001) and mixed TBI-severity samples, influence findings and therefore theory. For instance Van der Naalt et al. (2000) reported 86% of their sample had persistent symptoms but they restricted their sample to a GCS range of 9 -14 thus excluding the mildest TBI group, those with a GCS of 15. However, even within this mildest TBI group, some individuals continue to exhibit one or more persistent symptoms (McAllister et al., 2005) for months or years post injury.

Another methodological difficulty with investigations of MTBI recovery is the wide variety of neuropsychological test batteries, (comprehensive to very brief) which are used, thereby reducing comparability of studies. Additionally, sports concussion studies have the luxury of a pre-season neuropsychological assessment with which to compare post-MTBI performance. Choice of control group (e.g., other trauma, general population, volunteer status) and use of mixed severity samples are other issues which require studies of MTBI prognosis to be interpreted cautiously in clinical settings.

Models of PCS

Models of pathology such as PCS and PPCS currently tend towards a holistic or ecological perspective, moving away from polemical views such as neurogenic or psychogenic. This has been supported by neuroscience advances which have enabled increased knowledge of MTBI pathophysiology which give credence to both perspectives. Additionally, theorists accept that when constructing models related to the human condition, compartmentalization is restricting and does not satisfactorily answer either aetiology or intervention questions. In New Zealand the move towards adopting integrative models within the health sector has also been guided by consideration of Maori models of health and illness (Durie, 1984, 1994, 1998).

Diathesis stress model

Wood (2004) proposed a diathesis stress model, wherein pre-existing characteristics create a vulnerability upon which the stress of even a mild traumatic brain injury acts, leading to a rise of temporary physical and longer term psychological difficulties. Misattribution of symptoms to the MTBI, mistaken beliefs about pre- versus post-

MTBI function, expectation of difficulty and motivational factors such as financial gain or the need to apportion blame are factors contributing to Wood's explanation for persisting postconcussion symptoms.

Neuropsychological model

Kay et al.'s (1992) neuropsychological model described a complex interaction between neurological, physical, psychological, objective and subjective cognitive factors, and functional outcome. They proposed two, loop-type mechanisms to account for the maintenance of persistent PCS symptoms. Although Kay et al. described their model as neuropsychological, it contains elements which align it with the multifactorial models.

Another neuropsychological model (McCrea, 2008) accepts the evidence for a "clear neurological base for the acute symptoms and functional effects of the first several days to weeks post injury" (p.169). However, McCrea argues that there is little neurological evidence to support the later development of persistent postconcussion symptoms. He argues that PCS symptoms such as headache, dizziness, irritability, memory and concentration problems are not specific to PCS, can arise in a whole host of medical and psychological conditions, and can be influenced by motivational factors. Like Wood, (2002) he cites pre-existing and trauma related (anxiety and stress) psychological problems, demographic (female gender, older age) and psychosocial (social difficulties, and environmental stress) factors as well as somatic symptoms such as chronic pain and sleep disturbance as complicating factors associated with delayed recovery from MTBI. McCrea draws also on the writings of Larrabee (1997) to propose viewing PCS within a neuropsychological context as an undifferentiated

somatoform disorder. He argues that individuals with post-MTBI erroneously attribute their distress to physical causes, the MTBI, rather than looking more broadly at who they are (pre-existing psychological factors) and, how they have reacted to the MTBI and its impact on their lives (post-MTBI psychological and environmental factors). The model takes into account the overlap between PCS and posttraumatic stress disorder (PTSD) linking the trauma which caused the mild brain injury to the acute stress associated with the traumatic event such as threat, fear and anxiety (Harvey, Brewin, & Kopelman, 2003; Iverson, 2007; Parker, 2005).

Physiological models

Pall (2001, 2007) proposed a mechanism for this overlap. Stressors, such as physical or psychological trauma are associated with a rise in nitric oxide and initiation of the nitric oxide/peroxynitrite cycle. Once the cycle is chronically elevated it acts through biochemical sequences to shift parts of the body into a pathological state (Pall, 2007). According to Pall, the explanation for the observed differential development of pathology across a population, e.g., the MTBI population, lies in individual-specific characteristics such as genetic propensities e.g., to the development of PTSD (Koenen, 2007; Lee et al., 2005), hormonal factors (e.g., cortisol or oestrogen), strength of the stressor which is related to the magnitude of effect on the body's biochemical reaction, and diet (anti-oxidants and their interaction with peroxynitrite). Pall's model for explaining "unexplained illnesses" is comparatively new and neither he nor anyone else seems to have considered it within the context of PCS. However, given many of the illnesses (Chronic Fatigue Syndrome (CFS), Fibromyalgia and PTSD) have similar symptom clusters and to some extent similar neuropathology (Multiple Sclerosis (MS))

as PCS, his model could prove to have some relevance to understanding long term MTBI sequelae.

The role of pathophysiology in models of PCS is supported in the literature as summarized by Leddy et al. (2007). Phenomena such as increased sensitivity to physical exertion show physiological symptoms persisting many months after MTBI in otherwise asymptomatic individuals. Their model attempts to explain post-MTBI phenomena such as the tendency for athletes to exhibit postconcussion symptoms on exertion and to exhibit greater heart rate at rest and after cognitive or physiological exertion.

The model is summed up thus:

> concussion… involves more than just a disturbance of cerebral cognitive function: it is a systemic injury that affects multiple physiological systems throughout the body. PCS may reflect…a manifestation of persistently altered central and peripheral physiological state after concussion…some persistent cognitive deficits or symptoms are not directly the result of damage to neurons or their connections but secondary to the physiological dysregulation after concussion (Leddy et al., 2007, p.3).

Multifactorial models of postconcussion syndrome

An ecological, patient-oriented model (Ruff, 2005) proposes a comprehensive approach to the explanation of PCS. Ruff argues that the discipline oriented, neurogenic and psychogenic approaches do not promote a good understanding of the predicament of the "miserable minority", whose symptoms persist well beyond the expected recovery time of three to six months. The key element of this biopsychosocial

model is the complex interaction of the physical, emotional and cognitive symptoms with environmental (vocational, social, recreational, financial, and spiritual) factors. The inclusion of ecological factors makes this model more consistent with current thinking, and with the New Zealand Maori Te Whare Tapu Wha[2] model of health (Durie, 1985, 1998) which guides a bi-cultural (Maori and European) approach to psychology and neuropsychology in New Zealand.

When adopting a biopsychosocial approach to PCS modelling, there is a need to screen for co-morbidities and avoid erroneously attributing symptoms to PCS (Iverson, 2006). However, while recognizing that not all symptoms reported by each MTBI patient are attributable to the MTBI, the treatment approach has to take them into consideration. For instance, when a MTBI patient presents with prolonged fatigue as well as anxiety symptoms the treatment will have to address both in order to promote well-being.

Treatment for PCS

Models of PCS have spawned a wide variety of therapies including medications (e.g., anxiolytic, antidepressant, analgesic), psychotherapy (e.g., cognitive behavioural therapy, systematic desensitization, progressive muscle relaxation, cognitive retraining), hypnosis, biofeedback and graded exercise (Mittenberg et al., 1996). To date the most effective and widely used treatment has been an early education and

[2] Te Whare Tapa Wha model of Maori health is an holistic approach. "Te Whare Tapa Wha" literally translates as the four sides of the house. Durie (1985) described the Maori perspective of health as encompassing the four basic tenets of life - spiritual, psychic, bodily and family. The spiritual dimension includes traditional and modern religious beliefs and practices as well as a connection with the natural environment, the land and the ancestors. The psychic dimension encompasses thoughts, emotions and personality, while the bodily dimension includes not only the physical body but also the ritualised procedures which differentiate the sacred (e.g. the head,) from the common parts of the body. Finally, family, in the Te Whare Tapa Wha model, refers to the extended kinship system where identity, responsibilities and privileges, such as child rearing, are shared by all the adults of the kinship group not just the biological parents as in a nuclear family.

reassurance based approach which has been replicated in several countries. See Table 2.3 for a summary of the most frequently cited and most recent treatments for PCS.

Treatment outcome was usually reported as reduction of frequency, and sometimes of severity, of symptoms compared with pre-treatment profile. While significant reductions were found across the symptoms measured, this did not always mean symptoms had disappeared. For instance, Mittenberg et al. (1996) found the percentage of initially symptomatic participants who continued to experience symptoms at six months post psychoeducation treatment was significantly less in the treatment group than in the control group; with the exception of noise sensitivity which had not changed. Symptoms such as headache and fatigue continued to be prevalent in over forty percent of that group. Anxiety and depression frequency was significantly reduced in both treatment and non-treatment groups suggesting that the primary mechanism for treatment effectiveness was a reduction in these psychological factors. In another study, progressive aerobic exercise was shown to successfully reduce the number and intensity of PCS symptoms reported (Kozlowski, 2008; Willer & Leddy, 2007).

Table 2.3

Treatments for Mild Traumatic Brain Injury and Postconcussion Syndrome.

First Author	Treatment details and results
Alves et al. (1993)	Interventions providing education and support appeared to be associated with symptom resolution in some patients. *N* = 587.
Mittenberg et al. (1996)	Early intervention, randomized controlled trials, psychoeducation, incorporating information about concussion and recovery expectations combined with reassurance; significant reductions in number, frequency and severity of postconcussion symptoms at 6 months (headaches, fatigue, memory problems, poor concentration, blurred vision, anxiety, depression and dizziness). Routine hospital care for MTBI control group also produced significant reductions in anxiety, depression and dizziness. At 6 months treatment group reported comparatively high frequency of headache 44%, fatigue 47%, memory problems, 38%, poor concentration 29%, blurred vision 50% anxiety 38%, depression 27% dizziness 36%. 28% controls vs. 11% of treatment group met ICD-10 criteria for PCS at 6 months. Treatment and Control *N* = 29 each group.
Paniak, et al. (1998)	Education oriented single session vs. extensive assessment, education and treatment as needed, no significant difference at 3-4 months follow-up. Post-concussion symptoms and general health (SF-36): Significant change for time 0 - 3 months, but not for group. Average effect size of PCS symptom changes 0 to 3 months for combined treatment conditions was 0.36, clinically significant change. Community Integration Questionnaire no time or group or between groups differences, possibly because "many participants had already returned to pre-injury vocational activities before (initial assessment)" p1020. No control group. Single session *N* = 60, Treatment as Needed N = 59.
Paniak et al. (2000)	12 months follow-up of Paniak et al.'s 1998 study. Post-concussion symptoms: No significant change for time 3 – 12 months or between treatment groups. Average effect size of PCS symptom changes 3 to 12 months for combined treatment conditions was 0.05, negligible upward change. Effect size between groups was 0.11 favouring single session treatment, very small difference. Community Integration Questionnaire no group or time differences between groups. Treatment *N* = 53, Control *N* = 52.
Mittenberg et al. (2001)	Review of treatment of post-concussion syndrome. "ICD-10 …indicates…Depression, anxiety and fear of permanent brain damage exacerbate and maintain the acute symptoms" (p.829). Summary of treatments, pharmacological, psychological, physiotherapy (e.g., biofeedback, TENS), hypnotherapy, graded resumption of activity, cognitive restructuring for catastrophising, anxiety and depression secondary to MTBI. Effect sizes, Cohen's *d* for psychological therapies including education and reassurance ranged from .22 (*N* = *462, not* randomized or blinded) to .37 (*N* = 201, randomized controlled and blinded trial). Mean effect size = .32 (*N* = 1014), clinically as well as statistically significant p = .0004. (Continued)

First Author	Treatment details and results
Ponsford et al., (2002)	Randomized controlled trial; information booklet and neuropsychological assessment, reassessment at 3 months. Treatment group reported less PCS symptoms and were less stressed at 3 months. Sleep difficulty and anxiety were significant between groups. Based on inspection of Figure 3 (p 331) fatigue was the most frequently reported symptom and there was almost no difference between control and treatment groups. Problems with the study – attrition (38%), mean age of 3 month sample significantly younger than earlier sample, possibility that those who returned (62%) were more symptomatic than non-returnees. MTBI *N* = 84, Controls *N* = 53.
Borg et al., (2004)	Review of non-surgical intervention for MTBI. Lack of uniform and valid case definitions of MTBI made study comparisons difficult; no strong evidence for any non-surgical treatment being clinically relevant; some evidence for early limited education and activation; routine intensive assessment and treatment not additionally beneficial. Recommendation early structured educational information. Need for cohort studies to define the prevalence, character and risk factors for persisting symptoms and disability, especially with adults to inform treatment. Need for well designed treatment studies. MTBI intervention studies reviewed *N* = 10, Total participants *N* =2372.
Comper et al. (2005)	Review of treatments for MTBI; education, neuropsychological assessment, counselling, manual therapy, outward bound and pharmacology. Main problems were lack of rigour, need control groups, need to draw sample from community based population not just medical, short follow-up period did not allow for natural recovery. Pharmacotherapy *N* = 129, CBT *N* = 64, Patient education *N* = 1881, Other interventions *N* = 28.
Gemmel & Leathem (2006)	Waitlist control, 6-week course in Tai Chi, significant improvement on all VAMS scores (except fatigue) with decreases in sadness, confusion, anger, tension, fear and increases in energy and happiness, short-term benefits after TBI, *N* = 18.
Kozlowski et al. (2006)	Single case study design, two cases, controlled exercise as treatment for complicated (multiple concussions) PCS. Case A no improvement but symptoms found post-treatment to pre-date concussions. Case B reduced number and frequency of PCS symptoms both showed increase in aerobic conditioning. *N* = 2.
Leddy et al. (2007)	Single case study multiple baselines design. History of two concussions within 7 months and past history of two concussions within previous 2 years. Treatment - supervised progressive aerobic exercise programme based on 80% of exercise symptom threshold. Improvement during initial baseline with accelerated improvement after beginning exercise treatment programme. At 6 weeks symptom free aerobic fitness increased and individual returned to play with no recurrence of PCS symptoms. Significance of study was use of exercise, not rest, to treat PCS. *N* = 1
Elgmark et al., (2007)	Information, reassurance, counselling, pharmaceutical: MTBI, RCT, early intervention for PCS – no significant difference between groups. More PCS symptoms = longer recovery period. Treatment *N* = 264, Control *N* = 131.

(continued)

First Author	Treatment details and results
Bell et al., (2008)	Randomised controlled trial; treatment group – education about MTBI, initial phone call within 2 days of injury and 4 follow-up, subject centred phone contacts at 2, 4, 8, and 12 months post injury providing information and reassurance on the general course of MTBI recovery and assistance in managing specific MTBI symptoms. Phone calls lasted from less than 1 minute to 33 minutes, mean = 8 minutes, and had a general script to ensure specific issues e.g., physical, cognitive, emotional and activity status was covered. Techniques included clarification and reflective listening, suggestions of management strategies and problem solving modelling. Reinforcement of positive behaviour towards increased participation. Educational material was mailed as needed and participants advised to seek medical help when needed. Control group – standard ED care for MTBI, a patient instruction handout and standard outpatient treatment if prescribed. Telephone treatment most effective, significant difference between percentage of treatment and controls reporting symptoms of fatigue, sleep trouble and sexual difficulties ($p<.05$). No other PCS symptoms significant change. 26% of treatment group still reporting fatigue difficulties at 6 months. Treatment $N = 168$, Control $N = 193$.
Kozlowski (2008)	Controlled trial of aerobic exercise as a treatment for postconcussion syndrome. Based on a physiologic systemic model of PCS. Treatment period varied according to the time it took participants to be able to exercise at full capacity without a return of PCS symptoms; treatment for up to 10 weeks.
Leddy et al. (2010)	The majority of participants reported significantly reduced PCS symptom following participation in the exercise programme. Following the treatment participants' ability to meet physical demands returned to comparable non-injured levels. Rate of PCS symptom improvement was related to peak exercise HR (r = -0.55, P = .04). Athletes recovered faster than non-athletes (25 + or - 8.7 vs. 74.8 + or - 27.2 days, P = .01). No adverse events were reported. Athletes returned to sport and non-athletes to work. MTBI $N = 14$, Control $N = 10$.

ED = Emergency Department, ICD-10 = International Statistical Classification of Diseases and Related Health Problems, MTBI = Mild Traumatic Brain Injury, PCS = Postconcussion Syndrome, CBT = Cognitive Behavioural Therapy,
RCT = Randomised Controlled Trial,

Summary

MTBI is caused by external mechanical force to the head and results in comparatively minor signs and symptoms. Recovery is rapid (7 days to 3 months) but a small percentage of MTBI patients exhibit symptoms for months or years. Postconcussion syndrome generally refers to the cluster of persistent symptoms remaining for three months or more. Sometimes there are only one or two symptoms, e.g., headache, fatigue, dizziness, which persist. Most recent models of PCS take a biopsychosocial perspective. A wide range of PCS treatments have been evaluated with more or less robust research designs. The most effective treatments to date are early education about MTBI sequelae and expected recovery, combined with reassurance and progressive aerobic exercise. However, the psychoeducation treatment showed only limited success in treating post-MTBI fatigue which sometimes persists for years and is associated with poor outcomes such as reduced work capacity and/or engagement in alternative less financially rewarding work. The progressive exercise treatment study did not provide information about individual postconcussion symptoms and so it is not known how effective it was for treating post-MTBI fatigue. There is a need for further investigation into treatment approaches for post-MTBI fatigue.

Chapter 3

FATIGUE

Although subjective fatigue is one of the three most commonly reported and long lasting postconcussion symptoms, it is poorly understood. It is an enigmatic symptom, acknowledged by many researchers and clinicians and understood by few. This chapter provides a review of current knowledge about the natural history, aetiology, onset and prognosis of subjective fatigue, its base rate in the general population and, its epidemiology in the MTBI population. Comparison between post-MTBI fatigue and fatigue in other illness states or in the healthy population, and a brief examination of the difference between fatigue and sleepiness will contribute to the development of an operational definition of post-MTBI fatigue. Current models of post-MTBI fatigue and theories about its origins and maintenance factors are explored, and a preliminary ecological model of post-MTBI fatigue is proposed.

Definition of fatigue.

Fatigue is a non-specific, complex and multidimensional phenomenon which appears deceptively simple to understand and define but clinicians and researchers do not have a common understanding of the term or the condition of fatigue. Patients can use the word to mean different things in the same conversation (Krupp, 2003). It is non-specific because it has little or no diagnostic value as it is present across a broad range of conditions - from physiological (sleep deprivation), through medical (bacterial or viral infections), psychiatric disorders (depression and anxiety), lifestyle choices (excessive alcohol or caffeine or psychosocial stressors) and life events (trauma) (Torres-Harding & Jason, 2005). Early twentieth century opinion was that the concept

of fatigue should be entirely abandoned because of the difficulty of defining or objectively measuring it (Holding, 1983). Neurophysiologists discovered the electrophysiological fatigue of the myasthenic synapse over a century ago but, like pain, fatigue is a private and subjective experience which currently can only be measured through self-report (Wessely, 2005). Given the ongoing difficulty of objectively measuring mental and emotional fatigue, the primary focus of fatigue research within neuropsychology has been subjective fatigue, that is, the *experience of fatigue* as reported by community and clinical populations. For the remainder of this review, and body of research, the terms "fatigue" and "subjective fatigue" will be used interchangeably.

Subjective fatigue has been extensively studied in both the general population and specific illness populations such as CFS, MS, cancer, post-poliomyelitis, Parkinson's Disease, 'unexplained illnesses', autoimmune dysfunction, and depression.

The MTBI literature has addressed subjective fatigue to a significantly lesser extent, although that situation is changing. It is now more frequently directly addressed in comprehensive TBI books (Silver, McAllister, & Yudofsky, 2005; Zasler, Katz, & Zafonte, 2005) as well as TBI research papers including the MTBI literature (Allison, 1995; Borgaro, Gierok, Caples, & Kwasnica, 2004; Stulemeijer et al., 2006; Ziino & Ponsford, 2005a, 2005b, 2006). Definitions of subjective fatigue have common elements which can be combined towards a multidimensional view of fatigue as shown in Table 3.1. On the basis of the various perspectives of fatigue reviewed, a working definition of both normal and pathological subjective fatigue was constructed to guide this post-MTBI fatigue research.

Table 3.1

Common Elements in the Definitions of Subjective Fatigue Gleaned from the Literature.

Dimension	Descriptors
Endurance	• decreased mental and/or physical endurance • inability to rise to the occasion • performance that is short of one's expectations (as when healthy) • sense of loss of power • decreased ability to act • everything is an effort • decreased performance over a prolonged period of time • decreased performance during acute but sustained effort
Motivation	• decreased motivation • loss of inclination or motivation to engage in an activity • increased resistance to further effort
Resources	• depletion of reserves • imbalance between availability, utilization or retrieval of required resources • low energy • (not) responsive to rest • 'drained' feeling • fatigability • carriers of the APOE epsilon 4 allele
Sense of Tiredness	• lassitude • sense of tiredness or? overwhelming exhaustion • weariness following exertion • weariness without exertion • feeling of exhaustion
Functioning	• impaired physical, cognitive and/or emotional functioning • difficulty tracking and understanding conversation and/or lectures • tendency to abandon both household tasks or social activities • changes in information processing • modify the pace by reducing the number and speed of activities • weakness • decreased capacity for work • reduced efficiency to respond to stimuli • limited ability to sustain concentration and endure mental tasks • reduced concentration, motivation, initiation and/or 'zest for life' • fatigue-impaired executive functioning • reduced ability to plan or organize • staying home because it feels safe

Dimension	Descriptors
Objective/Subjective	• self-perceived • self-report • independently measurable • subjective feeling • objective performance decrement
Normal versus Pathological	• protective process • excessive relative to effort • boredom • accompanied by mood states (irritation, depression, jubilation, happiness, relief) • higher physiological costs (increase blood pressure) in severe TBI versus healthy controls
Physical, Mental, Emotional, Psychological, Neurological	• total body 'give-out' • somatic • central and peripheral fatigue • psychophysiological state resulting from sustained mental effort • reduction in perceived control • undermined confidence • issues around need to rely on others • grief and frustration for the loss of an active life • loss of the past self • isolation

The list was compiled from articles published by the following authors: - Aaronson et al., 1999; Belmont et al., 2006; Chaudhuri & Behan, 2000, 2004; Christodoulou, 2005; DeLuca, 2005a, 2005b; Dijkers & Bushnik, 2008; Krupp, 2003; Lange, Cook & Natelson, 2005; Ream & Richardson, 1996; Sundstrom et al., 2007; van der Linden & Eling, 2006.

Normal fatigue

Normal subjective fatigue is a sense of tiredness or exhaustion following extended effort accompanied by reduced power and motivation to engage in effortful activity, independent of mood. It implies depleted energy resources which can be replenished by rest and sustenance (De Luca, 2005; Krupp, 2003; Rao et al., 2005). For instance, the home gardener feels physically tired but satisfied after a big day in the garden, the athlete who has just won an Olympic race exhibits physical tiredness accompanied by elation (emotional energy) and the student who emerges from successfully completing a challenging exam exhibits mental tiredness but is happy with their effort. Normal fatigue could also be accompanied by despondency if despite significant effort success

was not achieved, but this temporary dip in mood is likely to be qualitatively different than depression.

Pathological fatigue

Pathological fatigue occurs when the amount of effort required to induce the sense of tiredness or exhaustion, reduced power and motivation is considerably less than would be expected in that individual when healthy. In pathological fatigue, energy resources are depleted more quickly and more extensively than normally expected and are not as responsive to rest and sleep (De Luca, 2005; Krupp, 2003; Rao et al., 2005). For instance, following an MTBI a significant proportion of individuals report becoming very tired just doing their normal daily activities and frequently report, in clinical settings, needing a nap or rest at the end of, or during, a normal working day and/or being unable to complete a full working day. The need for a nap or rest after regular activity was not normal for them prior to their MTBI. Many people who attend our Concussion Clinic report feeling very tired in the early afternoon, around 2 pm. While mood is not a defining characteristic, pathological fatigue is more likely to be accompanied by increased irritability, depression and/or anxiety than normal fatigue, and to be perceived as unpleasant.

Fatigue and Energy

Are energy and fatigue two separate constructs or polar opposites of a unidimensional construct? The psychological literature, to date, is inconclusive with variation in correlations ranging from r = .80, Profile of Mood States fatigue and energy subscales, to r = .50, Beck Depression Inventory – II fatigue and energy items (O'Connor, 2006). Van der Linden & Eling (2006) saw energy (determination and enthusiasm which

promotes persistence) as a personality trait, while O'Connor saw fatigue and energy as transient states. These apparently opposing views highlight the necessity to be clear about the concept under study. In this research the focus is on post-MTBI fatigue and energy as transitory states which vary from time to time.

Fatigue and Excessive Sleepiness

Fatigue is frequently confused with sleepiness both in lay and clinical contexts. Distinguishing between fatigue and sleepiness is crucial to choosing the most appropriate intervention as sleep, particularly in the case of post-MTBI fatigue, does not always relieve fatigue, but does, on the other hand, relieve sleepiness. Sleep dysfunction, including delayed sleep onset, frequent waking and early waking, is a common post-concussion symptom (Ayalon, Borodkin, Dishon, Kanety, & Dagan, 2007; Fichtenberg, Zafonte, Putnam, Mann, & Millard, 2002; Levin, 1989; Levin, Eisenberg, & Benton, 1989; Parsons & Ver Beck, 1982) and is a potential cause of fatigue. Both fatigue and excessive sleepiness have a neurophysiological substrates but just how much biological overlap there is between excessive sleepiness and fatigue is yet to be elucidated (Chaudhuri & Behan, 2004; Guilleminault & Brooks, 2001).

Fatigability

Sleep deprivation studies identified fatigability (resistance versus vulnerability to fatigue) as an individual characteristic which determines differential neurophysiological function (differences in cortical activation) and cognitive performance after prolonged sleep deprivation (Caldwell, 2005). This apparently

innate characteristic could help explain why some MTBI individuals suffer more from post-MTBI fatigue than others.

Base Rate of Fatigue in the General Population

One of the arguments against the existence of a Postconcussion Syndrome is the prevalence of many of the postconcussion symptoms in the general, non-brain injured population as shown in the synopsis of fatigue studies and reviews presented in Table 3.2. These studies are considered in further detail below.

Fatigue is a relatively common problem within the general population and epidemiological studies found between 10.5% and 41.2% incidence of prolonged, greater than one month, fatigue (Table 3.2). One outlier reported 76% fatigue in a population of litigants, where symptom exaggeration could be expected.

General medical practice was the primary source of epidemiological data, with a few studies drawing from the wider population. For instance, a large (N = 31,406) community study found 12.33% of the sample reported fatigue duration greater than or equal to one month, and 8.26% of the sample reported fatigue duration greater than or equal to six months (Evengard, Jacks, Pedersen, & Sullivan, 2005). Psychiatric history, substance abuse and neurological conditions were exclusion criteria as these conditions often include fatigue as a common symptom. However, there was no evidence that acquired brain injury including TBI was among the exclusion criteria. Hence the estimate of fatigue base rate within the community could have been inflated by inclusion of a sub-population known to have a high frequency of subjective fatigue complaint i.e., post-acquired brain injury and who could be expected to be part of a

Table 3.2

Base Rates of Fatigue in the General Population

First Author	Design and Sample	Fatigue Prevalence
David et al., (1990)	London general practice Questionnaire survey. *N* = 611 (Male 167, Female 444)	10.2% of men 10.6% of women
Cathebras et al., (1992)	Primary care, structured interviews for presenting complaints, self-report measures of symptoms and hypochondriasis, and the Diagnostic Interview Schedule (DIS). Fatigue complainants more likely have a lifetime diagnosis of depression or anxiety (45.2% vs. 28.2%). *N* = 686	93 (13.6%) fatigue symptom 46 (6.7%) primary complaint was fatigue
Lees-Haley & Brown (1993)	Litigants for psychological stress or distress without neurological claims or injuries, *N* = 170	79% reported fatigue
Kroenke et al. (1993)	Consecutive patients surveyed in two adult primary-care clinics. Fatigue was more prevalent in women than in men (28% vs. 19%). *N* = 1159	*N* = 276 (24%) fatigue a major problem.
Walker et al. (1993)	National Institute of Mental Health Epidemiologic Catchment Area Study. USA Fatigue associated with lifetime and current risk for affective, anxiety, and somatoform disorders, as well as increased utilization of medical services. Household sample *N* = 18,571	6 – 7 % with lifetime 24% in general population unexplained fatigue current 6%, lifetime 15.5%
Pawlikowska et al. (1994)	Postal survey. Comment: no indication of TBI or neurological status so could include post-TBI population as confound to true non-TBI base rates, general practice patients *N* = 15 283.	18.3% for ≥ 6 months
Fuhrer et al., (1995)	French primary care patients, associated factors - depression for woman, age for men, lower socio-economic status for both. *N* = 3784	41.2% fatigue symptom 7.6% primary complaint was fatigue
Jason et al. (1999)	Cross-sectional telephone screening of random community-based sample, *N* = 18 675	4.2% reported severe fatigue

First Author	Design and Sample	Fatigue Prevalence
Sundstrom et al (2004	Subset of Betula general population longitudinal prospective cohort study of ageing, memory and health, no head injury *N* = 62	26% Baseline 19% 5 year Follow-up not significant
Evengard et al (2005)	Twin study general population, non-clinical, individuals, telephone survey. Exclusions for psychiatric, neurological, substance abuse/dependence, sleep disorder, cancer, hepatitis B or C or HIV, significant rheumatological disorder, chronic pulmonary disease, significant endocrine disorder, or inflammatory bowel disease. No apparent screen for history of TBI. *N* = 31 406	Fatigue 21% whole sample Fatigue 17.17% with exclusions Fatigue ≥ 1 month 12.33% Fatigue ≥ 6 months 8.26%
Yang & Wu (2005)	Brief review of literature and development of a Situational Fatigue Scale - community samples or general practice patients; rates vary depending upon survey methodology and population. *N* = 232	10% - 45%

TBI = Traumatic Brain Injury; ED = Emergency Department; HIV = Human immunodeficiency virus,

general medical practice patient population. Predictors of fatigue across a range of populations include female gender, sociocultural, physiological and/or psychological variables, and being more likely to visit a health care provider (Fuhrer & Wessely, 1995b; Kroenke, Wood, Mangelsdorff, Meier, & Powell, 1988; Lewis & Wessely, 1992). Female gender has been reported as significant in many fatigue studies but usually with the unanswered question - are women more likely to report this symptom than men? Fatigue is a relatively common symptom in the general population as the studies in Table 3.2 have shown; its prevalence in a MTBI sample will be examined in Study One, Chapter 5.

POST-MTBI FATIGUE

Characteristics of Post-MTBI Fatigue.

The natural history of MTBI is full recovery within three months, usually much sooner. Excessive fatigue within that period is expected, and is deemed 'normal' until persistence is demonstrated by report of excessive or unusual fatiguing at three months or longer, post injury. Pathological post-MTBI fatigue may be defined as subjective fatigue or tiredness experienced by individuals who have a history of MTBI greater than three months prior to assessment. This proposed working definition of post-MTBI fatigue specifically excludes mood but does not delineate between physical, mental, emotional, central or peripheral fatigue. However, given the injury is to the brain, post-MTBI fatigue is likely to be explained by *central* mechanisms and manifest as a result of mental activity whether or not that mental activity controls physical or only mental output or performance.

Fatigue is one of the three most common, persistent, symptoms of MTBI, interfering with participation in work, home and social activities and, thereby reducing quality of life (Kashluba et al., 2004b; Mittenberg et al., 2001; Mittenberg, DiGiulio, Perrin, & Bass, 1992; Ziino & Ponsford, 2005a). A general picture that emerges from the studies and reviews in Table 3.3 is that there is a greater prevalence of fatigue in the MTBI population than in the general population. For instance, reviews report persistent post-MTBI fatigue prevalence rates of 22% to 59% at three months and longitudinal studies have listed post-TBI fatigue among the symptoms lingering for months and years (Olver et al., 1996) post injury. Comparative studies of post-concussion symptoms in both MTBI and healthy samples, listed in Table 3.3, have shown fatigue is more prevalent within the MTBI population than in the healthy controls (Kashluba et al., 2006; Kashluba et al., 2004b; Lundin, Boussard, Edman, & Borg, 2006; Mickeviciene et al., 2002; Mittenberg et al., 1996).

An association has been established between post-TBI fatigue and factors such as acute symptoms, mechanism of injury, time since injury and higher education levels (Stulemeijer et al., 2006; Ziino & Ponsford, 2005a). Litigation is frequently cited as a predictor of persistent postconcussion syndrome (PCS) including fatigue (Belanger, Vanderploeg, Curtiss, & Warden, 2007; Iverson, 2005) because those involved in litigation after a MTBI are often found to be more symptomatic than those who are not involved in litigation (Binder & Rohling, 1996). However, it has been argued (Hornstein, 2005; Iverson, Zasler, & Lange, 2007); that the litigation process is very stressful and likely to produce a range of stress reactions including fatigue and could also exacerbate actual postconcussion symptoms; that those individuals who have poorer outcomes, i.e., persistent symptoms, following a MTBI are more likely to

seek compensation than those who recover. Also Hornstein cited Thornhill et al.'s (2000) finding that 80% of a prospective sample of MTBI survivors were not involved in litigation despite over half of them continuing to exhibit disability at one year post injury. The role of litigation and symptom exaggeration is still unresolved and has to be considered when an individual presents with post-MTBI fatigue or other postconcussion symptoms (Iverson et al., 2007).

On the other hand, factors such as injury severity and mood (depression) have not been found to be significantly associated with post-TBI fatigue. This is somewhat surprising as fatigue and low energy are among criteria for the diagnosis of depression (American Psychological Association, 1994; World Health Organisation, 1992b); hence, there is a need for research to clarify the relationship between depression and post-MTBI fatigue. A 2009 study (de Leon, Kirsch, Maio, Tan-Schriner, Millis, Fredriksen, et al., 2009) found fatigue severity 12 months after mild head injury was associated with characteristics (fatigue, medical disability, marital status and litigation) present in the month preceding the injury but not with the Mild Head Injury (MHI) directly.

Recovery from MTBI can be complicated by a combination of symptoms such as a new mental health condition (e.g., depression) or pain (de Kruijk, Leffers, Meerhoff, Rutten, & Twijnstra, 2002). Sleep dysfunction and pain have been linked to fatigue in an investigation of postconcussive symptoms in a chronic pain sample (Smith-Seemiller et al., 2003), although Mooney (2005) and Rao et al. (2005) pointed out that fatigue and sleep dysfunction can also be mediated by psychiatric symptoms.

A current, oft quoted, neuroscience theory attributes post-TBI fatigue to injury in the Hypothalamic-Pituitary-Adrenal axis (Chaudhuri & Behan, 2000) and consequent interruption of the neurotransmitter (Serotonin, Dopamine, Norepinephrine, Acetylcholine) pathways associated with depression and euphoria (Zasler et al., 2005). This was particularly expected among the 'Miserable Minority', (Ruff, 1996; Rutherford, Merrett, & McDonald, 1978; R Wood, 2004) i.e., those MTBI patients who are high achievers who are anxious when they under-perform and when they can not resume their pre-accident participation as quickly as they would like.

Psychosocial issues play a part in recovery from MTBI and the reaction of professionals, family members, friends and colleagues impacts on recovery progress (Ruff, 1996).

While severity of injury has not been found to predict post-MTBI fatigue, many studies reporting on post-TBI fatigue do so from samples incorporating individuals with mild to severe TBI (Olver et al., 1996; Ziino & Ponsford, 2005a) Reporting findings for a mixed TBI severity group is likely to mask the 'real' picture for both the mild and the more severe injuries where disability is very often permanent and profound. Additionally, severity ratings, rather than frequency, were found to distinguish 'normal subjects' from those who had an mild traumatic brain injury (Kay et al., 1992).

After comparing normal, currently depressed and mild head injury (MHI, 12 months post-injury) groups, significant large correlations were found between postconcussion symptoms (including fatigue) and both depression ($r = .68$) and anxiety ($r = .64$)

(Trahan, Ross, & Trahan, 2001). While the MHI group scores more closely resembled the normal group scores, there were significant differences between the three groups for frequency and severity of fatigue and depression symptoms. Another study (Machulda, Bergquist, Ito, & Chew, 1998) found a positive relationship, which strengthened over time, between perceived stress and intensity of postconcussion symptoms. Treatment of depression in MTBI patients resulted in improvement of global and psychosocial functioning, postconcussive symptoms and neurobehavioural difficulties.

Another part of the post-MTBI fatigue picture that emerges from Table 3.3 is the variety of instruments used to measure fatigue; Postconcussion Syndrome Checklist (Gouvier et al., 1992), Problem Checklist (Kay et al., 1995), Rivermead Postconcussion Checklist (King et al., 1995), Rivermead Head Injury Follow-up Questionnaire (Crawford et a., 1996) Checklist Individual Strength (Vercoulen et al., 1994), SF-36 Vitality (Ware, Gandek, & IQOLA Project Group, 1994) are just a few (Christensen & Piper-Terry, 2004). The scales in the studies in Table 3.3 have all been used in several PCS studies but none have been specifically developed to measure post-MTBI fatigue.

Post-MTBI Fatigue and Other Illness-Related Fatigue

Mental fatigue can be classified as chronic, characterised as persistent or slow to recover, or acute, that is, temporary and linked to previous effortful activities (van der Linden, 2011). Chronic mental fatigue such as exhibited by people with CFS, is by the CDC/NIH[3] definition, not the result of ongoing exertion (Fukuda et al., 1994). Studies

[3] Centres for Disease Control and Prevention/National Institutes of Health

of acute mental fatigue in non-head injured samples noted a decline in performance or an adaptation of behaviour to maintain some aspects of performance (van der Linden, 2011). Post-MTBI fatigue is akin to acute mental fatigue but with sudden manifestation, particularly following mental effort, prompting Wrightson and Gronwall (1999) to use the term "like a curtain coming down" (p 47). This sudden manifestation of post-MTBI fatigue has been observed during neuropsychological assessment at our Concussion Clinic. An explanation for this apparent 'sudden onset' could lie in compromised executive functioning such as attentional and monitoring processes in the anterior cingulate cortex as a result of diffuse axonal injury (DAI) (Lorist, Boksem, & Ridderinkhof, 2005).

Post-MTBI Fatigue Onset

One of the arguments against recognition of fatigue as a post-concussion symptom is that onset appears to be quite variable among people with TBI. For instance, Ouellet & Morin (2006) reported onset of post-TBI fatigue varying from days (35.7%) to weeks (15.5%) to months (30.7%) post injury. Possible explanations are, firstly, that other symptoms such as headache or non-head injuries claim priority focus in the early period and only after many of these symptoms have resolved does fatigue get noticed. Secondly, medication, such as Amitriptyline, prescribed for headache prevention or sleep disruption can cause drowsiness or fatigue (AFT Pharmaceuticals Ltd, 2010), at least temporarily. Thirdly, in most circumstances the individual with an MTBI initially rests or reduces their daily activity, so fatigue is less likely to be seen as a separate symptom. Fourthly, once early symptoms such as headache, dizziness and nausea resolve or reduce, the individual with MTBI resumes their normal activity level before their brain is fully healed and they require extra energy to perform their normal

cognitive tasks (Leddy et al., 2007). Finally, compensation seeking and litigation are also known correlates of persistent PCS symptoms including post-MTBI fatigue (Binder & Rohling, 1996; Paniak, Toller-Lobe, Reynolds, Melnyk, & Nagy, 2000); however, the majority of those with financial incentives are not cured by a verdict (R. W. Evans, 1992) suggesting the fatigue was real.

Prevalence of Post-MTBI Fatigue

Dijkers & Bushnik's (2008) review of 16 articles concluded that the rate of post-TBI fatigue (30% to 70%) was significantly greater than the base rate in the population at large. As they point out, there are significant problems with fatigue prevalence studies both in the general population and those with TBI. Problems include the absence of a standard definition of fatigue and of clinical measures which operationalise fatigue, as well as the large number of different instruments used to measure fatigue across prevalence studies. Although Dijkers & Bushnik assert that most of the post-TBI fatigue research has involved individuals with mild TBI, many of the studies report findings for populations of mixed severity TBI making it difficult to clarify what is happening within the MTBI group.

However, several studies have reported no significant effect of TBI severity on post-TBI fatigue (Allison, 1995; Cantor et al., 2008; Ouellet & Morin, 2006; Stulemeijer et al., 2006). Despite using a mixed sample, Ouellet & Morin (2006), identified fatigue prevalence by severity and reported 73.9% of those with MTBI complained of significant post-MTBI fatigue. They also reported that 79.4% of significant others concurred with the fatigue complaint, providing corroboration for the subjective report of fatigue. Another clinic-based study (N = 586) compared a group with MTBI with a

group of patients with a non-MTBI injury (ankle and wrist) and found a significantly greater incidence of fatigue (32%) in the MTBI group than was found in the non-MTBI group (12%) at six months post injury (Stulemeijer et al., 2006). This study found no relationship between fatigue and age, educational level or social status and only a small gender difference in the control group with women reporting a higher level of fatigue ($p < .01$). No information about psychiatric or other conditions which could influence the findings was reported.

As with Ouellet & Morrin's (2006) study, most of the post-MTBI fatigue prevalence data is gleaned from studies of postconcussion symptoms in general. Studies of the prevalence and natural history of post-MTBI fatigue are summarised in Table 3.3 which reports prevalence rates from 28% to 82% at time periods from 1 month to over 7 years post injury. Post-MTBI fatigue is clearly a significant symptom for those recovering from a mild brain injury. Many of the studies in Table 3.3 compared TBI samples with non-TBI samples demonstrating that post-MTBI fatigue is more prevalent than fatigue in the general population. Given the distress associated with post-MTBI fatigue there is a need for investigation into the most effective ways to treat post-MTBI fatigue.

Table 3.3

Prevalence of Post-MTBI Fatigue in MTBI Samples

Author	Sample	Prevalence of post-MTBI fatigue	Fatigue Measure
Gouvier 1988	MTBI patients and relatives Pre-exam college students' relatives	'Tires easily', MTBI 33.3%, MTBI relative's perception 37.5% Students 27.6% Students' relatives perception 34.7 %	37 item checklist (Oddy et al. 1978)
Mittenberg et al. (1992)	Mild Head Injury *N* = 100	63.9 %	Single item in checklist
Mittenberg et al. (1996)	Randomised controlled trial Mild Head Injury *N* = 29 x 2 groups	At 6 months post treatment Treatment group 47% Control group 82%	Single item in checklist
Sawchyn et al. (2000)	Undergraduate students MTBI and non-MTBI groups	Base rate of fatigue 53% whole sample. No significant difference between groups on any PCSC symptoms	Postconcussion Syndrome Checklist (PCSC) (Gouvier et al., 1992)
Mickeviciene et al. (2002)	MTBI *N* = 131 Other minor injury *N* = 146	≥22 months MTBI fatigue 28%, tiredness 31% Control fatigue 28%, tiredness 29% Difference between groups p > .05	Visual Analogue Scale - Fatigue (0-100) Lee, et al. (1991)

(Continued)

Author	Sample	Prevalence of post-MTBI fatigue	Fatigue Measure
Sundstrom et al. (2004)	MTBI subset of ageing, memory and health study, *N* = 31	Baseline 16% 5 yr Follow-up 42 %	"Do you often feel fatigued?" Yes/No
Rao et al. (2005)	Review of post-MTBI fatigue (and more severe TBI)	Post-MTBI fatigue review 1 month 29% - 47% 3 months 22% - 37% 1 year ~20% 5 years 37%	Range of measures
Kashluba et al. (2004, 2006)	MTBI Controls healthy	1 month 90% vs. 33% 3 months 59% vs. 36%	Problem Checklist, (Kay et al., 1995)
Lundin et al. (2006)	MTBI, *N* = 102 Controls in good health, *N* = 35	3 months 21% 3 months 11%	RPSQ (King et al. 1995) RHIFQ (Crawford et al. 1996)
Ouellet & Morin (2006)	Clinic-based population, mixed severity (MTBI *N* = 69,416),	Fatigue 74% of MTBI *N* =51. Time since injury for whole sample 83.9 (79.94) months Onset of post-TBI fatigue varied from days (35.7%) to weeks (15.5%) to months (30.7%)	Purpose-designed questionnaire of pre and post-injury fatigue; Multidimensional Fatigue Inventory (Smets et al., 1995)
Stulemeijer et al. (2006)	Prospective controlled study; ED Clinic patients MTBI *N* = 299 ; minor injury no MTBI *N* = 287 postal survey 6 months post-injury	MTBI 32% fatigue at 6 months post-injury Controls 12% fatigue $p < 0.0001$	RPSQ CIS (Fatigue) (Vercoulen et al., 1994)

(Continued)

Author	Sample	Prevalence of post-MTBI fatigue	Fatigue Measure
Cantor et al. (2008)	TBI mild to severe, no history of neurological problems or previous brain injury, *N* = 223 and non-injured controls, no history of brain injury, *N* = 85	≥ 12 months fatigue; 75% TBI; 40% controls sig. $p<0.001$; sig. correlation of GFI with vitality (SF-36) $r= -0.49$ $p < 0.001$ and depression (BDI-II adjusted) $r = 0.18$ $p<0.01$	GFI; SF-36 Vitality subscale BDI-II adjusted removal of fatigue and energy items

RPSQ = Rivermead Postconcussion Symptoms Questionnaire, RHIFQ = Rivermead Head Injury Follow-up Questionnaire, CIS = Checklist Individual Strength; GFI = Global Fatigue Index from Multidimensional Assessment of Fatigue (MAF), BDI-II = Beck Depression Inventory 2nd Edition.

Correlates of Fatigue and Post-MTBI Fatigue

Fatigue, in general, has been found to be correlated with age, female gender, education, employment, social class, disease characteristics and depression in a number of different health-related populations (Kapella, Larson, Patel, Covey, & Berry, 2006; Tiesinga, Dassen, Halfens, & van den Heuvel, 1999). Cantor et al. (2008) reported finding, in a mixed TBI severity (37.9% MTBI) study, that post-TBI fatigue appeared to be unrelated to demographic and injury variables other than gender. However, other studies (Borgaro, Baker, Wethe, Prigatano, & Kwasnica, 2005; Ziino & Ponsford, 2005a) reported no relationship between gender and post-TBI fatigue. According to Cantor et al.'s (2008) review, post-MTBI fatigue did not limit the quantity and frequency of participation in life activities but they were unsure about the quality of post-TBI participation, i.e., how well or satisfactorily the individuals carried out daily activities including socializing. They found that fatigue was not associated with severity of TBI, time post injury or income. Several items on the Participation Objective Participation Subjective (POPS), (cleaning house, paying bills, visiting friends, engaging in sex, and speaking to neighbours) were significantly related to fatigue (Cantor et al., 2008).

Both commonly used sets of criteria for the diagnosis of depression, e.g., DSM-IV and ICD-10, include fatigue or tiredness. As a consequence, depression is frequently seen as a confound in fatigue research. However, several studies have found fatigue and depression to be independent even when co-occurring. Allison (1995) reported that when depression was held constant, a significant difference in fatigue was found between a group with closed head injury and non-head injured controls. According to an investigation of risk factors for depression following mild to moderate TBI, fatigue

added no additional unique variance when chronic stress and pain were held constant (Bay & Donders, 2008). In another study of a mixed TBI sample (37.9% MTBI), fatigue was not accounted for by depression, pain or sleep disturbance alone (Cantor et al., 2008). When depression and anxiety were held constant in a mixed severity TBI population (36.4% MTBI), performance on complex selective attention tasks, which have a higher working memory load, was significantly associated with subjective fatigue (Ziino & Ponsford, 2006). Greater subjective mental fatigue was associated with more errors, attribution of fatigue to the need for mental effort in performing tasks, slower reaction times and the reporting of fatigue having a greater impact on daily function (Johansson, Berglund, & Ronnback, 2009; Lorist et al., 2009; Ziino & Ponsford, 2006).Well-being and quality of life are also significantly negatively affected by post-TBI fatigue (Cantor et al., 2008).

Within the MTBI population, post-MTBI fatigue severity at six months post-injury was significantly correlated with headache and nausea on admission as well as post-injury concentration, motivation, physical and social activity (Stulemeijer et al., 2006). Keeping in mind that the following observations refer to a mixed TBI sample, Ouellet & Morin (2006) found post-TBI fatigue was significantly correlated with time since injury, inability to work, anxiety, depression, cognitive symptoms, irritability, insomnia and pain. They also reported no significant relationship for TBI severity and post-TBI fatigue as measured by the General Fatigue Index of the Multidimensional Fatigue Inventory. The participants' perceptions of changes in fatigue level from pre to post TBI were inconsistent with their results on self-report fatigue questionnaires. That is, 95% expressed the belief that their fatigue was worse post injury but, when they rated pre/post fatigue on scales, including an *ad hoc* version and the Multidimensional

Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995), only 68.5% were significantly more fatigued post-injury. This finding raises questions about the role of psychological factors such as distress, anxiety and coping styles in inflating the experience of excessive fatigue.

Pathophysiology of Post-MTBI Fatigue

Burgeoning understanding of the pathophysiology of post-MTBI fatigue during the early 21st century has enabled the development of the tailored treatment for post-MTBI fatigue which is investigated in this current study. This section provides a brief overview of the pathophysiology of post-MTBI fatigue which informs the treatment trial presented in this thesis.

Neurobiological changes, such as ionic shifts, altered metabolism, impaired connectivity, or changes in neurotransmission (Giza & Hovda, 2001), occur both immediately and in the days and weeks following an MTBI. To date it is not known, definitively, which biological substrates underlie fatigue in *normal* individuals, hence the pathophysiology of post-MTBI fatigue is also unclear. However, imaging advances, particularly fMRI, diffusion tensor imaging (DTI), diffusion weighted imaging (DWI) and proton magnetic resonance spectroscopy (PMRS) and animal-based studies over the last two decades have enabled increased understanding of brain changes post TBI. Study of mechanisms, such as DAI and the neurometabolic cascade and the way these events interact with specific neuroanatomical structures, has contributed to our understanding of the likely (patho)physiology of central and/or mental fatigue. Injury within neurological mechanisms such as the autonomic and central nervous systems has been proposed to explain central fatigue (Chaudhuri & Behan, 2000, 2004; Fellus &

Elovic, 2007). Neuronal hypometabolism, axonal damage, regional choline peaks, cell membrane instability, and demyelination have been associated with fatigue in a variety of disease states and TBI (Chaudhuri & Behan, 2004; Zhang, Chen & Graham, 2002; Zwarts, Bleijenberg & van Engelen, 2008).

The proposed mechanism for early post-MTBI fatigue is the metabolic cascade which is followed firstly by hypermetabolism and diminished cerebral blood flow. Then an energy crisis (hypometabolism) is triggered by disparity between energy supply and demand. The depressed glucose metabolism overtly manifests as acute post-(M)TBI fatigue which was observed to last two to four weeks post-TBI (Giza & Hovda, 2001)In some cases homeostasis is not re-established and one or more of these conditions - autonomic dysregulation, hypoperfusion, neuroendocrine and neurotransmitter disruption - continue well beyond the expected recovery period. This prolonged state of disequilibrium is proposed as an explanation for persistent postconcussion symptoms (Leddy et al., 2007; McCrea, 2008). Cerebral circulation can remain slowed for up to three years post MTBI (Alexander, 1995). Chaudhuri & Behan (2004) summed up the pathophysiological process of central fatigue as the disruption caused by metabolic and structural lesions of the usual process of activation in pathways interconnecting the basal ganglia, thalamus, limbic system and higher cortical centre. Another mechanism suggested to explain central fatigue (i.e., post-MTBI fatigue) is failure to maintain adequate levels of dopaminergic transmission to the striatum and anterior cingulate cortex (Lorist et al., 2005). Additionally, disruption within the glutamatergic, adrenergic and cholinergic systems following TBI (Giza & Hovda, 2001) is associated with post-TBI depression and fatigue. Fatigue is a known sequelae of neuroendocrine dysregulation (Payne, 2004) but the incidence of post-MTBI neuroendochrine

dysfunction is rare (Klose et al., 2007; van der Eerden et al., 2010). Systemic disruption could explain the persistence of post-MTBI fatigue for years post head injury.

Diffuse axonal injury

Diffuse axonal injury (DAI) is a mechanism which could explain systemic disruption both for late onset and for persistence of postconcussion symptoms, particularly, post-MTBI fatigue. A link between DAI and fatigue was established in two MS studies (Marrie, Fisher, Miller, Lee, & Rudick, 2005; Tartaglia, Narayanan, & Arnold, 2008). DAI is a common form of lesion following MTBI which results from rapid acceleration-deceleration and/or rotational-vibrational forces acting on the brain matter during a mild brain trauma (Bigler, 2001; Gentry, Godersky, & Thompson, 1988; Zhang et al., 2010). It is largely a result of secondary biochemical cascades with delayed onset, so a person with DAI who initially appears well may deteriorate later (Cohen et al., 2007; Smith, Meaney, & Shull, 2003; Zhang et al., 2010). In MTBI two thirds of DAI lesions occur in areas where grey and white matter meet (Wasserman & Koenigsberg, 2007) i.e., the lobar white matter, corpus callosum, basal ganglia, thalamus, dorsolateral upper brainstem and cerebellum (Gennarelli & Graham, 2005; Inglese et al., 2005). These brain structures are involved in maintaining and regulating alertness and maintaining motivation to act, thus most likely to be implicated in the subjective experience of post-MTBI fatigue.

DAI is associated with another common post-MTBI symptom, sleep dysfunction (Ayalon et al., 2007), and 80% of individuals with TBI-associated sleep dysfunction also report fatigue (Clinchot, Bogner, Mysiw, Fugate, & Corrigan, 1998). Sleep dysfunction does not necessarily co-occur with post-MTBI fatigue, however many of

the same brain areas (brain stem, basal forebrain and hypothalamus) and systems (neurotransmitters - serotonin, acetylcholine, dopamine, norepinephrine and other hormones and endogenous products) regulate the sleep-wake cycle as well as signal energy and fatigue (Rao et al., 2005). Despite the known neurophysiological commonalities, the search for clarity about the links between sleep and fatigue is still being pursued (Chaudhuri & Behan, 2004). Psychiatric symptoms resulting from TBI-related neurotransmitter disruption (Giza & Hovda, 2001) have been proposed as the mediating factor linking sleep dysfunction and fatigue following a TBI (Rao et al., 2005).

Psychological symptoms

Whether there is a causal role for psychological symptoms in the post-MTBI fatigue model is unclear. "Statistically, depression predicts fatigue and fatigue predicts depression in the general population" (Fellus & Elovic, 2007). Low energy and fatigue are among the DSM-IV criteria for depression (American Psychiatric Association, 1994) but this relationship does not imply causality. However, disruption in neurotransmitter pathways has been linked directly to post-TBI fatigue (Chaudhuri & Behan, 2000, 2004; Fellus & Elovic, 2007) and, independently, to psychological difficulties like depression and anxiety. Psychological factors are not a necessary mediating variable for post-MTBI fatigue but could be an exacerbating factor.

Genetic factors

Genetic vulnerability to more severe neuropathology is likely to be part of the explanation for some individuals experiencing post-MTBI fatigue while others do not. Having the Apolipoprotein E (APOE or ε4) genotype increases the risk of post-MTBI

fatigue (Sundstrom et al., 2007), an effect which was more likely to be present as time since injury increased (Teasdale, Nicoll, Murray, & Fiddes, 1997).

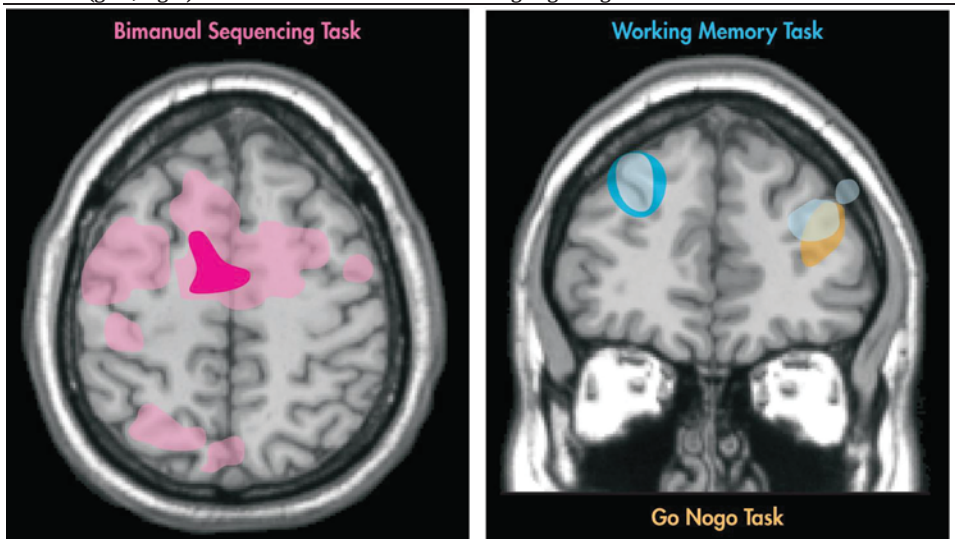
Advances in imaging technology

All of these factors - genetic predisposition, sleep dysfunction, psychological factors, and systemic disruption - could have a role in explaining the presence of post-MTBI fatigue. Traditional methods of brain imaging following MTBI - CT and MRI scanning - are notoriously poor at detecting DAI (Smith et al., 2003). However, relatively recent advances in more sensitive imaging techniques such as diffusion weighted imaging (DWI) and fMRI have enabled a better understanding of the impact of MTBI on brain function while performing cognitive tasks (Cook, O'Connor, Lange, & Steffener, 2007; G. Lange et al., 2005; Tartaglia et al., 2008).

Studies of sports related concussion based on pre- and post-MTBI neuroimaging have broadened our understanding of possible mechanisms which account for phenomena such as post-MTBI fatigue. For instance during cognitive activity such as a working memory task, fMRI found a more regionally dispersed and more lateralized pattern of activation post MTBI than was found in imaging of either pre-injury baseline or uninjured control groups (Chen et al., 2004; McAllister, 2005; Mendez et al., 2005; Tartaglia et al., 2008; Zhang et al., 2010). Figure 3.1 (Mendez et al., 2005) illustrates the difference between cortical activation of MTBI athletes compared with uninjured athletes. The figure shows that concussed athletes had widespread activations in areas not activated in comparison subjects. However, the concussed athletes' cognitive performance was unchanged compared to their baseline measures. This observation was supported in DeLuca's (2007) review of the neuropsychological perspective of fatigue

where he noted that subjective fatigue was not correlated with objective cognitive performance on neuropsychological tests. In a recent controlled study, Zhang et al. (2010) also demonstrated through fMRI and DTI that comparatively more regional dispersion and lateralisation occurs within the brains of individuals who have sustained an MTBI when they are doing common neuropsychological tests. Zhang et al.'s study found a trend towards more mental fatigue in the MTBI group. However, as the MTBI group was asymptomatic at the time of assessment, it is likely they did not still have

Task-related brain activation on fMRI may be changed post concussion.[1–3] Athletes with concussions (shown in light shades) have many more regions of activation than those without (shown in dark shades) during a bimanual sequencing task (pink, left) or working memory task (blue, right).[1,2] In addition, concussion may be associated with decreased activation in areas critical for task performance. Athletes with concussion had reduced activation in right dorsolateral prefrontal cortex during a working memory task (light blue, right).[2] In another study, comparison subjects showed more activation in left dorsolateral prefrontal cortex (gold, right) than athletes with concussion during a go no go task.



Reprinted with permission from Journal of Neuropsychiatry and Clinical Neurosciences, (Copyright 2005). American Psychiatric Publishing, Inc. Mendez et al. (2005) Figure 2, p300

1. (Jantzen, Anderson, Steinberg, & Kelso, 2004)
2. (Chen et al., 2004)
3. (Easdon, Levine, O'Connor, Tisserand, & Hevenor, 2004)

Figure 3.1. Task-related brain activation on fMRI.

the same level of brain injury and the same drain on their energy resources as appears likely from inspection of Mendez et al.'s illustration.

These studies contribute to the model of post-MTBI fatigue by illustrating the greater demands concussed brains make on energy resources through requiring greater and more diverse cortical input to achieve the same overt cognitive performance. That is, cellular energy demand outstrips energy supply at least temporarily after MTBI (McAllister et al., 2005). The injured brain compensates by recruiting more cells to perform the task than it required pre-injury.

Understanding the pathophysiology of MTBI and by extrapolation, post-MTBI fatigue, is very much in the developmental stage. Improved brain imaging helps growth in our knowledge of post MTBI. For instance, that mild to moderate TBI with loss of consciousness has been associated with whole brain atrophy (MacKenzie et al., 2002) and that lateralization and regionalization changes at least temporarily after MTBI (Marushi et al., 2006; Mendez et al., 2005).

This biological perspective is not without its detractors. Lees-Haley et al. (2003) believe the search for neurophysiological explanations for TBI sequelae is too reliant on novel, clinically unproven, neuroimaging techniques such as SPECT, and strongly encouraged researchers and clinicians to give precedence to the more obvious explanations for human behaviour (e.g., subjective fatigue) and to be wary of becoming over excited about new technology. In their commentary on Bigler's (2001) treatise on the implications for clinical neuropsychology of TBI lesion(s), they state that it is statistically and empirically unsound for us to presume MTBI patients to be suffering chronic effects of brain injury until proven otherwise. In response, Bigler (2003) cited the many neurobiological animal and human models of MTBI which showed both change and dysfunction post MTBI thus supporting the need for neuropsychologists to

consider the physical neurosciences, as well as their own science, when looking to explain subjective post-MTBI complaints such as fatigue.

Towards A Model of Post-MTBI Fatigue

A neurophysiological model

Drawing together significant components from the discussion brings this thesis a step closer to proposing a model of post-MTBI fatigue. Many neuropathological events follow the MTBI event itself and when these take a more detrimental pathway they can explain post-MTBI fatigue. Figure 3.2 sets out a preliminary neurophysiological model of post-MTBI fatigue. Combining this model with psychological (Rao et al., 2005), environmental and contextual factors (Kay et al., 1992; Ruff, 2005) will lead to the proposal of an ecological model of post-MTBI fatigue. Rao et al.'s (2005) algorithm proposed that not only fatigue but also sleep disturbance and psychiatric symptoms were directly linked to MTBI.

An Ecological Model of Post-MTBI Fatigue

Two other models of PCS (Kay et al., 1992; Ruff, 2005) took an holistic ecological approach, recognising that the MTBI occurred within the individual's internal (personal) and external (environmental) context. The context has an effect on how the individual reacts to their MTBI and also influences the development of feedback loops that reinforce and exacerbate these reactions. Hence the post-MTBI fatigue model, upon which any treatment approach is based, needs to be broader than that presented in Figure 3.2. The ecological model of post-MTBI fatigue, shown in Figure 3.3, takes into account the neurophysiological events which follow the initial application of

biomechanical forces to the head, either directly or through violent movement of the head, e.g., by shaking.

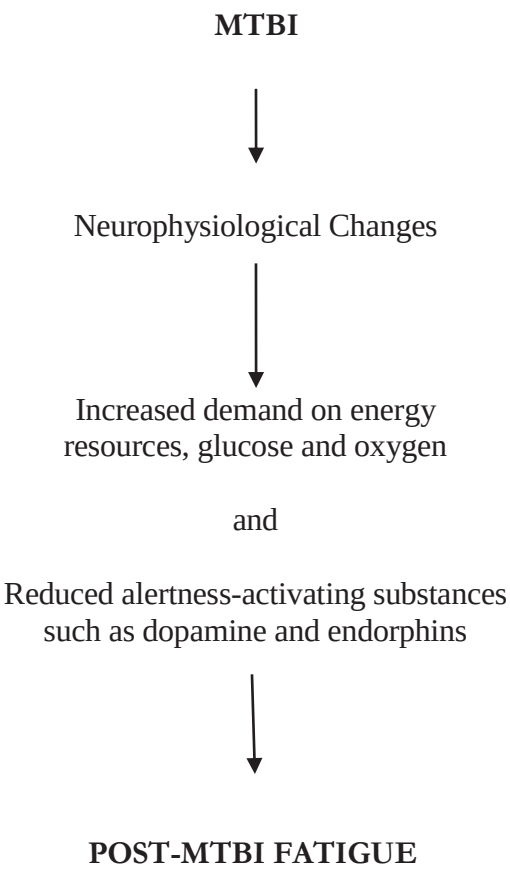


Figure 3.2. Neurophysiological model of post-MTBI fatigue.

As outlined in Figure 2.2 neurophysiological changes (Giza & Hovda, 2001; Leddy et al., 2007) lead directly to depleted energy reserves, i.e., post-MTBI fatigue, as well as to disruption in the sleep/wake cycle (Rao et al., 2005) and biopsychological symptoms such as depression and anxiety (Rao et al., 2005; Russo, 1997; Russo et al., 1996). Both loss of sleep and depression feed back into post-MTBI fatigue forming a secondary layer of fatigue-inducing factors. A tertiary layer arises when the individual

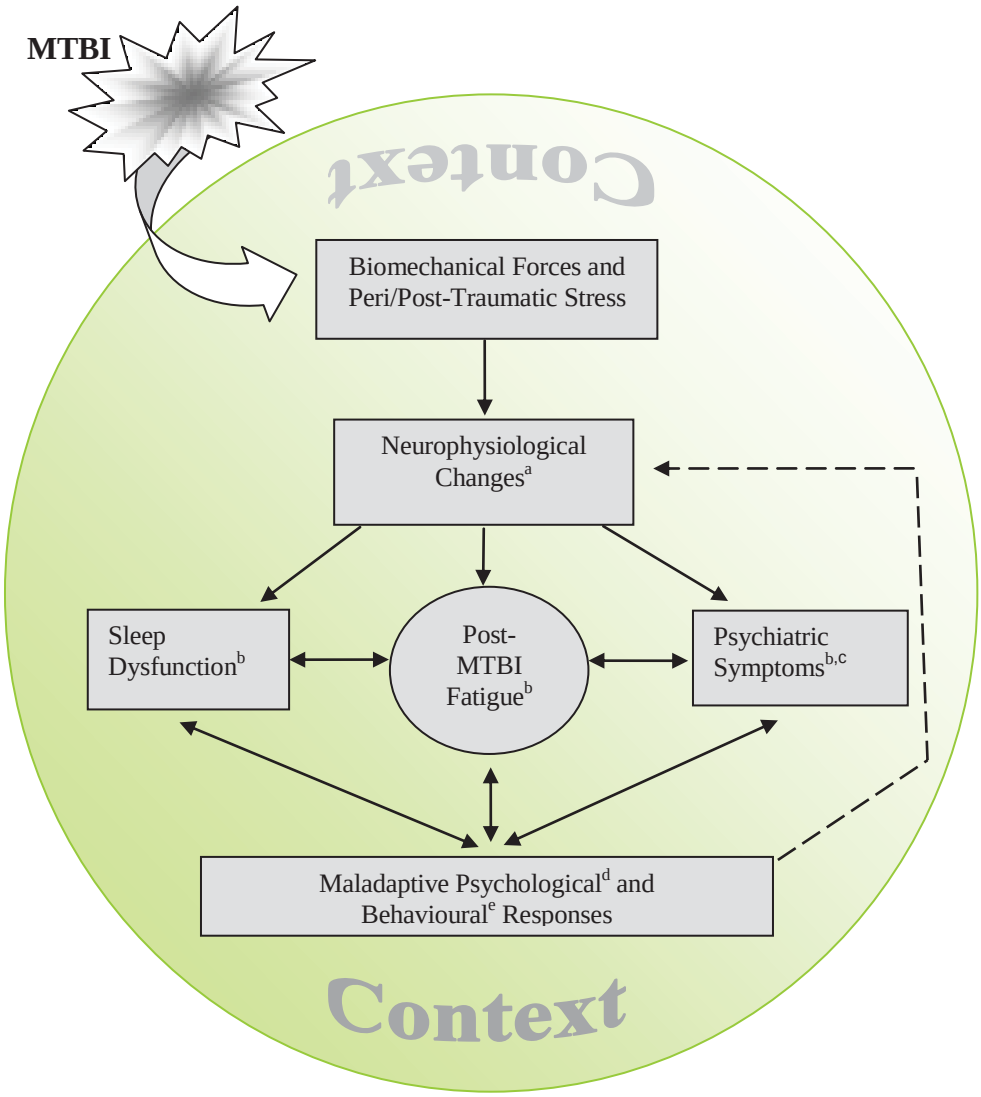


Figure 3.3. Proposed ecological model of post-MTBI fatigue.
a,(Giza & Hovda, 2001); b, (Rao et al., 2005); c, (Russo, 1997; Russo et al., 1996), d, Maladaptive cognitive coping responses resulting in feelings of anger, anxiety and depression which stimulate biological stress responses – the feedback loop (Friedberg & Jason, 1998) and persistent psychiatric illness (Fann et al., 2004); e, Inactivity, social isolation, too much activity e.g., full-time work or doing lots on "good days" followed by days of inactivity to recover; Context - Genetic, Personality, Emotional Intelligence, MTBI knowledge, Relational, Cultural, Vocational, Financial, Recreational, Social, Spiritual. (Ruff, 2005)

adopts maladaptive psychological and behavioural responses such as worry, fear, anger, blame, too little or too much activity, too little or too much social engagement, any or all of which stimulate biological stress responses creating a feedback loop which in turn maintains post-MTBI fatigue. These processes occur in a context of intra-individual and environmental factors which shape the individual's response to the MTBI event and the

likelihood they will have difficulty with post-MTBI fatigue. Intra-individual contextual factors which can affect the experience of post-MTBI fatigue are genetics, personality, emotional intelligence, spiritual beliefs and knowledge of MTBI prognosis and sequelae. External factors which can make a difference are relational, cultural, vocational, financial, recreational and social. (Ruff, 2005).

From a neuropsychological perspective, treatment for persistent post-MTBI fatigue could target many of the factors presented in this model. The most obvious are the psychiatric symptoms and sleep dysfunction as well as the maladaptive psychological and behavioural responses. However, the treatment literature for fatigue associated with other health problems such as CFS, MS and cancer provide some leads for treatment approaches which also address the neurophysiological changes associated with post-MTBI fatigue. In 2008, Kozlowski reported the results of a successful PCS treatment using progressive exercise, wherein the primary outcome measures were of physiological factors. The secondary outcome was the number of postconcussion symptoms participants reported. Chapter 5 contains a brief outline of the treatment literature for fatigue across a range of illnesses and conditions, as well as summarizing treatments for PCS.

Before moving on to the chapter on treatment studies, the first of two studies included in this thesis will be presented. The findings from this first study helped justify developing and evaluating a post-MTBI fatigue treatment approach by demonstrating that there is a sizable percentage of individuals who continue to report persistent post-MTBI fatigue beyond the expected three month recovery period. Chapter 4 outlines the history and findings of that study.

Chapter 4

STUDY ONE: PREVALENCE OF POST-MTBI FATIGUE IN A NEW ZEALAND SAMPLE

The base rate of fatigue in the general population was discussed in Chapter 3. It was found to vary between 10.5% and 41.2% across the majority of the studies listed in Table 3.1. One outlier study reported 76% of the sample had reported fatigue as a symptom in a population of litigants, where symptom exaggeration could be expected. Litigation is a confound in the study of the prevalence of persistent postconcussion symptoms. There are instances where the study has been carried out post-litigation settlement and the postconcussion symptoms were still being reported, suggesting that the financial settlement was not an active influence on the reporting of the postconcussion symptoms (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Iverson, 2005).

New Zealand has a unique system where all accident related rehabilitation is covered by a comprehensive no-fault personal accident insurance available to all New Zealand residents and visitors to New Zealand. Hence the issue of litigation as a predictor of persistent symptoms such as post-MTBI fatigue is minimised. The opportunity to study the prevalence of post-MTBI fatigue in a New Zealand population arose in 2005 and was seized as a good starting point for the current investigation of post-MTBI fatigue. Having a picture of post-MTBI fatigue prevalence, severity and persistence over time would and did inform the argument for developing a treatment programme for persistent post-MTBI fatigue within the New Zealand environment.

The opportunity arose when the principal researcher of the post-MTBI fatigue studies, reported herein, met with Marcus Heitger, PhD, after he presented on a poster detailing his pilot study into the usefulness of post closed head injury oculomotor movement as a predictor of persistent postconcussion symptoms. Later in that year Dr Heitger presented another paper during which he stated that he was about to commence a study to investigate the findings of his pilot study in a much larger sample, N = 500. The study was to be based on a prospective sample drawn from those individuals presenting to the Christchurch Hospital, Emergency Department with Closed Head Injury (CHI) and was longitudinal to six months post CHI injury. Having seen the possibilities presented by this study for advancing local and international knowledge about persistent post-MTBI fatigue in New Zealand's unique fully insured population, the current author approached Dr Heitger for permission to collaborate with him. As a result Study One in the current dissertation was conceived. Dr Heitger graciously agreed to add a fatigue questionnaire to his protocol and also to share any of his ancillary data (e.g., depression, anxiety, vitality, demographic, but not oculomotor data) with the Study One principal researcher (Norrie). Choice of the fatigue measure was made solely by Ms. Norrie. Other measures (Hospital Anxiety and Depression Scale) had already been included in Dr Heitger's protocol. The data was collected over a period from late 2006 until early 2009 and, while the oculomotor study managed to recruit N = 350 participants, a sufficiently large sample, N = 263, was available to the post-MTBI fatigue prevalence study.

Subsequently, the post-MTBI fatigue prevalence study was published in the December 2010 issue of *Brain Injury*, the journal of the International Brain Injury Association. It

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Norrie, J., Heitger, M., Leathem, J., Anderson, T., Jones, R., & Flett, R. (2010). Mild traumatic brain injury and fatigue: A prospective longitudinal study. *Brain Injury, 24*(13-14), 1528-1538. doi:10.3109/02699052.2010.531687

Abstract

Primary Objective: To examine fatigue prevalence, severity, predictors and co-variates over six months post mild traumatic brain injury (MTBI).

Research Design: Longitudinal prospective study including 263 adults with MTBI.

Procedures: Participants completed the Fatigue Severity Scale (FSS), Rivermead Postconcussion Symptoms Questionnaire (RPSQ), Hospital Anxiety and Depression Scale (HADS) and the Short Form 36 Health Survey-Version 2 (SF-36v2). Complete data were available for 159 participants. Key measures: prevalence - RPSQ Item 6: severity - FSS. The effect of time on fatigue prevalence and severity was examined using ANOVA. Multiple regression analysis identified statistically significant covariates.

Main outcomes and results: Post-MTBI fatigue prevalence was 68%, 38% and 34% at 1 week, 3 and 6 months respectively. There was a strong effect for time over the first three months and moderate to high correlations between fatigue prevalence and severity. Early fatigue strongly predicted later fatigue. Depression, but not anxiety, was a predictor. Fatigue was seen as laziness by family or friends in 30% of cases.

Conclusions: Post-MTBI fatigue is a persistent postconcussion symptom, exacerbated by depression but not anxiety. It diminishes in the first three months and then becomes relatively stable suggesting the optimum intervention placement is at three months or more post-MTBI.

Fatigue is one of the three most common symptoms of mild traumatic brain injury (MTBI) interfering with participation in work, home and social activities and, thereby reducing quality of life (Kashluba et al., 2004b; Mittenberg et al., 2001; Mittenberg et al., 1992; Ziino & Ponsford, 2005a). Reviews report persistent post-MTBI fatigue prevalence rates of 22% to 59% at three months and longitudinal studies have listed post-TBI fatigue among the symptoms lingering for months and years (Hillier, Sharpe, & Metzer, 1997; McCullagh, Oucherlony, Protzner, Blair, & Feinstein, 2001; Middleboe et al., 1992; Sundstrom et al., 2007).

Earlier studies demonstrated an association between post TBI fatigue and factors such as acute symptoms, mechanism of injury, time since injury and higher education levels (Stulemeijer et al., 2006; Ziino & Ponsford, 2005a). Litigation is frequently cited as a predictor of persistent postconcussion syndrome (PCS) which includes fatigue (Belanger et al., 2005; Iverson, 2005). On the other hand, factors such as injury severity and mood (depression) have not been found to be significantly associated with post TBI fatigue. As fatigue and low energy are among criteria for the diagnosis of depression (American Psychological Association, 1994; World Health Organisation, 1992b), the current study sought to clarify the relationship between depression and post-MTBI fatigue. The terms MTBI, mild head trauma and mild head injury are not synonymous as only MTBI implies brain injury; the others can refer to superficial injuries with no

brain damage. However, in the course of the literature review it was noted that the three terms are used interchangeably. As the context of the articles clearly indicated that authors were referring to MTBI rather than superficial injuries we have chosen to report these terms as they were used in articles cited.

A 2009 study (de Leon, Kirsch, Maio, Tan-Schriner, Millis, Fredriksen, et al., 2009) found fatigue severity 12 months after mild head injury (MHI) was associated with characteristics (fatigue, medical disability, marital status and litigation) present in the month preceding the injury but not with the MHI directly. However, while pre-morbid characteristics are relevant to recovery, our data collection was part of a larger study and there was no opportunity to investigate participants' pre-morbid characteristics in depth. We also sought to describe the temporal profile of post-MTBI fatigue with a view to guiding timing of an intervention and to study fatigue in a litigation-free population with mild TBI.

Psychosocial issues play a part in recovery from MTBI and the reaction of professionals, family members, friends and colleagues impacts on recovery progress (Ruff, 1996). The family's perception of post-MTBI fatigue in their injured relative is not well researched. Seeing the fatigued person as 'lazy' is likely to result in unsupportive interactions, exacerbate any pre-existing psychological conditions and generally undermine recovery. Our study aimed to provide data on the prevalence of post-MTBI fatigue being perceived as 'laziness' by family and friends of the person with post-MTBI fatigue.

Fatigue as experienced in the general population may be defined as a sense of tiredness or exhaustion following extended effort accompanied by reduced power and motivation to engage in effortful activity, independent of mood. This definition implies depleted energy resources which can be replenished by rest and sustenance. It is a relatively common problem within the general population and epidemiological studies report an incidence of between 10.5% and 41.2% incidence of prolonged fatigue i.e. greater than one month (Chan, 2001; Fox, Lees-Haley, Earnest, & Dolezal-Wood, 1995; Gouvier, Uddo-Crane, & Brown, 1988). An epidemiological study with a very large sample (N = 15283) found fatigue complained of by 18.3% of a general practice population (Pawlikowska et al., 1994).

Pathological fatigue, such as that associated with MTBI, occurs when the amount of effort required to induce the sense of tiredness or exhaustion, reduced power and motivation is considerably smaller than expected in a healthy individual. Energy resources are depleted more quickly and more extensively than normally expected and pathological fatigue is not as responsive to rest and sleep.

Comparative studies of post-concussion symptoms in both MTBI and healthy samples have shown fatigue is more prevalent within the MTBI population than in the healthy controls (Kashluba et al., 2004a; Stulemeijer et al., 2006; Yang, Tu, Hua, & Huang, 2007). Several studies of fatigue in the community (Cathebras, Robbins, Kirmayer, & Hayton, 1992; David et al., 1990; Fuhrer & Wessely, 1995a; Pawlikowska et al., 1994; Yang & Wu, 2005) drew their samples from primary care populations. The base rates of fatigue reported in these studies may be inflated by post-(M)TBI fatigue and other neurological-based fatigue conditions that were not screened out.

Severity of injury is another confounding factor in considering fatigue after TBI (e.g., (Olver et al., 1996; Ziino & Ponsford, 2005a). Reporting findings for a mixed TBI severity group is likely to mask the 'real' picture for both the mild and the more severe injuries where disability is very often permanent and profound. Since 80% of TBI are mild (New Zealand Guidelines Group, 2006), it is important to consider this group separately. Our study focused on a large sample including only participants with mild TBI. Additionally, severity ratings, rather than frequency, were found to distinguish 'normal subjects' from those who had an mild traumatic brain injury (Kay et al., 1992). The current study sought to examine both severity and frequency of post-MTBI fatigue and how each of these changed over time.

Regardless of whether fatigue is normal or pathological, psychological factors such as depression and anxiety have been closely linked with fatigue, e.g. in the formal diagnostic criteria for depression such as in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (American Psychological Association, 1994) and the International Classification of Diseases and Related Health Problems, 10th Edition (ICD-10) (World Health Organisation, 1992b). Depression has a potential role in producing, exacerbating and maintaining PCS-like symptoms. After comparing normal, currently depressed and MHI (12 months post-injury) groups, significant, large correlations were found between postconcussion symptoms (including fatigue) and both depression ($r = .68$) and anxiety ($r = .64$) (Trahan et al., 2001). While the MHI group scores more closely resembled the normal group scores, there were significant differences between the three groups for frequency and severity of fatigue and depression symptoms. Another study (Machulda et al., 1998) found a positive relationship, which strengthened over time, between perceived stress and intensity of

postconcussion symptoms. Treatment of depression in MTBI patients resulted in improvement of global and psychosocial functioning, postconcussive symptoms and neurobehavioural difficulties.

These studies used relatively small MTBI samples, whereas our study had a much larger MTBI sample within which to examine the relationship between post-MTBI fatigue, anxiety and depression. A significant relationship between depression and post-MTBI fatigue was expected for several reasons. Firstly, depression is a persistent symptom following MTBI (Zasler et al., 2005). Secondly, a current, oft quoted, neuroscience theory attributes post-TBI fatigue to injury in the Hypothalamic-Pituitary-Adrenal axis (Chaudhuri & Behan, 2000) and consequent interruption of the neurotransmitter (Serotonin, Dopamine, Norepinephrine, Acetylcholine) pathways associated with depression and euphoria (Zasler et al., 2005). Thirdly, the distress caused by ongoing excessive post-MTBI fatigue is likely to manifest as depression. For similar reasons, anxiety was also expected to have a significant relationship with post-MTBI fatigue prevalence and severity. This was particularly expected among the 'Miserable Minority', (Kay et al., 1992; Ruff, 2005; R. Wood, 2004) those MTBI patients who are high achievers; anxious when they under-perform and when they can not resume their pre-accident participation as quickly as they would like.

Recovery from MTBI can be complicated by a combination of symptoms such as a new mental health condition (e.g., depression) and pain (de Kruijk et al., 2002). Sleep dysfunction and pain have been linked to fatigue in an investigation of postconcussive symptoms in a chronic pain sample (Quality Standards Subcommittee of the American

Academy of Neurology, 1997), although Mooney (2005) and Rao et al. (2005) pointed out that fatigue and sleep dysfunction can also be mediated by psychiatric symptoms. While major sources of pain such as orthopaedic injuries were an exclusion criterion in our study, we examined the link between fatigue and single item measures of headache and sleep dysfunction as well a general pain perception as part of our symptom evaluation, in anticipation of an association between pain and fatigue in people with MTBI.

Another relevant issue in the context of MTBI is the role of litigation. New Zealand has a unique system where all accident related rehabilitation is covered by a 24-hour no-fault personal accident insurance, funded primarily by the New Zealand government. Hence the issue of litigation as a predictor of persistent symptoms such as post-MTBI fatigue (Binder, Rohling, & Larrabee, 1997; Paniak et al., 2002; Paniak et al., 2000) was minimised by conducting the current study in the New Zealand environment.

At the time our study was conducted the literature indicated that post-MTBI fatigue was significantly related to factors such as acute symptoms, mechanism of injury, time since injury and higher education levels. Less clarity existed around the relationship with factors such as injury severity, anxiety and depression and the temporal profile of post-MTBI fatigue. Also, litigation is frequently cited as a predictor of persistent postconcussion syndrome (PCS). We used a prospective longitudinal design, in a MTBI population, to address these factors in our study, which aimed to investigate the prevalence of post-MTBI fatigue and to track its temporal profile over the first six months post-injury.

Another important aspect of the present study was the examination of factors predicting persistent fatigue at an early stage post-injury. In a concussion clinic setting, a screen that predicted early on which individuals are at risk of developing pathological fatigue would be useful, as it would identify individuals in need of intervention as early as possible. The current study employed several measures of fatigue prevalence and/or severity. These varied from a single item through scales of four and nine items to allow comparison to test whether a single item, the most parsimonious solution, could effectively identify an early predictor of persistent post-MTBI fatigue.

The study also examined the association of psychological factors such as depression, anxiety, emotionality and mental health to post-MTBI fatigue. Previous studies noted the likely association between psychosocial issues, mood and persistent PCS (McClelland, Fenton, & Rutherford, 1994; Ryan & Warden, 2003); however, we sought to clarify the relationship with one PCS symptom, fatigue.

An understanding, well-informed social support network facilitates rehabilitation (Cavallo & Kay, 2005), while critical non-supportive beliefs among family and friends could potentially slow a person's recovery from post-MTBI fatigue and exacerbate psychological reactions such as depression, anxiety or personality disorders (Ruff, 1996). The opportunity was taken during the current study to explore the prevalence of post-MTBI fatigue sufferers being considered 'lazy' by their significant others. Such a perspective could impact both on the type of support received and the emotional health of the post-MTBI fatigue sufferer.

This investigation into post-MTBI fatigue was carried out in conjunction with a larger prospective, longitudinal study (Heitger et al., 2005) investigating outcome prediction after mild closed head injury.

Method

Participants

Participants were recruited from the body of patients presenting with mild closed head injury (Carroll, Cassidy, Holm, Kraus, & Coronado, 2004) to Christchurch Hospital (the main hospital for a population pool of >400 000 in the South Island of New Zealand). Patients had to have a Glasgow Coma Scale (GCS) score of between 13 and 15 on first assessment, without falling below 13 at any consecutive assessment at the hospital. Patients whose first GCS score was taken more than an hour post-injury but whose case history and injury mechanism was considered consistent with mild head trauma were eligible for the study if all subsequent GCS scores were above 13. Post-injury loss of consciousness (LOC) had to be less than 20 min and duration of post-traumatic amnesia (PTA) less than 24 hours. Duration of LOC was established based on available patient records or witness reports. Estimated PTA duration was established retrospectively at the time of study assessment following an iterative protocol applied in previous studies (Heitger, Jones, Dalrymple-Alford, et al., 2007; Heitger, Jones, Frampton, Ardagh, & Anderson, 2007). Potential participants were excluded if there was an abnormal CT scan, evidence of regular intake of psychoactive drugs or history of drug abuse, central neurological disorder or psychiatric condition, evidence of skull or facial fractures, or presence of multiple trauma or significant trauma to other parts of the body (e.g. broken limbs or ribs, spinal injuries, soft tissue injury requiring plastic surgery). All participants were made aware that their future health care, including

access to free public health care, would not be affected by their decision whether or not to take part in the study. Participants were offered compensation for travel costs to attend the study assessment but received no other payment. Several attempts were made to contact participants by phone and mail in order to improve the response return rate at follow-up. The project was approved by the Canterbury Ethics Committee/Upper South A Regional Ethics Committee, CTB/04/04/044, and this was endorsed by the Massey University Human Ethics Committee. Written consent was obtained from all participants.

Measures

The Fatigue Severity Scale (FSS) and a fatigue-related item from the Rivermead Postconcussion Symptoms Questionnaire were used to examine fatigue severity and prevalence respectively. As fatigue is consistent with low energy, the Vitality Scale of the Short Form 36 Health Survey Version 2 (SF-36v2) (Stewart & Ware, 1992; Ware, Kosinski, & Dewey, 2000) enabled comparison between fatigue and energy within the sample. All three measures have been used extensively in fatigue research.

Fatigue Severity Scale (FSS)(Krupp, La Rocca, Muir-Nash, & Steinberg, 1989). The FSS has 9 items which are rated on a seven-point Likert scale ranging from strongly disagree to strongly agree and the score is the average of the nine items. Krupp et al. (1989) developers of the FSS reported good internal consistency ($\alpha = 0.88$) and both test-retest reliability and sensitivity to change consistent with predictions (Krupp et al., 1989) . Kleinman et al.'s (2000) international study ($N = 1223$) reported good internal consistency ($\alpha = 0.94$ and test-retest reliability (intraclass correlation coefficient = 0.82) (Kleinman et al., 2000). FSS means in normal, healthy samples were 3.35 (1.11)

(Ziino & Ponsford, 2005a), 2.3 (0.7) (Krupp et al., 1989) and 2.53 (1.18) (Schwartz, Jandorf, & Krupp, 1993). Krupp (2003) stated a score ≥ 4 was indicative of severe fatigue (Krupp, 2003) . In our study the cutoff for post-MTBI fatigue caseness was set at 3.7, that is, one standard deviation above the mean for normal controls (Schwartz et al., 1993).

One item 'When I am tired my family, or partner, thinks I am being lazy' was added to the end of the FSS to assess significant others' attitude towards fatigue.

Rivermead Postconcussion Symptoms Questionnaire (RPSQ):.(King et al., 1995) On the RPSQ the participants rated the presence and problem-status of 16 possible postconcussional symptoms, including fatigue, on a scale from zero to four, comparing the presence and problem-status of each symptom with its premorbid status (0 = not experienced at all after the injury, 1 = experienced but no more of a problem compared to before the injury, 2 = a mild problem, 3 = a moderate problem, and 4 = a severe problem). For the initial assessment at approximately 1 week post-injury, the assessment period for answers on the RPSQ was extended from 'the previous 24h' to 'the time post-injury'. For the follow-up assessments at 3 and 6 months post-injury, the assessment period was 'the previous 2 weeks' in keeping with the time frame for the fatigue assessment. Fatigue prevalence was the frequency with which RPSQ-Item 6 was rated ≥ 2.

Vitality scale of the Short Form 36 Health Survey - Version 2: (SF-36v2) (Ware et al., 2000). The SF-36v2 is a multi-purpose, short-form, 36 item, health survey with 8 subscales, Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality,

Social Function, Role Emotional and Mental Health, (Ware et al., 2000). The Vitality subscale is a measure of both fatigue and energy with good internal consistency (alpha >0.70) and test-retest reliability across a wide range of illness conditions (McHorney, Ware, Lu, & Sherbourne, 1994; McHorney, Ware, & Razcek, 1993; Wang, Chan, & Deng, 2006). A high score on the vitality subscale indicates low fatigue. The correlation between the vitality scale and the FSS was r = -0.76) (Kleinman et al., 2000). Vitality subscale internal consistency for an MTBI group ranged from 0.83 to 0.91 across the SF-36v2 subscales (Findler, Cantour, Haddad, Gordon, & Ashman, 2001) indicating the Vitality subscale had good reliability within a MTBI sample. At the first assessment participants were asked to refer only to the time period since injury when answering the questionnaire items. At follow-up participants were asked to use the standard, preceding 4-week time period, when responding to the measure. The key measure for each scale was the 'Transformed Scale Score' with a best score of 100.

Psychological factors were measured using the Hospital Anxiety and Depression Scale (Snaith, 2003) which has been extensively used in health research.

Hospital Anxiety and Depression Scale (HADS) (Snaith, 2003) The HADS is a 14 item measure of generalised anxiety and depression. Items are rated 0-3. There are two scales: anxiety and depression. Both clinically and in research, it is a widely used instrument found to be reliable and valid (Herrmann, 1997). Cronbach alphas ranged from .68 to .93 (mean = 0.83) for anxiety and from .67 to .90 (mean = .82) for depression. An updated literature review (Bjelland, Dahl, Haug, & Neckelmann, 2002) reported the HADS cut-off score of ≥ 8, gave a sensitivity range of 0.90 to 0.66 and a specificity range of 0.78 to 0.83 across medical samples. A study of a small MTBI

sample (Whelan-Goodinson, Ponsford, & Schonberger, 2009) found, with a cutoff score of ≥ 8, the HADS-Anxiety scale had 0.75 sensitivity and 0.69 specificity and the HADS-Depression scale had 62% sensitivity and 92% specificity. The current study found the HADS to be a reliable measure of emotional distress but cautioned against using it as the sole diagnostic tool for depression or anxiety. Internal consistency of the English version is acceptable as is two week retest reliability ($r>0.8$). Over time the test re-test reliability reduces suggesting HADS is a suitable measure of change. The two factors, anxiety and depression, explain 50% of the variance, remain stable across subgroups and correlate highly with the corresponding subscales ($r>0.9$) (Herrmann, 1997). One major advantage of the HADS is that it excludes somatic symptoms such as insomnia, anergia and fatigue (Martin, 2005) making it a suitable instrument to use while exploring fatigue in an MTBI population.

Procedure

Consenting participants recruited from the Emergency Department of Christchurch Hospital between July 2006 and August 2008 were assessed as soon as possible but not later than 10 days post-injury. Participants completed a set of questionnaires including the SF-36v2, RPSQ, HADS and the FSS. Questionnaires were mailed out with freepost return envelopes for follow-up at 3 and 6 months post-injury. Participants who did not return their questionnaires within 3 weeks of mailing the follow-up letter were reminded via email and/or phone as required. Participants who failed to return their follow-up questionnaires after 2 reminder contacts were not further contacted.

Statistical Analyses

The Statistical Package for the Social Sciences (SPSS) was used for statistical analysis. Only participants for whom there was fatigue follow-up data at each time period and who had not reported confounding temporary illness during the project (n = 159) were retained for the primary analyses.

Results were considered significant at $p < 0.05$. Prevalence of fatigue was based on RPSQ Item 6 and severity on the Fatigue Severity Scale (FSS). Pearson correlation coefficients were calculated to examine the relationship between the primary dependent variables, fatigue prevalence and severity, energy, depression and anxiety for each time period and across time periods. A one way analysis of variance was carried out to explore how fatigue prevalence, severity and energy changed over time. An hierarchical regression analysis was carried out to examine the relationship between the dependent variable six month fatigue severity and independent variables three month fatigue severity, depression and anxiety. The Receiver Operating Characteristic (ROC) curve (Kinnear & Gray, 2008) was used to calculate sensitivity and specificity of the RPSQ fatigue item in discriminating individuals who exhibited pathological fatigue (FSS) at six months from those who did not.

Results

Of the 263 recruited participants, full fatigue-related follow-up data was available for 180 but 21 of these had to be withdrawn because they had had another accident or illness which would have distorted the fatigue analysis. Comparison between the group with fatigue data at all three data points (N = 180) and the remainder of the initial sample (N = 83) showed a small ($\cong$ 0.02) significant group effect for GCS score at 1

hour post injury, time since injury and anxiety, vitality and prevalence of sleep difficulties at 1 week. Of the 159 participants on whom most of the analysis was based, 57 were female and 102 male, aged between 16 and 70, mean 35.92 SD 15.63 years. Almost 37.1% were ≤ 25 years old and 41.5% were ≥ 40 years, the age after which MTBI recovery takes longer (McCrea, 2008). First GCS scores were available for 158 participants, mean 14.8 SD 0.49. Of the 86 for whom PTA information was available, 80% had PTA ≤ 60 minutes. Mean years of education was 14.64 SD 2.8. Sixty-five participants reported LOC with a mean duration of 2.82 minutes and standard deviation of 3.98 minutes. Almost 35% had sustained a previous TBI.

While only 159 of the 263 recruited participants had full follow-up fatigue data, it was available for 228 (86.7%) at three months and 202 (76.8%) at six months. The majority of participants reported post-MTBI fatigue in the immediate weeks after their injury and this number reduced to just over a quarter of the population at six months. Approximately 50% reported fatigue one standard deviation above the norm (Krupp, 2003) in the early period (one week) and over 30% still reported this severity of fatigue at three and six months post injury (Table 4.1).

Table 4.1

Prevalence and Severity of Post-MTBI Fatigue at 1 Week, 3 and 6 Months for All Participants

	Prevalence [a] (*N*)	Severity[b] (*N*)
1 week	68.1% (263)	54.9% (255)
3 months	31.4% (226)	37.6% (218)
6 months	28.2% (202)	34.4% (195)

[a]Rivermead Postconcussion Symptom Questionnaire Item 6 ≥ 2 ; [b]Fatigue Severity Scale ≥ 3.7

It has been argued (McCrea, 2008) that findings of problems with fatigue can be distorted due to a greater likelihood that those with pathological fatigue would remain participants of the project. To address this argument, the fatigue percentages for those for whom data was available at each measurement point (N = 180) less those reporting a health condition are reported in Table 4.2, (N = 159).

Table 4.2

Prevalence and Severity of Post-MTBI Fatigue at Each Interval for Population with Data Available at All Three Intervals

N = 159	Prevalence [a]	Severity[b]
1 week	67.3%	54.1%
3 months	29.6%	35.8.4%
6 months	26.4%	34.0%

[a]Rivermead Postconcussion Symptom Questionnaire Item 6 ≥ 2 ; [b]Fatigue Severity Scale ≥ 3.7

There were moderate to high correlations ($p < 0.001$) between FSS (severity), RPSQ Item 6 (prevalence), and the Vitality subscale (energy) at most time periods (Table 4.3). These findings suggest convergent validity between the two fatigue measures but the relationship with the vitality measure is less clear. At one week, the relationship between vitality and the fatigue measures was not significant, however, at three and six months there were moderate to high correlations with the other fatigue measures ($p < 0.001$). Moderate to high correlations were found between depression and post-MTBI fatigue severity, and most of the correlations between anxiety and fatigue severity were moderate. Table 4.3 also shows that depression and anxiety were strongly correlated within each stage (one week, three and six months), but across stages, correlations for these two factors were in the moderate range.

Table 4.3

Comparison of the Single Item Measure of Fatigue (RPSQ item 6), the Nine Item FSS, the Four Item SF36v2 Vitality Subscale, Depression and Anxiety Over Time and Within the Measures (N = 159)

	FSS1	FSS3	FSS6	RPSQ1	RPSQ3	RPSQ6	Vit1	Vit3	Vit6	Dep1	Dep3	Dep6	Anx1	Anx3	Anx6
FSS1	1														
FSS3	0.53**	1													
FSS6	0.49**	0.76**	1												
RPSQ1	0.57**	0.16*	0.20*	1											
RPSQ3	0.30**	0.45**	0.40**	0.24**	1										
RPSQ6	0.38**	0.50**	0.62**	0.34**	0.60**	1									
Vit1	ns	ns	ns	ns	ns	ns	1								
Vit3	0.42**	0.66**	0.56**	-0.20*	-0.57**	-0.52**	ns	1							
Vit6	0.40**	0.39**	0.59**	-0.20*	-0.51**	-0.70**	ns	0.69**	1						
Dep1	0.52**	0.34**	0.34**	0.52**	0.31**	0.37**	ns	-0.35**	-0.36**	1					
Dep3	0.30**	0.44**	0.50**	ns	0.45**	0.44**	ns	-0.54**	-0.57**	0.37**	1				
Dep6	0.32**	0.54**	0.65**	ns	0.44**	0.65**	ns	-0.49**	-0.75**	0.46**	0.61**	1			
Anx1	0.37**	0.40**	0.28**	0.34**	0.29**	0.28**	ns	-0.35**	-0.28**	0.67**	0.31**	0.40**	1		
Anx3	0.26**	0.32**	0.32**	0.16*	0.39**	0.40**	-.18*	-0.38**	-0.36**	0.29**	0.63**	0.38**	0.31**	1	
Anx6	0.26**	0.48**	0.51**	ns	0.38**	0.51**	ns	-0.43**	-0.62**	0.35**	0.45**	0.75**	0.44**	0.45**	1

FSS = Fatigue Severity Scale; RPSQ = Item 6 of Rivermead Postconcussion Symptoms Questionnaire; Vit = SF36v2 Vitality subscale where high values are equivalent to low fatigue; Dep = HADS Depression ; Anx = HADS Anxiety. * $p \leq 0.05$ ** $p \leq 0.001$

Given the strong relationship between depression and anxiety at each interval a hierarchical regression analysis was carried out and both depression and anxiety were independently found to make significant unique contributions to fatigue. However, when depression (which had a stronger correlation with fatigue) was held constant, anxiety did not make a significant unique contribution to fatigue. Depression regression coefficients ranged from $\beta = 0.34$ to 0.66 for fatigue at each interval and from $\beta = -0.49$ to -0-66 for vitality at three and six months ($p < .001$). There were no significant regression coefficients for anxiety (all p's > 0.05).

Pain and sleep dysfunction

A combination of pain, anxiety, depression and sleep difficulties predicts post-MTBI fatigue severity accounting for 37.7%, 28.4% and 47.6% of the variance at each data point respectively. However, when fatigue prevalence and depression are held constant stepwise then the other symptoms (pain, sleep difficulties and anxiety) added very little to the variance (< 1% to 3%) across the data points.

Fatigue over time

Table 4.4 shows the means and standard deviations for fatigue prevalence and severity and for energy (vitality). Each of the measures shows a larger reduction between one week and three months than between three months and six months.

To determine whether these changes were significant over time, each of the dependent variables, prevalence (RPSQ), severity (FSS) and energy (SF-36v2 Vitality) was analysed using a one way repeated measures ANOVA. There was a large effect of

Table 4.4

Descriptive Statistics for Fatigue and Energy for 1 Week, 3 Months and 6 Months Post Injury

Time period	RPSQ	FSS	SF36v2 Vitality
N =159	*M(SD)*	*M(SD)*	*M(SD)*
1 week	2.09(1.24)	3.99(1.53)	46.57(24.72)
3 months	1.03(1.05)	3.29(1.44)	60.21(19.68)
6 months	0.96(1.05)	3.20(1.39)	62.11(20.18)

RPSQ = Item 6 of Rivermead Postconcussion Symptoms Questionnaire
FSS = Fatigue Severity Scale

time, over the six months post injury, for all three measures (Table 4.5). Post hoc analysis (paired-samples t-test) indicated that while significant change occurred for all three measures over the first three months, there was no further significant change over the second three months suggesting a recovery plateau and/or fatigue and low energy becoming persistent postconcussion symptoms.

The relationship between duration of loss of consciousness (LOC) and FSS at 3 months was significant ($r = 0.3$, $p < 0.05$). The Glasgow Coma Scale score, length of PTA, gender, years of education, occupation, and alcohol at time of accident were not significantly correlated with FSS.

In the sample for whom full data was available (n=159), early fatigue severity (FSS at 1 week) predicted later fatigue severity at three ($r = .53$, $p < 0.001$) and six months($r = 0.49$, $p < 0.001$) and accounted for 28% and 24% of the variance respectively. Fatigue severity at three months accounted for 56.7% of the variance, and was a stronger

Table 4.5

ANOVA Summary of the Within-Subjects Effects for Fatigue Prevalence and Severity, and Energy Over the First 6 Months Post MTBI

N =159	*df*	*F*	*partial* η^2
Fatigue Prevalence (RPSQ)	2,157	60.556**	0.44
Fatigue Severity (FSS)	2,157	23.60**	0.23
Energy (SF36v2-Vitality)	2,157	17.573**	0.18

**p <0.001 RPSQ = Item 6 of Rivermead Postconcussion Symptoms Questionnaire;
FSS = Fatigue Severity Scale; SF36v2 = Short Form 36 Health Survey - Version 2

predictor of fatigue at six months ($r = 0.76$, $p < 0.001$) than fatigue at one week. Indeed, in the whole sample (n =263) fatigue severity at 1 week ($r = .40$, $p < 0.001$) and 3 months ($r = .53$, $p < 0.001$) predicted persistent PCS (RPSQ total) at 6 months.

As neuropsychological function is frequently found to be restored in the early weeks post MTBI (McCrea, 2008) many attribute persistent postconcussion symptoms to psychological factors rather than to the effects of the injury itself (Sigurdardottir, Andelic, Roe, Jerstad, & Schanke, 2009). We found moderate to strong relationships between measures of fatigue and psychological factors such as depression and anxiety (Table 4.3) which seemed to support the argument for psychological factors being a strong predictor of ongoing post-MTBI fatigue. Multiple regression analysis showed fatigue severity, depression and anxiety at three months together accounted for 59.6% (adjusted R square) of the variance in fatigue severity at six months. The beta values in Table 4.6 demonstrate that, of the three independent variables included, fatigue severity at three months is the strongest significant predictor of fatigue severity at six

months, and depression at three months is also a significant predictor but anxiety at three months is not.

The RPSQ fatigue item served as a quick screen to identify the presence of post-MTBI fatigue and accounted for approximately 32.6%, 20.1% & 37.4% of the variance in fatigue severity at each interval respectively (N = 159, $p < 0.001$). Hierarchical regression analysis showed that when fatigue severity was held constant for any particular time period then the RPSQ fatigue item at that time period added little to the variance of fatigue severity in the next time period. For instance fatigue severity at one week (FSS1) accounted for 28% of the variance of fatigue severity at three months (FSS3) and fatigue prevalence at one week (RPSQ1) added just 3.1% to the variance of fatigue severity at three months (Table 4.6). The sensitivity and specificity of Item 6 within the first ten days after injury to correctly identify pathological fatigue at six months (FSS6) was 0.74 and 0.63 respectively. Both type one and two errors became increasingly more likely when Item 6 was used to predict persistent fatigue severity at three or six months post injury (Table 4.7).

A potentially unsupportive interpretation of fatigue-related behaviours as ‘laziness’ by family members was reported by up to 30% of all participants at each interval. The correlation between post-MTBI fatigue severity and being thought lazy increased from time 1 ($r = 0.21$, $p < 0.01$) to time 2 ($r = 0.51$, $p < 0.001$) then remained stable over the next three months suggesting a less supportive environment for rehabilitation.

Table 4.6

Summary of Hierarchical Regression Analysis with Fatigue Severity, Depression and Anxiety, at 3 Months, as Predictors of Fatigue Severity at 6 Months Post MTBI (*N* = 159)

Variable	*B*	*SE B*	*β*	Semi-partial correlation	Sig.
Constant	0.92	0.18			0.001
FSS3	0.64	0.05	0.69	0.69	0.001
Depression3	0.12	0.04	0.25	0.25	0.001
Anxiety3	-0.01	0.03	-0.04	-0.04	0.610

FSS = Fatigue Severity Scale

Table 4.7

Sensitivity and Specificity of RPSQ Item 6 (Fatigue) ≥ 1.5 in Discriminating Pathological Fatigue at 6 Months (FSS6 ≥ 3.7). (*N* = 192)

	Sensitivity	1 - Specificity
RPSQ 1 week	0.74	0.63
RPSQ 3 months	0.42	0.24
RPSQ 6 months	0.55	0.12

RPSQ = Item 6 of Rivermead Postconcussion Symptoms Questionnaire

Discussion

The current study examined fatigue in the first six months after MTBI using a prospective longitudinal design whilst excluding known confounding factors such as litigation, presence of psychological or neurological disorders, and substance abuse. Importantly the study focused on a participant sample including only MTBI thus providing specific evidence on the role of fatigue after mild head trauma not easily identifiable in previous studies that used mixed severity samples.

Our results show that over half of the participants reported pathological fatigue, immediately after injury and that a third to a quarter of the sample continued to report pathological fatigue three and six months later, respectively. For those reporting fatigue problems at three months, there was a strong likelihood they would report fatigue at six months post-MTBI. Clinically this is an important finding of our study as post-MTBI fatigue appears to move into the realm of persistent postconcussion symptoms at about three months post MTBI. The implication of this finding is that a sizeable proportion of the MTBI population are likely to be in need of an intervention to reduce fatigue, build energy levels and return to a pre-injury participation level.

Epidemiological studies of persistent fatigue in the general population reported rates of between 10.5% and 41.2% (Chan, 2001; Fox et al., 1995; Gouvier et al., 1988). Hence our finding of 31.4% fatigue prevalence and 37.6% mild to severe post-MTBI fatigue at three months suggests that fatigue is more common after MTBI than base rates within the general population.

The prevalence and severity of post-MTBI fatigue in our study was consistent with previous evidence e.g., (Rao et al., 2005) showing that 29%–59% of patients experience problems with fatigue at three months post injury. Importantly, there were no differences for these measures between our entire study sample and the sub-group of participants for whom data was available at all time points. There was a small significant group effect for time since injury, GCS at one hour, anxiety, vitality and prevalence of sleep difficulties at 1 week between those who were included in the

study and those who were not because of incomplete data. Given that those whose data was incomplete or not present had higher scores on all these measures there is a likelihood that the findings under-estimate the prevalence and severity of post-MTBI fatigue in the long-term.

There was no significant change in the percentage of individuals with MTBI reporting fatigue prevalence (RPSQ) or severity (FSS) between three and six months. However, there was a significant increase in the percentage of those reporting depression and/or anxiety above the cutoff for mild problems at six months compared with reports at three months. This increase coincides with a levelling-off of the fatigue percentages within the sample population. A strengthening positive relationship has been found between perceived stress and intensity of postconcussion symptoms over time (Machulda et al., 1998). Our study examined this relationship in more detail, with respect to fatigue, anxiety and depression and found a pattern which suggests persistent symptoms are associated with increased distress as illustrated by enduring elevated fatigue, anxiety and depression scores. Also, contrary to Ziino and Ponsford (Ziino & Ponsford, 2005a) we found depression (but not anxiety) *was* a significant predictor of post-MTBI fatigue. We also found that when depression was held constant other factors such as pain and poor sleep did not contribute significantly to post-MTBI fatigue. The clinical implications of these findings are that both fatigue and psychological factors require treatment early to prevent symptoms worsening. However, whether the increased psychological symptoms are related to fatigue, to neurological sequelae (neurotransmitter disruption within the HPA pathway) or to pre-

morbid psychological conditions remains unclear and could not be determined from the current study.

The search for a parsimonious 'one-item-screen' to predict persistent post-MTBI fatigue is unlikely to be satisfied by using RPSQ Item 6. Within the sample for which there was data at each time point, the initial RPSQ response accounts for about 12 percent of fatigue prevalence and four percent of fatigue severity at six months.

We hypothesised that as fatigue symptoms persisted significant others would become less sympathetic towards the person with post-MTBI fatigue. Our findings that 28% of participants with MTBI faced this type of attitude gives impetus to including family in interventions promoting recovery from post-MTBI fatigue.

There are several limitations of the current study. The HADS is widely used in research, but despite this, it is not a diagnostic tool for anxiety and depression. It indicates the possibility of depression and anxiety but a follow-up psychiatric or psychological assessment is required to determine whether there is a clinical level of anxiety or depression difficulties (Schönberger & Ponsford, 2010). The HADS was originally developed to look for symptoms in non-psychiatric inpatients and while Bjelland et al. (2002) reviewed 747 studies involving the HADS there is minimal research on its validity and reliability following MTBI. A general problem with assessing depression and anxiety in patients who have a brain injury, acquired or traumatic, is the crossover of symptoms between psychological conditions and the sequelae of MTBI. This is particularly true of HADS items such as Item 8 "I feel as if I

am slowed down" which can refer to the slowed information processing of brain injury or to depression-related low motivation and lassitude. Hence the HADS scales must be interpreted with caution (Bailey, Barth, & Bender, 2009; Schönberger & Ponsford, 2010).

Another limitation was that there was no systematic attempt to measure pre-injury fatigue status. However, many clinicians and researchers are of the belief that the individual's perception of their pre-injury status is not reliable. It is likely to be coloured by their post-injury status and other issues such as personal resilience and secondary gain factors such as financial or emotional support (Davis, 2002).

Another limitation of the current study is the lack of available information about treatments provided to the participants after their head injury. This confounds the findings related to the effect of time on fatigue as treatment effects are likely to be influencing the findings.

The primary purpose of the larger 'mother-study', under which the present investigation into post-MTBI fatigue was conducted, was the examination of eye movement control and the relationship of oculomotor control with health recovery after MTBI. As a result, no explicit record was kept of participants' medications, other than those referred to in the exclusions (e.g., psychoactive medication). Medications which might have caused fatigue could potentially inflate the numbers reporting fatigue during their recovery period and this potential inflation constitutes another limitation.

In conclusion, the current study examined post-MTBI fatigue in a non-litigious population and found that not only does it persist for at least six months post-injury, but also that it does not improve significantly after about three months. As the fatigue becomes more persistent, psychological factors such as anxiety and depression tend to worsen. These findings are useful in guiding interventions for post-MTBI fatigue and have helped to inform the design of a post-MTBI fatigue treatment programme developed by the lead author.

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Chapter 5

TREATMENT FOR POST-MTBI FATIGUE

Some studies of the effectiveness of treatment for postconcussion symptoms list the effect for each symptom including post-MTBI fatigue (Bell et al., 2008; Kashluba et al., 2004b; Mittenberg et al., 1996). However, there has only been one treatment study, specifically targeting post-(M)TBI fatigue, published to date (May 2010). This was a randomised placebo controlled study of the effectiveness of Modafinil for treating fatigue in a mixed TBI-severity (25.5% MTBI) sample (Jha et al., 2008). No clinically significant difference was found between the treatment and the placebo.

Since the literature on post-MTBI fatigue is so very sparse a review of treatment for fatigue in other illnesses which have similarities to traumatic brain injury sequelae was conducted.

Treatment of Fatigue in Other Illnesses

There is an extensive literature on treatment of fatigue in other illness states, e.g., Chronic Fatigue Syndrome (CFS), Multiple Sclerosis (MS), cancer. A review of this literature suggests that aerobic exercise and cognitive behaviour therapy (CBT) combined hold out the best hope of reducing subjective fatigue and increasing subjective feelings of energy in the post-MTBI population (see Table 5.1). Because fatigue is multidimensional, treatment must be tailored to the needs of the individual and the aetiology of their presenting condition (Lange, Cook & Natelson, 2005).

Table 5.1

Treatment Approaches for Fatigue Across a Range of Illness Conditions

First Author	Details
Reviews	
Krupp (2003)	Recommendations for treatment – psychoeducation, nutrition, energy conservation, exercise, CBT, pharmacology *N* = 74
Kujala (2004, 2006)	RCT, benefits of exercise therapy for chronic diseases, improvement in conditioning; beneficial effects on all metabolic syndrome components, recommended individualised programmes tailored to patient and disease type; long term adherence is a problem and face to face or telephone contact is recommended to improve compliance. Studies *N* = 171, Participants *N* ≥ 14,034 (not all studies listed specified *N)*
Lange et al. (2005)	Treatment needs to be tailored to each individual; combination of behavioural, pharmacological, and physical interventions, CBT better for tertiary settings, for patients with low self-efficacy to begin exercise programme, pharmacological for severe illness cases to enable mobilisation, or when fatigue is resistant to CBT or exercise. Exercise training resulted in decreased self-reported fatigue and improved QOL. *N* = 47
Rao et al., (2005)	Review fatigue and sleep problems following TBI; pharmacological – few TBI studies, fatigue improved in postpolio patients, MS patients; CBT effective for CFS
Fellus et al. (2007)	Review post-TBI fatigue. Recommended interdisciplinary team, home exercise programme to optimize cardiovascular health and physical well being as well as enhancing emotional and immune system functions. Education about brain injury and fatigue, energy conservation strategies, diet – weight management and energy efficiency, sleep hygiene therapy, psychotherapy to minimise stress, anxiety and depressive states, pharmacological therapy including pain treatment, antidepressants (including dopaminergic action to address abulic features) and elimination of fatigue causing agents where possible, stimulants (no well designed studies to support), ginkgo biloba and ginseng shown to be effective fatigue treatments and citicholine has been used in Europe and Asia for stroke and TBI treatment, improvement in attention and vigilance.

(continued)

First Author	Details
Friedberg et al. (1998)	5 of 6 CFS treatment studies showed improvement in fatigue after CBT plus graded activity, coping skills or graded aerobic exercise. Envelope theory – individually tailored balance between rest and activity with the goal of building up tolerance for activity. Monitoring levels of subjective expended energy, perceived energy and subjective fatigue over time useful approach to management of CFS. Matching perceived and expended energy reduced subjective fatigue. 8 session coping skills treatment programme for CFS groups.
Stulemeijer et al., (2005)	RCT, CBT for adolescents aged 10-17 years with CFS, 10 sessions over five months. Significant decrease in reported fatigue severity post treatment. *N* = 71
van Kessel (2007, 2008)	RCT MS-related fatigue, CBT significantly more effective than relaxation training. *N* = 72
Aerobic Exercise	
Shapiro et al., (1975)	Graded exercise improved slow-wave sleep (SWS), reduced rapid-eye-movement sleep and, at higher exercise levels, reduced stage 2 sleep supporting the hypothesis that SWS is involved in the recovery process from fatigue. *N* = 2
Dustman et al. (1990)	Two studies: Older adults and, cross-sectional study young sedentary adults and older adults; four months aerobic exercise exhibited improvement in response time, visual sensitivity, and performance on a battery of cognitive tests. *N* = 60
Fulcher et al. (1997)	RCT crossover design, CFS, 12 weeks graded or flexibility exercises and relaxation therapy showed improvement in fatigue, functional capacity and fitness. 3 month and 1 year follow-up improvements maintained. No effect for mood or sleep or mental fatigue. *N* = 59
Mostert et al. (2002)	RCT, MS-related fatigue, 4 weeks 5 x 30 minutes aerobic exercise training, SF36-Vitality significantly increased but only trend towards reduced fatigue severity. Treatment *N* = 37, Control *N* = 26
Schulz et al., (2004)	RCT, impact of aerobic training on immune-endochrine parameters, neurotrophic factors, QOL and coordination in MS. 8 week, 2 X 30 mins. cycle. No significant training effects for endochrine and immune parameters or neurotrophins. Improvements in QOL, physical fitness and coordinative function. *N* = 67

(continued)

First Author	Details
Puetz et al., (2006)	Meta-analysis, chronic aerobic exercise or exercise training, no health issue 16 studies, health problems 54 studies, total *N* = 2216. 94% of all studies had effect size > 0. Mean effect size = 0.37. Improvement on measures of feelings energy and fatigue, clinically relevant. Moderators included additional therapy e.g., health education, mode of exercise aerobic, strength or flexibility training. Other possible moderators included age, baseline anxiety and/or depression. Strength training associated with reduced depression.
Motl et al. (2008)	Meta-analysis, 13 studies, *N* = 484. MS. Significant effects of aerobic exercise training for fatigue (0.19) as a measure of QOL, duration of exercise training intervention related to effect size - larger for < 3 months (0.34) , smaller for ≥ 3 months (0.16). Training for >90 min./week (0.44) larger effect size than ≤90 min. (0.12).
Meeusen (2005)	Brief review; animal and human studies; exercise influences the central dopaminergic, noradrenergic and serotonergic systems, reduces depressive symptoms. Voluntary exercise in rats increases cell proliferation and recruitment of new neurons in several brain areas which parallel improvement in learning and memory and enhances Long Term Potentiation and spatial learning. *N* = Not available
Pharmacology	
Friedberg et al. (1998)	Review CFS treatment: Moclobemide resulted in small significant reduction in fatigue. Selective serotonin reuptake inhibitors and blood pressure medications not usually effective in treating fatigue in CFS.
Tenovuo (2005)	Review; Donezipil, Galantamine, Rivastigmine; 63% responded to one or more of the drugs, vigilance, concentration, initiation and general functioning improved but tiredness for 11% of the whole sample. MTBI amantadine, venlfaxine and paroxetine had been ineffective but rivastigmine resulted in diminished fatigue and subsequent return to work. *N* = 111.
Choi-Kwon et al., (2007)	Double-blind placebo controlled trial of 20mg Fluoxetine daily was ineffective in reducing fatigue in post-stroke patients but both depression and emotional incontinence were improved in Fluoxetine group. Hypothesized that post-stroke fatigue was not related to serotonergic dysfunction. *N* = 83
Jha et al., (2006, 2008)	Mixed severity TBI group (25.5% MTBI), No improvement in fatigue found for Modafinil. *N* = 51

(continued)

First Author	Details
Milman, et al., (2008)	Animal MTBI, Dehydroepiandrosterone sulphate, neuroactive neurosteroid, regular weekly dose to injured animals associated with improvement in long-term cognitive and behavioural effects induced by MTBI. *N* = Not available.
Other	
Tsai (2008)	E-therapy: Controlled quasi-experimental design, 18 week e-therapy (web-based) for fatigue management programme for older adults with congestive heart failure. Lowered Global Fatigue score, increased knowledge of fatigue management, and diminished impact of fatigue on daily activities. *N* = 29

CBT = Cognitive Behavioural Therapy; RCT = Random Controlled Trial; QOL = Quality of Life; CFS = Chronic Fatigue Syndrome; MS = Multiple Sclerosis; MTBI = Mild Traumatic Brain Injury

Their review of fatigue treatment approaches included CBT, pharmacology, and exercise training. Diet (dairy, red meat, whey, protein and eggs) and dietary supplements (creatine) are effective in reducing mental fatigue and improving cognitive performance (Fellus & Elovic, 2007; Sakellaris et al., 2008; Watanabe, Kato, & Kato, 2002; Yamamoto, 2007).

Two New Zealand studies found CBT to be an effective treatment for fatigue in individuals with either CFS or MS. The techniques they used were cognitive restructuring of symptom perceptions and anxiety (catastrophising), as well as, teaching coping strategies (Moss-Morris, Sharon, Tobin, & Baldi, 2005; van Kessel, 2007).

Psychoeducation

The most effective psychological (CBT) intervention for preventing the development of persistent postconcussion symptoms to date is psychoeducation and reassurance about sequelae and recovery period following MTBI (Mittenberg et al., 1996). They measured a range of PCS symptoms including fatigue. The percentage of those reporting fatigue was reduced from 82%, pre-treatment to 47% at six months. However, this result means that almost half the sample was still having fatigue problems suggesting that psychoeducation alone was insufficient. Additionally, there was no indication of the severity of post-MTBI fatigue reported by the participants in the study.

Exercise as Therapy for Fatigue

Animal concussion studies support a period of rest during the immediate post-acute stage (Griesbach, Gomez-Pinilla, & Hovda, 2007) and avoidance of intensive rehabilitation input at that stage. However, extended use of rest as therapy is not recommended as it leads to deconditioning and increased feelings of tiredness or fatigue (Puetz, O'Connor, & Dishman, 2006). Physical inactivity exacerbates fatigue by creating a vicious cycle of cardiovascular and musculoskeletal deconditioning that has a negative impact on quality of life.

Aerobic exercise therapy, on the other hand, consistently results in subjective reports of increased energy, decreased fatigue and other symptom improvements (Lange et al., 2005a). A metanalysis of the use of exercise to treat fatigue in a broad range of conditions, including cancer, chronic fatigue, fibromyalgia, unexplained illness with fatigue, anxiety or depression, found increased feelings of energy and reduced feelings of fatigue and was best in combination with additional psychological therapy (Puetz et al., 2006). As shown by the studies reviewed in Table 4.1, aerobic exercise was found to be an effective fatigue treatment in illnesses such as MS and some types or stages of CFS (Clark & White, 2005; Moss-Morris et al., 2005; Powell, Bentall, Nye, & Edwards, 2004). MS sufferers reported discovering for themselves the need to remain active in order to reduce their experience of fatigue (Stuifbergen & Rogers, 1997). Graded exercise training effectively alleviates the fatigue found in numerous conditions, some of which are associated with damage to the mitochondrial sheath, e.g. MS. Thus aerobic exercise training seems relevant to treatment of post-MTBI fatigue as MTBI also involves damage to the mitochondria via diffuse axonal injury. A controlled exercise programme (Kozlowski, 2008; Kozlowski, Willer, Leddy,

Chevalier, & Scarsaletta, 2006; Willer & Leddy, 2006) was found to be effective in promoting return to play for elite athletes with persistent PCS. While examining the effect of physical activity (aquatic physical intervention) on post-TBI depression, Driver and Eade (2009) reported a significant improvement in the fatigue subscale of the Profile of Mood States (POMS).

Stimulation of the production of brain derived neurotrophin factor (BDNF) is one proposed mechanism by which exercise helps recovery from persistent PCS. BDNF has a role in the reorganisation and rejuvenation of injured circuits through neuroplasticity and neuroprotection (Berchtold, Chinn, Chou, Kesslak, & Cotman, 2005; Griesbach, Hovda, & Gomez-Pinilla, 2006; Hennigan, O'Callaghan, & Kelly, 2007; R. Meeusen & Watson, 2007; R. Meeusen, Watson, Hasegawa, Roelands, & Piacentini, 2007; Rojas Vega et al., 2006; Vaynman & Gomez-Pinilla, 2005). Increased expression of BDNF as a response to exercise may be a central factor in exercise-derived benefits to brain function (Berchtold et al., 2005; Ferris, Williams, & Shen, 2007; Gold et al., 2003; Soya et al., 2007). It offers an explanation for the findings that aerobic exercise improves PCS and, potentially, reduces post-MTBI fatigue (Vaynman & Gomez-Pinilla, 2005). Exercise seems like a natural and non-invasive way to promote neuroplasticity (Vaynman & Gomez-Pinilla, 2005) and hence recovery from PCS and post-MTBI fatigue. Not all exercise based fatigue treatments have found significant training effects for endocrine and immune parameters or neurotrophins (K. Schulz et al., 2004). However, a literature review (Cotman, Berchtold, & Christie, 2007) reported positive BDNF outcomes following exercise and gave many examples of how exercise has been shown to be effective in promoting brain health. They asserted that growth factors, including BDNF,

"orchestrate most, if not all, of the brain responses to exercise through direct or indirect effects" (p 468).

Both the timing of the exercise-based intervention and exercise intensity are important considerations, as too intense or too early are potentially counterproductive in reducing fatigue (Ang & Gomez-Pinilla, 2007; Chaudhuri & Behan, 2004). Berchtold et al. (2005) investigated dose response in an animal study and discovered that aerobic exercise on alternate days was as effective as daily exercise in stimulating BDNF production as measured by hippocampal response. This finding is relevant to programme design particularly if human participants are unused to regular exercise or lack motivation to begin an exercise regimen. Graded aerobic exercise training over an extended period, e.g., 12 weeks, was associated with improved physical and cognitive functioning in CFS sufferers (Wallman, Morton, Goodman, Grove, & Guilgoyle, 2004).

Motivating a group of fatigued individuals to engage in exercise is likely to be challenging for the therapist. Ridsdale, Darbishire & Seed (2004) found graded exercise training (GET) was not superior to CBT in alleviating symptoms in a group presenting to primary care with a three month history of fatigue and that CBT was easier to "sell".

Other Targets for Fatigue Treatment

Sleep, depression, anxiety (catastrophising) and lack of exercise are all correlated with fatigue and could be considered as targets for treatment of fatigue (Wessely, 2005). Pain, particularly headache, is another common postconcussion symptom and as it is

likely to be associated with post-MTBI fatigue, it could also be targeted in conjunction with a post-MTBI fatigue treatment programme.

Summary

In summary, psychoeducation, CBT and aerobic exercise have all been found beneficial in treating postconcussion symptoms. However, only one study has specifically targeted post-(M)TBI fatigue. An intervention which will reduce post-MTBI fatigue and enable resumption of pre-injury activities will be a valuable addition to the MTBI rehabilitation tool box. The general fatigue treatment literature informed the design of a programme targeting post-MTBI fatigue. This programme is hypothesized to bring about reduction of fatigue and improved function in those who take part in the programme. The hypotheses about the effects of this programme are set out in the next chapter.

Chapter 6

DEVELOPMENT OF THE TREATMENT PROGRAMME FOR POST-MTBI FATIGUE

While data on prevalence of post-MTBI fatigue in a New Zealand population was being collected for Study One, preparations were being made for Study Two - planned to be an evaluation of the effectiveness of a treatment for post-MTBI fatigue. This involved putting together an intervention programme - the Postconcussion Energy Recovery Training (PERT) programme, the development of which will be reported in this chapter. The 12 week PERT programme combines two well established rehabilitation approaches – psychoeducation and aerobic exercise. The psychoeducation module provides information, explanation and reassurance all of which have been demonstrated as effective interventions for the prevention or reduction of PCS (Mittenberg et al., 1996; Paniak et al., 1998).

Rationale

The PERT programme contains two primary CBT treatment approaches, psychoeducation and aerobic exercise, both of which are well-established in the literature as therapies for a wide range of conditions including postconcussion symptoms, depression and anxiety (see Chapter 5). Neither approach, psychoeducation nor aerobic exercise, had been specifically tested for its effect on post-MTBI fatigue as the primary outcome; however, given their effectiveness in treating other related conditions (Moss-Morris et al., 2005; van Kessel et al., 2008) they were included in the PERT programme. The PERT programme was designed to treat post-MTBI fatigue by targeting factors which have been incorporated into the proposed model of post-MTBI fatigue (Figure 3.3). Aerobic exercise has been shown to be effective for addressing

postconcussion symptoms such as the neurophysiological changes (Kozlowski, 2008) as well as psychiatric symptoms such as depression and anxiety (Barbour, Edenfield, & Blumenthal, 2007) which spawn maladaptive psychological and behavioural responses (Beck, 2008).

The PERT programme has a one week baseline followed by 11 weeks of treatment and is delivered through a combination of personal and phone sessions. During the baseline session the therapeutic relationship is established, the programme is explained and the Mendoza et al. (2005) model of post-MTBI fatigue is discussed. Baseline fatigue, mood, anxiety and social reintegration measures are administered and the baseline diary for recording exercise, naps, fatigue and energy for the ensuing week is explained. Week two sees the beginning of the aerobic exercise module, and the method for determining the appropriate aerobic range for each individual client is explained. Sessions three to 12 cover the topics: barriers to exercise, planning and pacing, mood and irritability problems arising from post-MTBI fatigue, sleep hygiene, self-managing activity load and asking for help, feelings and bad dreams (posttraumatic stress symptoms) and reassurance through anecdotes from those who have experienced post-MTBI fatigue.

Throughout the programme the participants record their daily fatigue, energy, naps and exercise on the days when they are required to exercise (five of the seven). Choice of the content of the psychoeducation module was based on the principal researcher's experience in the Concussion Clinic and on manuals and books e.g., (Mittenberg et al., 1996; Roberts Stoler & Albers Hill, 1998) written to assist recovery and/or prevention of persistent postconcussion symptoms as well as those written for other rehabilitation

programmes e.g., Pain Disability Prevention (Sullivan & Stanish, 2003). The exercise component of the PERT programme consisted of engagement in aerobic range (age-based) exercise such as walking for 30 minutes per day, five days a week. Delivery of the PERT programme was guided by client and therapist manuals.

Psychoeducation

For over 35 years, the value of providing information, explanation and encouragement has been discussed within the MTBI literature and several studies have shown its effectiveness in reducing the reporting of postconcussion symptoms (Mittenberg et al., 1996; Paniak et al., 1998; Paniak et al., 2000). The rehabilitative purpose of psychoeducation combined with reassurance was succinctly stated in Mittenberg et al.'s (1996) paper on cognitive behavioural prevention of postconcussion syndrome. Patients in their study were given a manual and met with a therapist who discussed the symptoms and expected outcome with them. "The manual was intended to support the reattribution of symptoms to selective attention, normal transient responses to stress, and anxiety arousing or depressive self-statements." (pp. 141-142). Although Mittenberg et al. were targeting the postconcussion syndrome, they reported their results as individual symptoms and showed that psychoeducation reduced the incidence of reported post-MTBI fatigue from 82% to 47% six months after the psychoeducation treatment was applied.

Paniak et al.'s (1998) literature review, noted above, compared individuals who had no input with those who had been given education and reassurance and found that the latter had earlier return to work and fewer postconcussion symptoms which resolved more quickly. Reassurance as well as education was found to be more effective than

education alone (Alves et al., 1993) although as Paniak pointed out this study's value was reduced by a large attrition rate.

Psychoeducation following MTBI can serve four purposes according to Paniak et al. (1998, 2000) Firstly, the individual's post-MTBI experience can be legitimized as being 'real' rather than being brushed aside as trivial or their being told that there is nothing wrong. Secondly, psychoeducation can educate the individual about common post-MTBI symptoms. Thirdly, the post-MTBI individual can be taught strategies for coping with the common post-MTBI symptoms and advised about not using less helpful strategies such as extensive rest beyond the first week or so. Fourthly, they can be reassured of a good outcome and given an understanding of the expected length of the recovery period.

In the context of post-MTBI fatigue, the four purposes of providing a psychoeducation programme would be firstly to acknowledge fatigue as a legitimate long-lasting postconcussion symptom and reassure the individual that they are not just being 'lazy' when they find themselves very low in motivation to act mentally or physically. Providing an evidence-based explanation for post-MTBI fatigue reinforces this legitimization and lays the foundation for the introduction of the proposed treatment approach – aerobic exercise. Teaching coping strategies such as planning and pacing activities during the post-MTBI fatigue recovery period helps prevent the 'boom and bust' cycle which has been observed in many Concussion Clinic clients as well as those who present to the Psychology Clinic at Massey University with chronic pain.

Anecdotally, the effects of providing information about MTBI and post-MTBI fatigue have been observed in the Concussion Clinic when clients and their significant others express relief at having an explanation for the difficulties experienced or observed. The client with post-MTBI fatigue worries about whether their symptoms are indicative of further brain injury and their significant others and employers become annoyed and frustrated and are in some instances subsequently less supportive. Providing information and reassurance helps clients to alter their maladaptive thoughts and beliefs, to feel less stressed (maladaptive psychological reactions) and to recognise their maladaptive behaviours (excessive resting or trying to do too much). Psychoeducation also increases the individual's readiness to take action to help relieve their fatigue. Similarly their significant others and employers benefit from education about MTBI and post-MTBI fatigue and are able to alter their own maladaptive (intolerant) behaviour and to understand the need for programmes which encourage a graduated return to work.

The psychoeducation provided to participants in Study Two targets maladaptive thoughts and beliefs about post-MTBI fatigue by providing information about a model of post-MTBI fatigue (Mendez et al., 2005) and about strategies for living with post-MTBI fatigue so as to conserve energy and reduce fatigue. The aerobic exercise component targets maladaptive behaviours such as excessive rest and depleting energy reserves by trying to do too much work or other activity; behaviours which are believed to increase post-MTBI fatigue.

Aerobic exercise

Chapter 5 summarised the evidence for using aerobic exercise as a treatment approach for fatigue and this strategy was included in the PERT programme. Animal and human studies have demonstrated that extended rest was not a suitable strategy in the postconcussion stage (Griesbach et al., 2006; Puetz et al., 2006). There are many studies (Fulcher & White, 1997; Moss-Morris et al., 2005; van Kessel et al., 2008; Wallman et al., 2004) which demonstrated that exercise reduced fatigue in MS and CFS. Also Kozlowski's (2008) study showed that aerobic exercise reduced postconcussion symptoms in elite athletes and Driver and Eade (2009), while evaluating an aquatic physical intervention for post-TBI depression, found a reduction of fatigue in their sample after the intervention.

Aerobic exercise addresses many factors in the proposed post-MTBI fatigue model, Figure 3.3. It stimulates the production of brain derived neurotrophic factor (BDNF) which plays a role in neuroplasticity and neuroprotection thus helping the brain to heal after a MTBI (Cotman et al., 2007). That is, it addresses the postconcussion neurophysiological changes which result in temporary cognitive impairment (McAllister, 2005) and dysfunction in the autoregulatory system in some instances (Leddy et al., 2007). It also addresses psychiatric symptoms and maladaptive psychological and behavioural responses such as stress, depression, anxiety and excessive resting.

Once it was decided to include aerobic exercise in the treatment there was a need to operationalise the key factors, (frequency, intensity and duration) of the exercise programme. These were arrived at through both literature review and consideration of

a primary intention of the programme, clinical relevance, which in this instance was seen as: ease of accessibility for the participants and low cost to providers and funders.

Successful exercise-based programmes for treatment of fatigue in illnesses such as MS and CFS were 8-12 weeks long (Fulcher & White, 1997; van Kessel et al., 2008). Programme length was set at 12 weeks including a one week baseline during which participants were asked to record what they did but not to change their routine from their usual practice. The exercise dose (intensity of exercise, duration of individual sessions and frequency per week) for the PERT programme was set at 30 minutes per day, five days a week of aerobic-level exercise. Choice of these parameters was informed by studies of frequency and intensity (Dishman, Thom, Puetz, O'Connor, & Clementz, 2010; Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005). Additionally, at the time the PERT programme was being developed, the Pain Disability Programme (PDP) using aerobic exercise and cognitive behavioural therapy including psychoeducation was being rolled out in New Zealand, supported by ACC (Sullivan & Stanish, 2003). The PDP exercise schedule was 30 minutes per day, five days a week and had been shown to reduce deconditioning in people with persistent pain. The reason for five rather than seven days of exercise was to enhance compliance by allowing an exercise 'holiday' of two days per week. Dunn et al. (2005) found that moderate intensity of exercise was more important than frequency (3 days/week versus 5 days/week) but they cited the (Texas) public health recommendation as being ≥ 30 minutes per day most days if not all days of the week. This recommendation is also well publicised by Sports and Recreation New Zealand using the slogan "30 minutes a day, Push Play". Hence all participants were already primed to think of this frequency and duration as an appropriate strategy to engage in.

Client and Therapist Manuals (see Appendix I for Therapist Manual which encompasses the Client Manual material[4])

Since the 1960's manuals have become an increasingly popular tool used both in research and clinical practice. The advantages that manuals offer are the provision of a precise and organized way of training and supervising therapists, speeding up the training, enhancing the possibility of replication and facilitating comparison of common components of the treatments (Kazdin, 2004; Lambert & Ogles, 2004). Lambert and Ogles also report on a review of studies investigating the potential benefits of using manuals; for instance, that manualised treatments are transportable from efficacy studies into clinical settings. Additionally, Kazdin (2004) observed that for a treatment to be evaluated and replicated in research and generalizable beyond the research situation to the clinical environment it needs to be operationalised, preferably through a treatment manual. However, Lambert and Ogles (2004) noted studies which have shown that use of a manual does not guarantee good outcomes, nor the quality of the therapist's input and Kazdin (1994) highlighted the disadvantage of using the manual in a rigid slavish manner which does not allow for adaptation to each individual client. On the other hand, the manual signals the limits of that adaptation so that integrity of the treatment is maintained (Kazdin, 1994).

A manual provides a permanent record of the treatment content and approach which is valuable not only for researchers and therapists, but just as importantly it is a valuable

[4]Appendix I contains the Therapist Manual. The Client Manual has not been reproduced in this document for reasons of economy but is embedded and easily identifiable on inspection of the Therapist Manual. For instance on page 11 of the Therapist Manual halfway down the page is a reference to the relevant page in the Client Manual, e.g., "Client Manual P4". From this point on page 11 to the solid line mid-page 16 the content is a direct copy of the Client Manual. Then follows further therapist instructions in blue ink until mid-page 17 where the black printed text is again a copy of the Client Manual text. Each section of the Therapist Manual is set out in a similar manner with therapist instructions in blue print and Client Manual content in black print. Each new Client Manual section is referenced to the actual Client Manual with the title "Client manual P..". The choice of blue ink for the instructions was deliberately chosen as it is consistent with many of the commonly used psychological tests i.e, the Wechsler suite of intelligence tests.

resource for the client with MTBI. In the early days, weeks or months post injury the three most commonly observed cognitive symptoms of MTBI are impaired memory, attention and information processing speed (McAllister, 2005; McCrea, 2008). Hence, at least for those participants still in that early period, it is essential to provide a written record of the sessions so they can review the information provided during a session. For those with post-MTBI fatigue, whose cognitive function has returned to normal, it is still essential as few if any people have perfect memories. Finally, as the PERT programme was partly presented through phone interviews, having a manual meant that each participant had the information already in front of them, thus facilitating communication between therapist and client.

Postconcussion Energy Recovery Training (PERT)

Two manuals (Appendix I) one for the client and the other for the therapist were developed to guide the implementation of a treatment programme for post-MTBI fatigue.

The participant's manual (contained within the Therapist Manual in Appendix I) contains information about topics which were relevant to recovery from post-MTBI fatigue such as planning and pacing, communication with significant others about mood and needs, and sleep hygiene. It also contained anecdotes written by people who had recovered from post-MTBI fatigue. Figure 6.1 shows the topics the PERT programme covered each week. The therapist's manual (Appendix I) begins with an introduction briefly outlining the programme and emphasizing the experimental nature of its current use. The therapist's manual also contains a copy of the demographic

Week 1 • Introducing PERT • Theory of Post-MTBI fatigue • Plan and Diary	Week 7 • Saying 'NO', Asking for help • Plan and Diary
Week 2 • The Aerobic Zone • Plan and Diary	Week 8 • "Beat Fatigue Slowly but Surely" Ken Jelinek • Plan and Diary
Week 3 • Barriers to Exercise • Plan and Diary	Week 9 • Feelings and Bad Dreams • Plan and Diary
Week 4 • Planning and Pacing • Plan and Diary	Week 10 • Denise Hansen's Story Part I • Plan and Diary
Week 5 • Problems associated with Fatigue • Plan and Diary	Week 11 • Denise Hansen's Story Part II • Plan and Diary
Week 6 • Getting a Good Night's Sleep • Plan and Diary	Week 12 • Maintenance of exercise • Plan and Diary

Figure 6.1. List of topics covered each week of the PERT programme

questionnaire and the fatigue, mood, anxiety and social reintegration questionnaires, for which technical information is provided. Within the complete copy of the therapist manual each of the modules from the client manual is reproduced, with instructions for the therapist on what to emphasize during the session. To avoid excessive duplication in the current document the abridged version, i.e., without the client manual content, has been reproduced in Appendix J.

In the interest of keeping the programme accessible and based on the successful treatment programme for fatigue in people with MS (van Kessel et al., 2008), the PERT programme included both personal and phone consultations. This reduced the number of times that participants had to travel to the Concussion Clinic for a session. It also reduced the overall cost of providing the programme as the phone contacts were 15 to 20 minutes versus 60 minutes for a personal session, thus using significantly less

therapist time and consequently costing the funder less than if all sessions were an hour long. Figure 6.2 shows the treatment group schedule of contact with the therapist over the 24 weeks of the study.

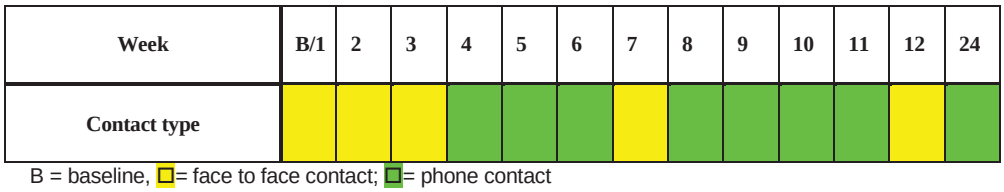

Figure 6.2 Schedule for delivery of the PERT programme

PERT programme content week by week

In this section the content and rationale for each of the 12 weeks of the programme is discussed. This is the content which appeared in the Client Manual (Appendix I). As stated earlier, the Therapist Manual (Appendix J) had all of the client manual content as well as specific instructions to guide the therapist in administration of the programme.

PERT Week 1 - In keeping with the research regarding reassurance and creating expectations of success (Mittenberg et al., 1996; Paniak et al., 1998) the PERT programme begins with a reassuring message that the post-MTBI fatigue can get better but that it will require the active participation of the client. The structure of the programme is briefly outlined and then an explanation of the Mendez et al. (2005) explanation for post-MTBI fatigue is provided. The explanation for fatigue was presented with illustrations to give the participant an image and metaphor to explain why they are feeling tired and to show them that they were not just being lazy. The baseline measures are taken by having the participant complete the online fatigue,

anxiety and depression and social reintegration measures during this session. Then the participant is asked keep a record of their exercise, naps, fatigue and energy levels over the next week. They are also asked not to change their current activity routine. The fatigue and energy ratings are based on a Likert scale in the manual (Figure 6.3).

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7...…..8...…..9…..10
No fatigue/tiredness Exhausted

0…….1……..2..……3..……4..……5..……6..……7...…..8...…..9…..10
No Energy Full of Energy

Figure 6.3 PERT manual fatigue and energy rating scales

Each chapter presented the topic for the week, the diary blank and a place to record the time and place for the next session.

PERT Week 2 – the objective was to introduce the aerobic exercise component and to teach the participant to be able to measure their own heart beat so that they are able to monitor the intensity of their exercise. The widely accepted Karvonen (McMurray, 1999) formula - maximum heart rate, for age, per 15 seconds = (220 – age)/4 was used to calculate the rate for the Study Two participants (age range 15–65). The aerobic range graph was calculated as a heart rate between 60% and 80% of the recommended maximum rate for age. Besides the heart beat chart (Appendix I, Client Manual – Week 2), they were also given the Talk Test (Persinger, Foster, Gibson, Fater, & Porcari, 2004) as another way of monitoring exercise intensity while actually engaged in exercise.

PERT Week 3 - In anticipation of difficulties non-active participants might have motivating themselves to do the prescribed exercise, barriers to exercise and possible solutions were discussed (Myers & Roth, 1997; Osuji, Lovegreen, Elliott, & Brownson, 2006).

PERT Week 4 - During the years of working in the Concussion Clinic I heard a proportion of clients report that they because they felt good they would engage in an activity one day only to find it took them several days to recover. So I included a session on planning and pacing to encourage participants who were reporting persistent post-MTBI fatigue to adopt a steady planned approach. For instance they were encouraged to set a time limit on an activity and to stop at the end of the time even if the job was not finished. Time limits could be increased over successive days or weeks as their stamina built up. Planning and pacing is recommended in both MTBI and chronic pain workbooks as a way of avoiding the "burn and bust" cycle of high activity on 'good days' followed by long recovery periods (Denton, 2008; Roberts-Stoller & Albers-Hill, 1998; Sullivan & Stanish, 2003).

PERT Week 5 – Three other common postconcussion symptoms - headache, irritability and loss of concentration - are the focus of the fifth session. Here I have drawn on general principles of therapy and problem solving such as *recognising* there is a problem gleaned from over twenty years as a therapist. The individual is encouraged to notice the signs of fatigue before it becomes a factor in poor control of frustration and irritability reactions. Also during this session suggestions for helpful strategies which can enable the individual to avoid conflict with the people around

them, such as taking a rest or time out and communicating their need to withdraw rather than just leaving.

PERT Week 6 – "say NO or ask for help" To some extent this is a continuation of the "Planning and Pacing" concept. The objective of this session is to encourage the individual to avoid taking on more than they can handle and to educate others by saying "No" when asked to take on more than their energy resources can tolerate. MTBI is an invisible injury and clients report that people, e.g., employers and/or family forget or do not know that their capacity for activity is temporarily curtailed. These significant others expect the same performance as pre-accident and some individuals with MTBI try to oblige only to find that fatigue prevents them and then there is often conflict. Also, the high achievers (Kay et al., 1992; Ruff, 1996; R Wood, 2004) try to tough it out and are not used to asking for help. Seeking support from other people is a valuable stress management tool. Giving the individual with post-MTBI fatigue permission to decline work or social activities or to ask for help and time to rest or to plan for stressful activities gives them access to strategies for living with post-MTBI fatigue.

PERT Week 7 – Sleep disruption is another common persistent postconcussion symptom (Williams, Lazic, & Ogilvie, 2008) which can have neurogenic and/or psychogenic aetiology and which leads to tiredness or fatigue. There is a multitude of websites providing sleep hygiene advice so I decided that writing yet another one was a waste of effort and I downloaded one set of advice and referenced others.

PERT Week 8 – Social learning theory (now social cognitive theory) (Bandura, 1977, 2004) proposes that people learn from each other using observation, imitation and modelling and adopt health promoting behaviours. By providing anecdotes from people who have either experienced MTBI or been a therapist in that area I have built in models and broadened the social context of endorsement for the activities I am asking the participants to engage in. The Week 8 section of the manual also has a short review summarising the hints that have been presented so far and adding a few extras to help with cognitive function such as "repeat things that need to be remembered…and write them down" (Client Manual p27).

PERT Week 9 – Many accidents resulting in MTBI occur in life threatening circumstances and while there is controversy about whether traumatic brain injury and posttraumatic stress disorder can co-exist (Sbordone & Liter, 1995), there is evidence that post-MTBI acquired stress, anxiety and depression disorders are observed in a proportion of individuals who have sustained a MTBI (Iverson et al., 2007; Moore, Terryberry-Spohr, & Hope, 2006). The PERT programme was psychoeducational rather than therapeutic but it was important to validate the psychological difficulties participants presented with and to guide them towards those who could provide help if needed. Hence the suggestion at the end of this module that the participant request a referral to a psychologist at the Concussion Clinic if they were having any of the posttraumatic stress symptoms mentioned.

PERT Weeks 10 and 11 - Following the same principles as in Week 9 (i.e. Bandura's (2004) Social Cognition Theory), that is, providing models for the participants, these

two sessions were built around the two-part story written by Denise Hanson (2006) telling of her recovery from a MTBI.

PERT Week 12 – Another story by a person who was working well over 100 hours per week before the accident and came to experience post-MTBI fatigue afterwards. She tells her story briefly and then lists suggestions for living with post-MTBI fatigue, encouraging good sleep and exercise in particular. Week 12 is also the final week so participants were asked to complete the primary fatigue, anxiety, depression and psychosocial measures and encouraged to keep up their exercise and other fatigue management practices.

Another form of motivation which was built into the manual was a chart of fatigue and energy levels which allowed the participants to track their progress over the sixty days they were involved in the programme.

The Manuals – physical appearance

Apart from designing the content of the manuals to reflect evidence-based practice I also wanted it to be attractive, nice to hold and to look at. I saw the manual as one more way of motivating the participants to engage in the PERT programme and commit to self-driven rehabilitation. I decided that the age group I would recruit from was 16 to 65 year olds so I needed something that would appeal to all age groups. Hence I included pictures and diagrams which would either impart knowledge or entertain, or in the case of the walking man  I wanted to cue the

participants into doing the exercise and remembering to fill in their daily diary. I also wanted a figure which looked like he/she was enjoying their exercise, and their life, to reinforce the expectation that life could be enjoyed even with post-MTBI fatigue. Through observation and a magazine article (source unknown) I was aware that the younger generation were accustomed to busy print material. While I recognised that MTBI often brings difficulty with too much stimuli I added some busyness to the text by using different font sizes and styles and page layout and pictures.

Other postconcussion manuals

Researchers presenting the successful postconcussion syndrome prevention psychoeducation programme developed by Mittenberg et al. (1996) gave their participants a manual - "Traumatic Brain Injury: A guide for patients" (Mittenberg, Zielinski, & Fichera, 1993). This manual covers a range of relevant topics of interest such as the cause and diagnosis of TBI, postconcussion symptoms and helpful hints for specific symptoms (including fatigue). The manual is presented in monochrome with long tracts of prose interspersed with tables of symptoms and boxes containing the helpful hints. Given that lack of concentration is a regularly observed postconcussion symptom (with a prevalence of 14% according to information in page five of the manual), these long tracts present a barrier to gaining information about MTBI symptoms. PERT on the other hand presented information using a variety of print styles, pictures, diagrams and relatively short paragraphs. This approach was designed to permit engagement with the material in short bursts which fitted better with shorter concentration periods. Inspiration for the PERT style of presentation was also drawn from the information booklets originally prepared by Dorothy Gronwell and Philip Wrightson in New Zealand and adapted by Catherine Wilson and the team at Epworth

Hospital in Melbourne. This information booklet is illustrated with colourful sketches illustrating the short paragraphs discussing postconcussion symptoms. A number of other manuals were examined for ideas about structure and presentation in the preparation of the PERT manuals. For instance the client and therapist manuals of the Pain Disability Prevention programme (Sullivan & Stanish, 2003) and the BrainSTARS manual which guides interventions for children who have an acquired brain injury (Dise-Lewis, Calvery, & Lewis, 2002).

To summarise, the PERT manual was developed to guide the clinicians and participants in their journey towards reduced post-MTBI fatigue and increased post-MTBI energy. Having a manualised treatment allows other clinicians to replicate the programme in a research or clinical context (Sanderson & Woody, 1995). The various modules included in the manual were based on evidence drawn from the literature both for MTBI as well as other conditions such as sleep disruption and barriers to doing exercise. The manual was designed with features such as pictures, diagrams and colour to appeal to participants and also to facilitate record keeping, which benefited both the gathering of data for the research as well as ongoing engagement of the participants. In the next chapter, Chapter 7, the development of Study Two, the evaluation of the effectiveness of the PERT programme and the confound which interfered with this purpose are discussed.

Chapter 7

STUDY TWO: EVALUATION OF THE EFFECTIVENESS OF A TREATMENT FOR POST-MTBI FATIGUE

Introduction

Study One established that fatigue is a persistent problem after MTBI in New Zealand, consistent with other countries. The problem of post-MTBI fatigue affects all aspects of life, keeping people from returning to work and from gaining back their pre-morbid sense of well-being. Thus it impacts not only the individual but also their family and the community at large.

In spite of the impact of post-MTBI fatigue, there is little in the way of evidence based intervention to assist with it. One post-MTBI fatigue study has evaluated the efficacy of medication (Jha, 2006; Jha et al., 2008a), while other studies using a range of methods did not single out fatigue from other PCS symptoms (e.g., Mittenberg et al, 1996; Kozlowski et al., 2008). Given the extent to which post-MTBI fatigue interferes with the resumption of pre-accident quality of life, the lack of research is puzzling as there is an obvious need for an effective treatment. Accordingly, the focus will now move to looking at interventions which might reduce fatigue in the MTBI population.

Guided by the literature on PCS, a model of post-MTBI fatigue was developed. The proposed ecological model of post-MTBI fatigue outlined in Chapter 3 suggested several intervention targets; neurophysiological changes, sleep dysfunction, psychiatric symptoms and maladaptive psychological and behavioural responses. These formed the basis for the development of the PERT programme as outlined in Chapter 6. This was based on the model above and incorporated evidence-based treatment approaches

for fatigue as described in Chapter 5, which covered treatment of fatigue as well as the cluster of symptoms associated with PCS.

The need to evaluate the PERT programme as an intervention to reduce post-MTBI fatigue led to Study Two. The study was designed and conducted as a 2 x 3, group by time, controlled trial of the effectiveness of the PERT programme on subjective post-MTBI fatigue prevalence and severity, anxiety and depression, psychosocial factors, sleep dysfunction and negative attitudes of family towards the person with post-MTBI fatigue.

However, as will be described below, the study did not develop as planned. Instead of there being two different groups – one receiving the PERT programme and the other not (treatment as usual), both groups engaged in similar activities (treatment or independently) as contained within in the PERT programme. This occurred due to changes made, without warning, to the treatment received by the control group.

This was revealed when initial analysis showed a main effect for time but no time by group effect – both groups improved. In reflecting on why this might be, it was decided to contact the control participants to find out more about what they had been doing over the 6 months study period. Most, it was discovered (80%), had *also* engaged in exercise during their recovery period. Further over half had had contact with an Occupational Therapist or a Clinical Psychologist after their initial assessment thereby exposing them to additional opportunities for accessing psychoeducation about MTBI**.** While the treatment group received more systematic presentation of

information about post-MTBI fatigue as well as fatigue focused treatment, the fact remained that both groups had received input along the same lines.

Accordingly the results are presented in three parts later in this chapter. Part 1 briefly presents the results of the controlled trial and the findings from the analysis of the treatment participants' diaries. Part 2 presents results from analysis of the data from the whole sample and also the results of the analysis of intraindividual reliable clinically significant change (RCSC). Part 3 presents responses to post hoc questions regarding the differences between the RCSC distribution within the treatment and control groups.

The original hypotheses for Study Two, which were adopted for Part 1 of the analysis, were:-

1. That participants who complete the PERT programme (compared to those who receive 'treatment as usual') following their MTBI will
    a. report significantly less subjective fatigue prevalence and severity as measured by Item 6 of the Rivermead Postconcussion Symptoms Questionnaire (RPSQ) and scores on the Fatigue Severity Scale (FSS) and the Fatigue Assessment Scale (FAS) and their daily diary records.
    b. maintain gains (reduced fatigue) at follow-up, three months after treatment concludes.
    c. show no significant effect of time since injury on outcome measures. That is, there will not be a significant correlation between post-MTBI fatigue scores and time since injury.
2. That PERT participants will report significantly less anxiety and/or depression than the control group at three and six months post-baseline. That is, their

scores on the Hospital Anxiety and Depression Scale (HADS) will be significantly less than they were at baseline in comparison with those of the control group.

3. That a positive side-effect of both the aerobic exercise and the specific sleep focused module will be an improvement in sleep. It is hypothesized that PERT participants will report a greater reduced incidence of sleep disturbance as measured by Item 5 of the Rivermead Postconcussion Symptoms Questionnaire.
4. That PERT participants will report significantly increased participation in occupational activities, interpersonal relationships, and independent living skills compared with the control group's participation at three and six months post-baseline. That is, their scores on the Sydney Psychosocial Reintegration Scale (SPRS) will be significantly lower than they were at baseline in comparison with the scores of the control group.
5. If the individual with post-MTBI fatigue believed they were seen as lazy by their partner or family when exhibiting fatigue behaviours, they would report more severe post-MTBI fatigue.

Method

As stated earlier, the original objective of Study Two was to evaluate a 12 week manualised combined aerobic exercise and psychoeducation programme for post-MTBI fatigue, comparing outcomes over time with a control group. The quasi-experimental design used a pretest-posttest-follow-up format. All participants completed measures at baseline, at 12 weeks and 24 weeks. The PERT programme

was provided to the treatment group according to the procedure set out in the manual while the control group received the comparatively unstructured treatment as was normally provided in their local Concussion Clinics. Outcomes included post-MTBI fatigue prevalence and severity, depression, anxiety and psychosocial reintegration factors.

In order to estimate the number of participants required for Study Two, previous meta-analyses of studies of the effectiveness of exercise and/or psychoeducation in treating either postconcussion symptoms or, fatigue in other illnesses were reviewed.

Mittenberg et al.'s (2001) meta-analysis of five treatment studies for postconcussion symptoms reported an average effect size of d = .32 (range d = .22 to d = .37). However, none of these studies included fatigue-specific data or used exercise as a treatment for postconcussion or fatigue. To examine fatigue specifically, studies of fatigue treatment when associated with other conditions were reviewed. A meta-analysis of 55 studies of exercise treatment for cancer-related fatigue reported an average effect size of d = .27 (range d = .18 to d =.37) (Cramp & Daniel, 2008). A study of exercise treatment for post TBI mood problems (not fatigue) revealed an effect size for fatigue of d = 1.00 (Driver & Eade, 2009). Another study comparing two psychoeducation programmes for postconcussion symptoms found the average effect of PCS symptom changes was d = .36 (Paniak et al., 1998).

A power analysis for Study Two was conducted using the GPower 3.1.3 calculator (Faul, Erdfelder, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007). The effect size used in this calculation was d = .42, the average of the effect sizes

reported in the studies above. With 80% power, α = .05 significance and *d* = .42 the recommended total group size is 76 for repeated measure within-between interaction analysis of variance (ANOVA), that is, for analysis of time by group. If Cohen's *d* = 1.00, (Driver & Eade, 2009), was entered into the calculator, the total group size is 16. Hence Study Two would need a total of between 16 and 76 participants. If the design were altered to a repeated measures design based on one group (whole sample) then according to the GPower 3.1.3 calculations, the sample size would need to be between 14 and 62. As Driver & Eade's fatigue effect size is much higher than those of the other studies reviewed, a conservative approach was adopted and the target sample size range for Study Two was set at *N* = 62 to *N* = 76.

An estimate of attrition during treatment and follow-up phases was based on a study of exercise and CBT with a MS population (van Kessel et al., 2008). On this basis, it was estimated that approximately 10% of participants would drop out during the treatment phase and that fewer participants would be available for follow-up. Thus estimating a maximum attrition of 20% at six-month follow-up the goal was to recruit at least 55 and up to 80 participants. Sixty-four participants agreed to be part of Study Two and analysis was carried out with the 37 for whom there was complete data at the end of the study. Attrition was greater than predicted and the details are presented in the "participants" section of this chapter.

Study setting

Concussion Clinics were established in New Zealand in 2000 by the Accident Compensation Corporation (ACC), a government sponsored organisation which provides comprehensive, no-fault personal injury cover for all New Zealand residents

and visitors to New Zealand. Individuals referred to the clinics attended an initial medical specialist and neuropsychological assessment from which recommendations for further services were made. Upon approval by ACC, the Concussion Clinic client was provided with psychological and/or occupational therapy and could be referred for additional services such as physiotherapy. The provider of the initial assessment was required by ACC to give the Concussion Clinic client printed information about MTBI and PCS. Information about post-MTBI fatigue varied between service providers. The material on post-MTBI fatigue, written by a psychologist in the 1980s and used by the Palmerston North Concussion Clinic occupational therapist was outdated and not well founded in the literature. Once the current study got underway, both the clinical psychologist and the occupational therapists used the PERT manual to guide therapy for post-MTBI fatigue. The Concussion Clinic model described here was superceded in July 2010 by a different ACC funded Concussion Service model developed after consultation with representatives from all the New Zealand Concussion Clinics. Data collection for the current study had ceased prior to the introduction of the new Concussion Service model.

Participants

Participants were recruited from consecutive clients presenting to Concussion Clinics in Palmerston North, Porirua and New Plymouth over an 18-month period. There were insufficient numbers of clients in any of these Concussion Clinics for the whole study to be based in one clinic. As the principal researcher worked in the Palmerston North clinic, this was chosen as the source of treatment group participants, thus saving costs involved with travel to other centres. Recruiting participants from Porirua and New Plymouth was based on convenience as there were already well-established networks

between the principal researcher and the Concussion Clinic clinical psychologists in the other centres.

All participants had been diagnosed as having sustained a MTBI and had reported a score between 2 and 4 on the Rivermead Postconcussion Symptoms Questionnaire item 6 ('Fatigue, tiring more easily') at their initial Concussion Clinic assessment. Potential participants were provided with written information (Appendices A and B) about the study by the clinical psychologist doing the initial neuropsychological assessment. The control group participants were asked to give consent to be contacted by the principal investigator to explain the study and to invite them to become participants. All participants were made aware that their future health care would not be affected by their decision regarding participation in the study.

Potential participants were excluded if there was evidence of regular excessive intake of psychoactive drugs or history of drug abuse, central neurological disorder or psychiatric condition, evidence of skull or facial fractures, or presence of multiple trauma/significant trauma to other parts of the body (e.g., broken limbs or ribs, spinal injuries, soft tissue injury requiring plastic surgery). As the treatment was exercise based, participants had to be free of injury and other conditions such as drug use which would prevent or significantly inhibit physical activity.

Of the 64 individuals who met the inclusion criteria, 18 treatment and 23 control participants were recruited[5] and completed the outcome measures at baseline, 12 and 24 weeks. Two control participants missed the week 12 follow-up but provided data at

[5] Unanticipated difficulties with recruitment arose from staffing changes at two of the Concussion Clinics, meaning there were fewer treatment and control group participants than was planned.

week 24, and two dropped out of the study after providing baseline data. Neither responded to several attempts to contact them to ask for the week 12 data. Eight control participants agreed to take part at the initial contact but then did not provide any data and a further two potential control participants did not respond to several messages left on their phones and no contact was made with them.

Table 7.1 sets out the demographic information for the two groups. There was no significant difference on any of the fatigue, anxiety, depression and psychosocial reintegration measures between the treatment and control groups at baseline and no significant differences between the groups on the following demographic variables (Table 7.1): age, gender, time since injury, loss of consciousness, length of loss of consciousness, length of time in posttraumatic amnesia, Glasgow Coma Scale score, previous TBI history, accident type (aetiology of MTBI), other injury or previous history of depression or anxiety.

Seven participants in the treatment group provided baseline data but did not continue for a variety of reasons including another serious accident involving multiple fractures plus a diagnosis of sarcoidosis, decision to withdraw from all contact with the Concussion Clinic, inconsistent attendance at the clinic, failure to respond to attempts to set up appointments, or subsequent diagnosis of depression rather than post-MTBI fatigue as primary problem. Concussion Clinic clients who reported post-MTBI fatigue but declined to take part in the programme were provided with treatment as usual for their fatigue. Table 7.1 lists participant characteristics by group.

Table 7.1

Demographic and Injury-related Factors

Factors	Categories	Treatment	Control	All
Age	Years	20 – 58	16 – 61	16 – 61
Gender	Female	8	13	21
	Male	10	10	20
Time Since Injury	Days	44 – 663	33 - 1380	44-1380
LOC	No	7	8	15
	Yes	8	6	14
	Unknown	3	9	12
LOC – minutes		1 - 30	1 - 30	1 - 30
PTA	No	10	5	15
	Yes	6	14	20
	Unknown	2	4	6
PTA - minutes	<1hr	0	2	2
	<12hrs	4	8	12
	<24hrs	1	4	5
	Unknown	14	9	23
GCS	14	1	2	3
	15	4	3	7
	Unknown	13	18	31
TBI history	No	8	6	14
	Yes	6	15	21
	Unknown	4	2	6
Accident type	Vehicle Accident	6	7	13
	Fall	5	4	9
	Sports	2	2	4
	Assault	3	1	4
	Stand/Hit object	3	7	10
	Unknown	0	2	2
Work type	Professional	2	5	7
	Trades/Farming	7	4	11
	Sales/Service/Office	5	5	10
	Labour	2	0	2
	Student	2	4	6
	Unknown	0	5	5
Time off work	No	3	2	5
	Yes	15	18	33
	Unknown	0	3	3
Other injury	No	8	9	17
	Yes	10	9	19
	Unknown	1	5	6

Exercise during the first 12 week period*	No	0	4	4
	Yes	18	16	34
	Unknown	0	3	3
Exercise minutes**	≤30	16	5	21
	>30	2	9	11
	Unknown	0	9	9
Previous history of depression/anxiety	No	10	11	21
	Yes	5	10	15
	Unknown	3	2	5

LOC = loss of consciousness; GCS = Glasgow Coma Scale; PTA = Posttraumatic Amnesia; TBI = Traumatic Brain Injury; **p < .01

There was no significant difference between the treatment and control groups for age, gender, GCS, time since injury, LOC and length of LOC ($p > .05$). The cell count in the category cells of the remaining variables was too small for application of the chi-square test.

Measures

Four measures of fatigue using the Rivermead Postconcussion Symptoms Questionnaire Item 6, Fatigue Severity Scale, Fatigue Assessment Scale and daily fatigue and energy rating scales of fatigue and energy were selected as outcome measures. Item 6 on the RPSQ was used to screen all new Concussion Clinic clients for post-MTBI fatigue and then to measure the prevalence of post-MTBI fatigue within the sample at baseline, three and six months. Inspection of items in the two fatigue severity measures, FSS and FAS, suggests that the FSS, which was developed with populations of people with MS and Systemic Lupus Erythematosus (Krupp et al., 1989), has a bias towards physical activity and fatigue. Whereas the FAS, which was developed using a large (N = 2779) community based sample (Michielsen, De Vries, Van Heck, Van de Vijver, & Sijtsma, 2004) has five items which refer to cognitive processes characteristic of post-MTBI fatigue. Additionally, factor analysis of the FAS found it was a unidimensional measure of the fatigue construct. A final measure of

fatigue was a Likert scale where participants made daily ratings of fatigue and energy. This method was chosen for convenience to the participants.

Fatigue

Rivermead Postconcussion Symptoms Questionnaire (RPSQ)

The 16 item Rivermead Postconcussion Symptoms Questionnaire **(**RPSQ) (King et al., 1995) is rated on a scale from zero to four (0 = not experienced at all after the injury, 1 = experienced but no more of a problem compared to before the injury, 2 = a mild problem, 3 = a moderate problem, and 4 = a severe problem). Participant ratings, greater than or equal to 2 on Item 6 of the RPSQ, were used to determine presence of post-MTBI fatigue. Participants who rated item 6 $\geq$ 2 at their first visit to the Concussion Clinic were provided with information about the study and invited to take part. At baseline participants again rated the RPSQ items and the Item 6 rating was the baseline measure for prevalence. Test-retest reliability is r = .90 at 1 week post injury and r = .89 at 6 months post injury (King et al., 1995)

Fatigue Severity Scale (FSS)

There are no fatigue severity scales specifically developed for TBI populations; however one scale, the Fatigue Severity Scale (FSS) (Krupp et al., 1989), has been used as an outcome measure in several recent TBI studies investigating fatigue (Belmont, Agar, & Azouvi, 2009; Bushnik, Englander, & Katznelson, 2007; Ziino & Ponsford, 2005a). It has 9 items rated on a Likert scale from 0 = completely disagree, to 7 = completely agree. Internal consistency on the FSS is 0.94 and test-retest reliability is 0.82 (Kleinman et al., 2000). The FSS reported means for a normal healthy population are 3.35 (1.11) (Ziino & Ponsford, 2005a) and 2.53 (1.18) (Krupp

et al., 1989). Ziino & Ponsford reported a mean of 4.36 (SD=1.52) for a group of mixed severity TBI at six months (*M* (*SD*) = 241.67 (214.24) days) post injury.

An additional item 'When I am tired my family, or partner, thinks I am being lazy' was added to the end of the FSS questionnaire to assess the participant's perception of their significant other's attitude towards fatigue. However, it was not included in the FSS total and was analysed as a single item.

Fatigue Assessment Scale (FAS)

The Fatigue Assessment Scale (Michielsen, De Vries, & Van Heck, 2003; Michielsen, Willemsen, Croon, De Vries, & Van Heck, 2004) has 10 items drawn from three well known fatigue or quality of life measures: Fatigue Scale (Chalder et al., 1993), World Health Organization Quality of Life assessment instrument (Harper & Power, 1998) and Checklist Individual Strength (Vercoulen et al., 1994). The FAS has good reliability (Cronbach alpha = 0.87) (Michielsen, De Vries, et al., 2004), good internal consistency, unidimensionality, a single factor (fatigue) and it explained 48% of the variance (Michielsen, De Vries, et al., 2004). It was designed for universal use so does not exclude non- workers. It has good construct validity compared with other measures of fatigue, r = .61 to .79, p < .001 (Michielsen et al., 2003). The normal population mean and standard deviation; *M(SD)* = 19.26(6.52).

Daily ratings of fatigue and energy

Throughout the 12 week PERT programme the treatment group rated their fatigue and energy, five days a week, on the 10 point Likert scale featured in Figure 6.3. The weekly fatigue and energy means were analysed to explore change over time within the treatment group.

Anxiety, depression and psychosocial factors

Two measures, the Hospital Anxiety and Depression Scale and the Sydney Psychosocial Reintegration Scale allow monitoring of depression, anxiety and psychosocial factors.

Hospital Anxiety and Depression Scale (HADS).

The HADS (Zigmond & Snaith, 1983) is a measure of generalised anxiety and depression with 14 items rated 0 to 3. There are two subscales, Anxiety and Depression, with seven items each. The authors suggested a score greater than 7 on either scale indicated the presence of a *possible* case of anxiety or depression and a score greater than 10 indicated the presence of a *probable* case. The HADS manual (Snaith & Zigmond, 1994) describes specific categories for the scale scores; mild = 8 - 10, moderate = 11 - 13, and severe ≥ 14.

Despite these categories the HADS is designed to identify, not diagnose, emotional disorders in non-psychiatric patients within a hospital setting. It excludes somatic symptoms such as insomnia, anergia and fatigue, hence is a suitable measure of depression and anxiety during the study of post-MTBI fatigue. The HADS has good reliability and validity with Cronbach alphas of .80 for anxiety and .81 for depression (Herrmann, 1997). A cut-off score of ≥ 8 gave .80 sensitivity and specificity respectively (Bjelland et al., 2002). Test re-test reliability reduces over time suggesting the HADS is a suitable measure of change.

Sydney Psychosocial Reintegration Scale (SPRS)

The SPRS is a 12-item measure of specific types of psychosocial disabilities and handicaps that occur after TBI (Tate, Hodgkinson, Veerabangsa, & Maggiotto, 1999).

It has three subscales (Occupational Activities, Interpersonal Relationships, and Independent Living Skills) and asks the individual to compare their current status with their pre-morbid level of functioning. Items are rated on a 5 point scale with higher scores indicating better psychosocial functioning. The SPRS is based on the WHO's framework for conceptualising health and disability (World Health Organization, 1980, 1997). The self report (Form B) version is suitable for use with participants with MTBI as they are not significantly cognitively impaired and can therefore report on their own situation. Internal consistency was high, Cronbach alpha = .90. The three domains also have high reliability (r = .86 to .94) and stability co-efficients (McHugh et al., 2006).

Procedure

Figure 7.1 shows the procedure from first presentation to the clinic through recruitment to follow-up post PERT programme, to data analysis and reporting of the results.

Treatment group

After informed consent was obtained the participants in the treatment group were commenced on the PERT programme. The manualised programme was delivered by either an occupational therapist or clinical psychologist over twelve weeks. The therapists manual (Appendix I) contained both the entire content of the client manual as well as instructions on how to deliver each module to the client.

Treatment group participants met individually with their therapist who introduced the

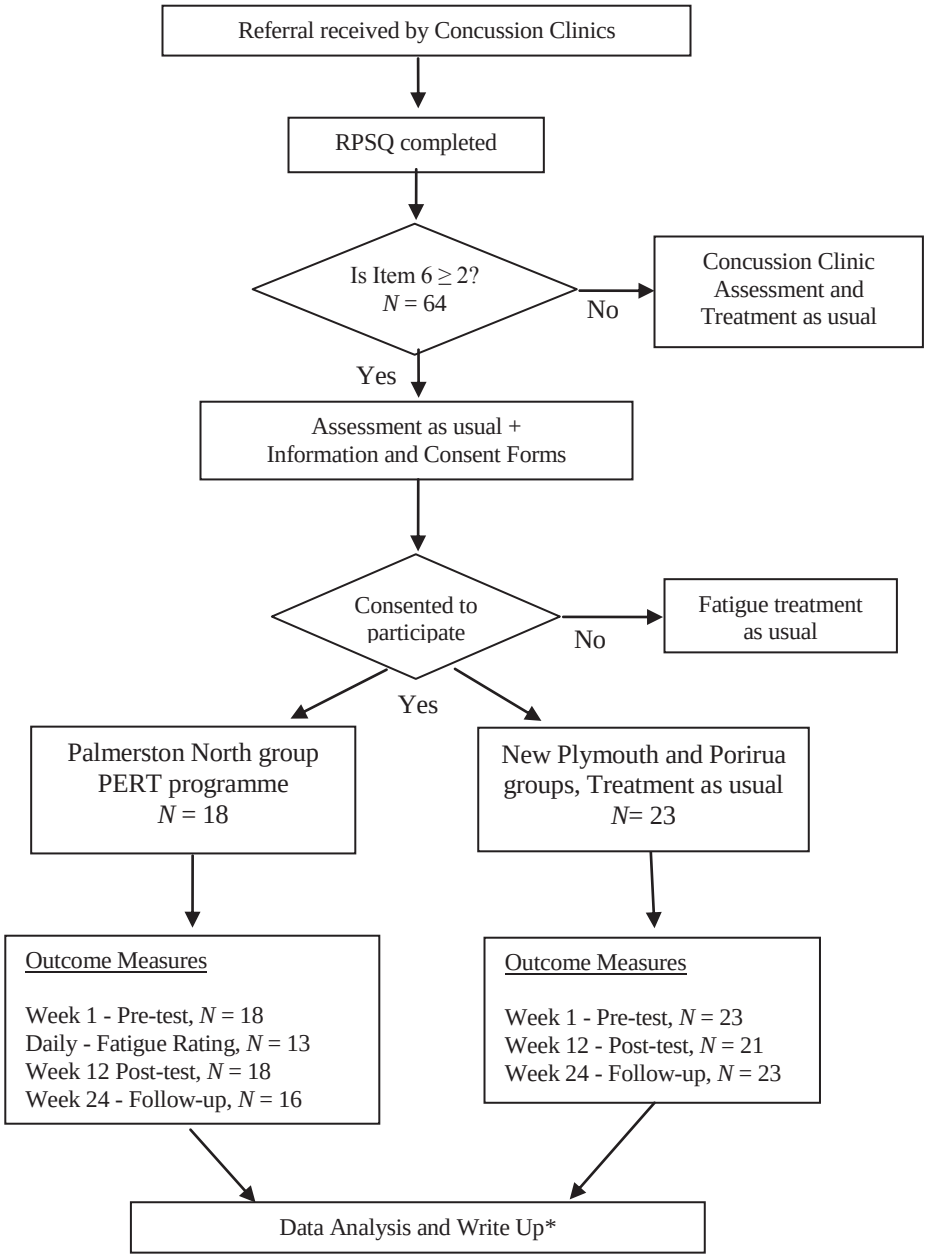

Figure 7.1. Flowchart of post-MTBI fatigue treatment evaluation research design

PERT = Postconcussion Energy Recovery Training; Daily - Fatigue Rating; Everyday the treatment participants rated their fatigue and energy levels on a Likert scale (1 = low to 10 = high) and recorded the ratings in their diary. *A complete set of data was available for *N* = 16 treamtnet and *N*= 21 control participants hence total *N* = 37.

PERT programme, and gave them a client manual. The manual included a diary in which the participants recorded their exercise, naps, and fatigue and energy ratings at the same time every day. The participants were also asked to chart their fatigue and energy ratings on a chart in the back of the manual. During the first session, the theory

of post-MTBI fatigue was explained and the participants were asked to commit to engaging in the regular exercise portion of the programme. During the first week of the programme, participants were asked to not change their routine but to keep a record of their exercise, naps, and fatigue and energy ratings in their manual in order to establish the baselines for those factors. During the ensuing 11 weeks, participants were asked to engage in 30 minutes of aerobic exercise five times a week. Participants were trained to take their own heart rate and to use a diagram in the manual which illustrated the aerobic range of heart rate by age. Participants were also encouraged to reduce nap time to a maximum of 30 minutes, and preferably to nil, over the duration of the PERT programme.

Control group

Information about the treatment provided for fatigue in the Porirua and New Plymouth Concussion Clinics was obtained through phone calls between the principal researcher and the occupational therapists working in those clinics. The occupational therapists in those Concussion Clinics indicated that return to work or school was the major focus of their contact with the Concussion Clinic clients. Under the Concussion Clinic contract with ACC individuals could be referred to the occupational therapist for a functional assessment if, during the initial medical and neuropsychological assessment, problems with return to work, school or home based functioning were identified. Other problems which prompted a referral to the occupational therapist were fatigue and/or sleep dysfunction. One of the occupational therapists said she talked with her Concussion Clinic clients about "why they have fatigue" and that Vitamin B1 deficiency was related to fatigue. She said she made recommendations for relaxation and rest, a diet that prevents weight gain, activity planning and adjustment and

encouragement to do gentle walking. Treatment provided by the Concussion Clinic psychologist targeted psychological symptoms such as depression, irritability and anxiety including posttraumatic stress symptoms using cognitive behavioural therapy.

Potential control group participants were identified by the Concussion Clinic clinical psychologists in Porirua and New Plymouth and given the information sheet about the study and asked if they would consent to being contacted by the principal researcher. Those who agreed were contacted by phone, their role in the study explained and they were invited to participate. Once informed consent to be contacted (Appendix C) was obtained they were asked to provide their email address and were sent the webpage address and the instructions for completing the outcome questionnaires. Hardcopies of the outcome questionnaires were sent to participants without computer access.

Schedule of contact for treatment and control group participants

Figure 7.2 sets out the schedule and type of contact with a therapist and/or the principal researcher throughout their involvement with Study Two.

At 12 and 24 weeks post baseline control participants were contacted by phone and asked to complete the questionnaires again. Some participants were reminded several times by phone and/or email at each data collection point. Between weeks 12 and 24 participants were contacted to obtain demographic information according to the semi-structured interview schedule in Appendix E. As noted earlier, they were also asked about the post-assessment contact they had with the Concussion Clinic professionals e.g., occupational therapist, psychologist, medical specialist. It was only at this point did it become clear that 13 (56.5%) had limited input (not necessarily focused on post-

MTBI fatigue) from an occupational therapist and/or a psychologist. Of the remaining control group members five (21.7%) had declined or not needed intervention and, the intervention status of another five was unknown.

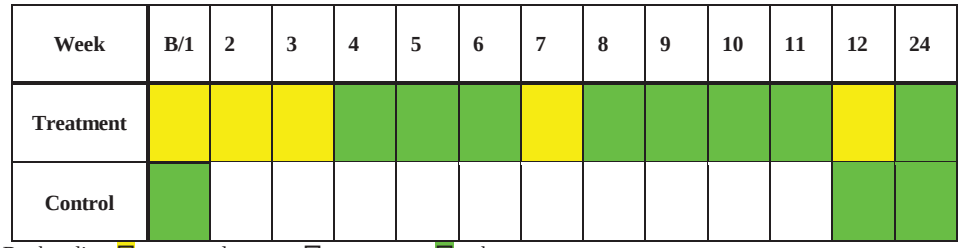

Figure 7.2 Schedule of contact for treatment and control groups

Control group participants were also asked whether they had engaged in exercise, and, if they answered "yes", they were asked about the frequency and duration of that exercise. Of the 20 control participants who provided information the majority (80%) indicated they had done regular exercise during the portion of their recovery period covered by the current study. Five exercised five times a week, one 30 minutes or less per session and four more than 30 minutes Nine exercised three times a week, four 30 minutes or less per session, and five more than 30 minutes. Two of the 16 did not provide information about frequency and duration of their exercise. None of these participants indicated they were keeping records of the exercise they were doing nor whether they were working to a pre-determined intensity.

Statistical Analysis

The statistical analyses were performed using SPSS 17.0. Prior to analysis all variables were examined using the SPSS explore and missing variables functions. Missing values analysis found missing values were randomly distributed. Subsequent

calculations were made to reduce the number of missing values. In instances where less than 25% of items from a composite variable were missing for any particular participant, the variable for that participant was computed by replacing the missing item values with the mean score calculated from existing item values. The mean is the best guess when all other information is missing and this approach is conservative. Other methods such as replacing missing scores with expectation maximization scores produces data which are only useful for exploratory and not inferential statistics (Tabachnick & Fidell, 2007), hence not suitable for the current study.

Data analysis was carried out and presented in three parts; Part 1 deals with comparison of treatment with control data to evaluate the effectiveness of the PERT programme. Part 2 presents the results of the analysis of the combined data from all the participants to determine the effects of time on the outcome measures. In this part, data were also analysed to determine whether individual participants were exhibiting reliable clinically significant change. The findings of the reliable clinically significant change analysis led back to questions about whether there were differences between the treatment and control groups in fatigue-related RCSC and/or secondary outcome measures. Part 3 presents the discussion of these questions.

Part 1

Part 1 contains a brief report of the results of the mixed between-within analysis of variance (ANOVA) which was initially used to evaluate the impact of the PERT programme on post-MTBI fatigue prevalence and severity, anxiety, depression, and psychosocial reintegration factors. Subsequent analysis of the combined group data is presented in Part 2. Part 1 also contains the results of the comparison of the baseline characteristics of the treatment and control groups (Table 7.1). A *t*-test for independent

samples was used for the interval variables and a chi square test for the nominal variables in Table 7.1.

The distributions of fatigue severity, depression and anxiety were found to be normal as assessed with the Kolmogorov-Smirnov statistic (Pallant, 2005), with the exception of treatment group FSS at three months, and control group depression at three and six months. However, for the SPRS scales there was a suggested violation of normality for 33% of the treatment group outcomes and 75% of the control group outcomes. Skewness and Kurtosis results on all measures were greater than zero. Given the participants were not randomly assigned to the treatment and control groups and were chosen because they were exhibiting difficulties with the factors being studied, zero skewness and kurtosis values were not expected.

Part 2

Following discovery of the way in which the control groups' independence (by exercise) was compromised, data from all participants were combined into one group and one-way repeated measures ANOVA were employed in the analysis. Additionally, that data for the whole sample was examined to determine if reliable clinically significant change had occurred for individual participants.

While comparison of group means is common research methodology, in clinical practice, the psychologist is interested in knowing whether an individual client's change in score is reliable (i.e., not due, simply, to measurement error) and, is also clinically significant (i.e., there is a greater likelihood of the score being in the normative rather than dysfunctional distribution) (C. Evans, Margison, & Barkham, 1998; Jacobson, Follette, & Revenstorf, 1984; Jacobson & Truax, 1991; Strauss,

Sherman, & Spreen, 2006). One measure of intra-individual change over time is the minimum clinically important difference (MCID), that is, the smallest change which is perceived as beneficial and able to justify implementation of the treatment (Jaeschke, Singer, & Guyatt, 1989; Pouchot et al., 2008). MCIDs can be either distribution or anchor based. Given the current study design did not include an anchor type question on which to base the MCID, the distribution-based Reliable Change Index (RCI) (Christensen & Mendoza, 1986; Jacobson et al., 1984; Jacobson & Truax, 1991) was used to determine both reliability and clinical significance of changes in scores. Jacobsen et al., proposed three tests of clinical significance (C. Evans et al., 1998; Jacobson & Truax, 1991; Jaeschke et al., 1989) and the third Criterion C was chosen because the clinical and normal distributions were overlapping and, normative data was available for measures such as FSS, FAS and HADS. Criterion C requires that there be a greater likelihood of the score being in the normative distribution than in the clinical distribution after treatment.

The Reliable Change and Clinically Significant calculator on Evans' (1998) website (http://www.psyctc.org/stats/rcsc.htm) was used to derive each RCI and clinically significant "cutoff" score. That is, the score below which there is a greater probability the individual's score has moved into the normal range. Formulae developed by Jacobsen et al., (1984, 1991) and revised by Christensen and Mendoza (1986) underpin the calculator (Evans et al., 1998). For the current study, baseline means and standard deviations together with published Cronbach α values were entered into the calculator. The RCI and cutoff indices were then used to identify the proportion of participants who had made reliable, clinically significant changes over the course of the current study. As there was no normative data for the daily diary records of fatigue, energy,

naps and exercise completed by the treatment group, clinical significance was defined as an RCI larger than ±1.96 giving a 95% probability that the observed change in scores following treatment was 'real' (Jacobson et al., 1984).

Part 3

Post hoc questions regarding the differences between the RCSC distribution within the treatment and control groups arose from findings of RCSC analysis of the whole sample. Chi square was used to determine whether there was a significant difference in RCSC status between the two groups. Mixed between-within ANOVA were used to explore relationships between RCSC distribution and secondary outcomes between the treatment and control groups.

Results

Part 1: Evaluation of the Effectiveness of the PERT Programme

Primary outcome - post-MTBI fatigue

Table 7.2 shows the means and standard deviations of the fatigue measures (Rivermead Postconcussion Symptoms Questionnaire (RPSQ); Item 6, Fatigue Severity Scale (FSS) and the Fatigue Assessment Scale (FAS)) for group, (treatment and control) by time period (baseline, 3 months and 6 months).

T-tests for independent groups established that there was no significant difference between the treatment and control groups at baseline for any of the fatigue measures - RPSQ Item 6 $t(35) = .66$, $p = .51$, FSS $t(35) = -.83$, $p = .41$ or FAS $t(35) = -.1.36$, $p = .18$.

The mixed between-within groups ANOVA found no significant time by group effects for fatigue: RPSQ Item 6, prevalence, Wilks-Lambda = .995, $F(2,34) = .09$, $p = .91$, partial eta squared = .005, and severity FSS, Wilks-Lambda = .99, $F(2,34) = .056$, $p = .95$, partial eta squared = .003, and FAS Wilks-Lambda = .99, $F(2,34) = .18$, $p = .84$, partial eta squared = .01. The treatment group changes in post-MTBI fatigue were not significantly different from the control group changes. However, as there was low power (Item 6, 18.6%; FSS, 11.2%; FAS, 35.9% respectively) for each of the ANOVAs calculated there is a risk of a Type 2 error (failing to reject the null

Table 7.2

Descriptive Statistics for Prevalence and Severity of Post-MTBI Fatigue in the Treatment and Control Groups. Treatment N = 16, Control N = 21

	Post-MTBI Fatigue Prevalence RPSQ item 6	**Post-MTBI Fatigue Severity FSS**	**Post-MTBI Fatigue Severity FAS**
	M(*SD*)	*M*(*SD*)	*M*(*SD*)
Baseline			
Treatment	3.06(.77)	5.47(1.04)	30.94(7.03)
Control	3.24(.83)	4.92(1.34)	25.92(9.16)
3 months			
Treatment	2.50(1.03)	5.14(1.19)	27.01(6.16)
Control	2.52(1.09)	4.35(1.57)	23.90(5.67)
6 months			
Treatment	2.06(1.00)	4.35(1.57)	23.97(7.79)
Control	2.14(1.32)	4.09(1.31)	21.71(4.98)

M = Mean; *SD* = Standard Deviation; RPSQ = Rivermead Postconcussion Symptoms Questionnaire; FSS = Fatigue Severity Scale; FAS = Fatigue Assessment Scale; Only participants with data at each time period were included in this analysis, hence two treatment group participants have been excluded from this analysis and total *N* = 37.

hypothesis when it is false). In real terms this means that because the treatment and control samples were small, the power was low so the usefulness, or otherwise, of the PERT programme as a treatment for post-MTBI fatigue is not able to be confidently asserted.

The mixed between-within groups ANOVA also showed there was a large[6] main effect for time for post-MTBI fatigue and this will be further explored in Section 2. The main effect for time results were: RPSQ Item 6, prevalence, Wilks-Lambda = .575, $F(2,34) = 12.55$, $p < .001$, partial eta squared = .43; and severity FSS Wilks-Lambda = .572, $F(2,34) = 12.70$, $p < .001$, partial eta squared = .43 and FAS Wilks-Lambda = .692, $F(2,34) = 6.45$, $p < .005$, partial eta squared = .31. These results show that there was a significant change in post-MTBI fatigue over time but do not give any clues as to what independent variables, apart from time, contributed to the change or how individual participants fared.

The treatment gains were expected to be maintained at follow-up, three months after completion of treatment, and inspection of Table 7.2 shows that to be true. Both treatment and control groups and the whole sample continued to report lower levels of post-MTBI fatigue on all three measures.

Time since injury

The correlations between time since injury, measured in days, and post-MTBI fatigue prevalence and severity measures ranged from $r = .01$ to $r = .4$ for the treatment group and from $r = .001$ to $r = .25$ for the control group. None of these relationships were significant. That is, the length of time since injury measured in days did not impact on severity or prevalence of fatigue after MTBI for any of the participants from either group.

[6] The effect size was reported using the statistic partial eta squared as calculated by SPSS. Partial eta squared effect size guidelines are as follows: - small .01, moderate .06 , large .14. Pallant (2010) referenced these guidelines to pp 284 – 287 in Cohen 1988. Cohen states "SMALL EFFECT SIZE…An $f = .10$ is equivalent to (eta) $\eta = .100$ and (partial eta squared) $\eta^2 = .0099$…MEDIUM EFFECT SIZE… $\eta^2 = .0588$…LARGE EFFECT SIZE… $\eta^2 = .1379$" pp 285-287.

PERT diary of fatigue, energy, naps and exercise duration

Throughout the 12 week PERT programme the treatment group kept a daily record of their fatigue and energy ratings. The weekly fatigue and energy means were analysed to explore change over time within the treatment group.

Figure 7.3 illustrates the change in the treatment group mean for fatigue and energy over the 12 weeks of the PERT programme. Fatigue can be seen to drop steadily throughout the period of the programme. A paired samples *t* test found a significant large reduction in mean fatigue ratings from baseline to the end of the programme at week 12, (t (10) = 3.49, $p < .005$; Cohen's $d = 1.43$).

Inspection of the curves in Figure 7.4, suggested that most of the reduction in fatigue

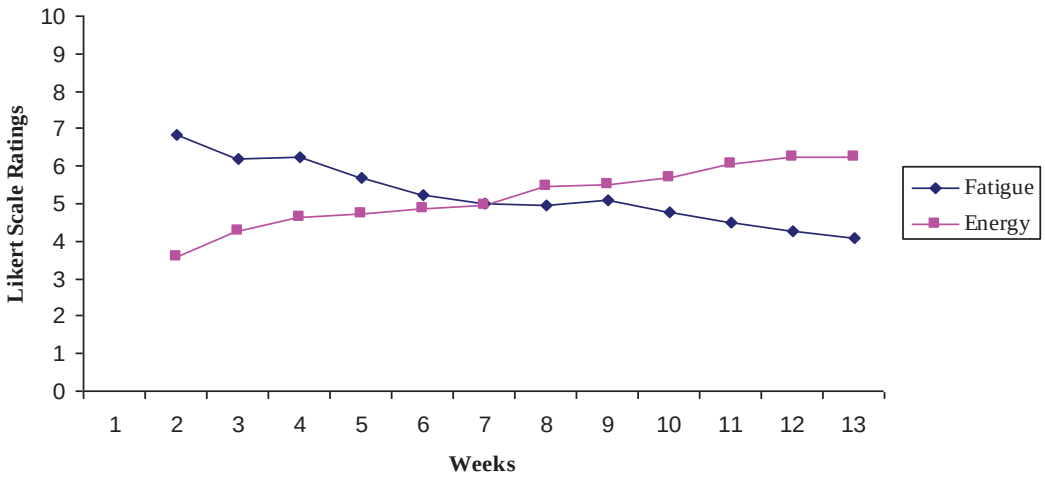

Figure 7.3. Change in energy and fatigue over the 12 week PERT programme

occurred in the first seven weeks and this was confirmed when a large significant effect for time was found between weeks one and seven ($t(10) = 4.04$, $p < .002$;

Cohen's *d* = .99). The smaller change between week seven and week 12 was not significant (t(10) = 1.08, p = .31).

The participants also recorded the duration of their naps and exercise periods in minutes in their diary. As shown on Figure 7.4, there was a significant reduction in nap time over the twelve week programme, $F(1,9) = 9.86$, $p < .05$. However, there was no significant change in exercise duration over the programme, a finding which was consistent with the programme manual which encouraged participants to limit naps to 30 minutes or less and to do 30 minutes exercise each day.

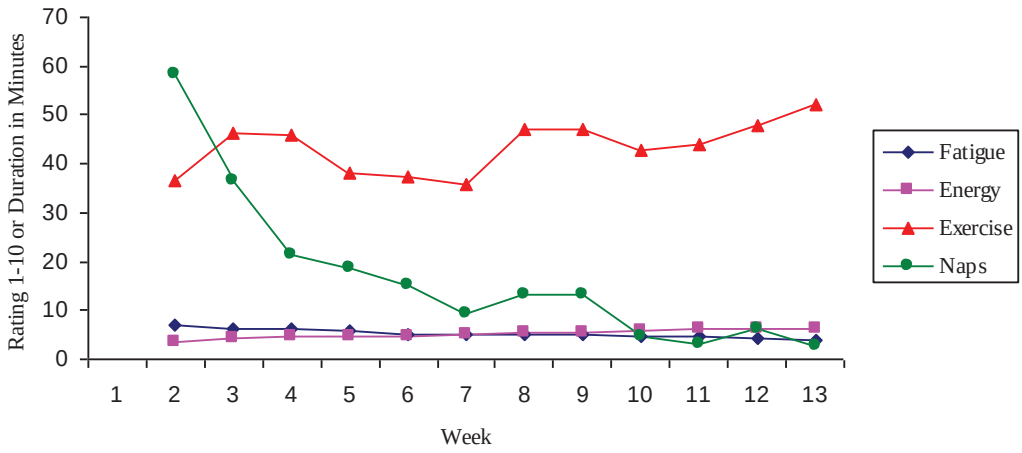

Figure 7.4. Fatigue and energy, exercise and naps in minutes

At baseline the majority of participants (81.2%) were having a nap and by week 12 only (8.3%) while their exercise had increased from a range of 9–102 minutes daily to 18–102 minutes daily. The control group was not asked to keep a similar diary so there is no record of how their fatigue or energy changed within the treatment period.

Daytime naps

One participant was removed from the analysis of daytime naps because his nap time trebled in week 6 when he had the flu, and after that, other major issues going on in his life meant that he did not supply any further diary data although he said he was continuing to exercise regularly. There was no noticeable effect on this or the other analyses when this man's data was withdrawn from the sample. Figure 7.5 illustrates the dramatic drop in nap time over the first six weeks of the PERT programme. Fatigue and energy on the other hand have comparatively flat curves. During the second half of the programme fewer participants were having naps and by week nine the three participants who were still having naps had reduced them to 30 minutes maximum. Only one participant was still reporting naps (mean = 30 minutes) at week 12.

Impact of the PERT programme on secondary outcome measures

As in the case of the post-MTBI fatigue measures, the time by group effects for the secondary measures, HADS Anxiety and Depression and SPRS Occupational Activities, Interpersonal Relationships and Independent Living Skills were not significant. Table 7.3 summarises the results of the mixed between-within subjects ANOVA. There was a trend for a time by group effect for Occupational Activities (SPRS OA) Wilks' Lambda, $F(2,30) = 2.71$, $p = .08$, partial eta squared = .08. However at 50% power this result does not give sufficient confidence to allow rejection, or retention, of the null hypothesis. Whether the PERT programme had any effect, beneficial or otherwise, on the participants' engagement in occupational activities is not made clear by this result.

By this stage in the analysis it was clear that there was little evidence of a positive effect of the PERT programme on post-MTBI fatigue or on most of the secondary outcomes, postconcussion syndrome (RPSQ Total) depression, anxiety, occupational activities, independent living skills, interpersonal relationships, overall psychosocial reintegration (SPRS Total) and the item relating how participants thought their relatives perceived their fatigue-related behaviour.

Table 7.3

Summary of Results of the Within Subjects ANOVA for Secondary Outcome Measures

Outcome Measure	Baseline *M*(*SD*)	3 months *M*(*SD*)	6 months *M*(*SD*)	*F*	*df*	*p*
RPSQ Total				.21	2,33	.81
Treatment	36.44(9.99)	27.56(8.13)	24.06(9.36)			
Control	34.30(10.30)	24.53(8.65)	19.50(10.62)			
HADS Dep				.04	2,33	.21
Treatment	7.96(3.52	6.74(3.69)	5.87(3.74)			
Control	7.29(3.94)	5.67(3.54)	4.97(3.95)			
HADS Anx				1.59	2,33	.22
Treatment	10.13(4.60)	9.87(4.76)	7.80(4.35)			
Control	9.21(4.00)	7.27(3.89)	7.05(3.06)			
SPRS – OA				2.71	2,30	.08*
Treatment	10.33(3.92)	9.85(4.06)	11.08(3.40)			
Control	9.70(3.42)	11.48(2.65)	12.15(2.87)			
SPRS – IR				.33	2,33	.73
Treatment	11.43(2.37)	13.13(2.52)	13.11(2.88)			
Control	11.76(3.45)	12.58(3.49)	13.00(3.22)			
SPRS - ILS				1.05	2,29	.36
Treatment	13.26(2.81)	14.77(1.64)	15.00(1.96)			
Control	14.42(1.74)	14.95(.97)	15.32(.75)			
SPRS Total				.05	2,32	.96
Treatment	34.89(7.69)	38.37(7.47)	39.41(7.31)			
Control	35.6497.33)	39.66(5.61)	40.82(5.54)			
Lazy Item				.82	2,33	.45
Treatment	2.56(2.13)	2.63(2.25)	2.69(1.85)			
Control	2.85(1.95)	3.30(1.84)	2.60(1.43)			
Sleep Disruption				.22	2,34	.80
Treatment	2.06(1.34)	1.87(1.36)	1.56(1.26)			
Control	2.29(1.15)	2.00(1.34)	1.52(1.25)			

RPSQ = Rivermead Postconcussion Symptoms Questionnaire; HADS = Hospital Anxiety and Depression Scale; Dep = Depression; Anx = Anxiety; OA = Occupational Activities; IR = Interpersonal Relationships; ILS = independent Living Skills; Lazy item - "When I am tired my family or partner thinks I am being lazy"; Sleep Disruption = RPSQ Item 5; * $p \leq .1$

The focus will now shift to analysis of the data from the combined groups and this will be presented in Part 2 below.

Part 2: Analysis of Combined Treatment and Control Group Data, i.e., All Study Two Participants

Primary outcome – post-MTBI fatigue

The one-way repeated measures ANOVA revealed a significant large main effect for time for all measures of subjective post-MTBI fatigue (see Table 7.4). RPSQ Item 6, prevalence ($F(2,35) = 13.35$, $p < .000$; partial eta squared =.43) and severity

Table 7.4

Descriptive Statistics for Prevalence and Severity of Post-MTBI Fatigue in the Whole Sample. N = 37

Time	Post-MTBI Fatigue Prevalence RPSQ item 6 *M*(*SD*)	Post-MTBI Fatigue Severity FSS *M*(*SD*)	Post-MTBI Fatigue Severity FAS *M*(*SD*)
Baseline	3.16(.80)	5.17(1.21	28.22(8.54)
3 months	2.52(1.04)	4.85(1.12)	25.36(6.08)
6 months	2.11(1.17)	4.24(1.40)	22.70(6.43)

M = Mean; *SD* = Standard Deviation; RPSQ = Rivermead Postconcussion Symptoms Questionnaire; FSS = Fatigue Severity Scale; FAS = Fatigue Assessment Scale; Only participants with data at each time period were included in this analysis, hence two treatment group participants have been excluded from this analysis and total *N* = 37.

FSS ($F(2,35) = 13.04$, $p < .001$; partial eta squared =.43) and FAS ($F(2,35) = 7.533$, $p < .005$, partial eta squared = .30).

Time since injury

The correlations between time since injury (measured in days) and post-MTBI fatigue (prevalence and severity measures) ranged from r = .02 to r = .14. None of these relationships were significant. Additionally, there were no significant correlations between time since injury and depression, anxiety, total RPSQ, SPRS or its subscales.

Post-MTBI fatigue - reliable clinically significant change

Reliable clinically significant change (RCSC) indices were calculated for the whole sample using Evans' (1998) online calculator by entering the baseline standard deviation and Cronbach's α for each of the fatigue severity measures (FSS SD = 1.21 α = .82; FAS SD = 8.54, α = .90). The resulting RCSC criterion for the FSS measure was ± 1.42 and for the FAS measure was ± 7.49. Change in an individual participant's score (Table 7.5) could be considered reliable and clinically significant if its absolute value was greater than or equal to the relevant criterion. Improvement in fatigue status is indicated by a negative change score hence a change ≤ -1.42 or ≤ – 7.49 indicated RCSC in FSS or FAS respectively. For example, participant 6 in Table 7.5 is exhibiting a reliable clinically significant change (reduction or improvement) in post-MTBI fatigue both at three months and six months post-baseline for both post-MTBI fatigue measures, FSS and FAS. Whereas participant 1 did not exhibit a change in the first three months and despite having negative scores on both measures at six months, there was only reliable clinically significant change (reduction) in the FAS, but not the FSS score, at 6 months (FSS > -1.42, FAS < -7.49). It can be seen from Table 7.5 that there were some participants whose post-MTBI fatigue increased over the six month study period.

Some of the participants' post-MTBI fatigue scores showed a reliable clinically significant deterioration during some part of the six months of the study. For example, participant 32 exhibited a reliable clinically significant change, an increase of 2 points on the FSS and, an increase of 10 points on the FAS at three months. Increases in both scale scores indicate increased post-MTBI fatigue and therefore deterioration in that symptom. However, at six months, the same participant is showing positive changes (FSS change score = -.89; FAS change score = 1.00) in the scores compared with the baseline score. Nevertheless, the changes are not reliable clinically significant changes as the change scores are greater than the reliable change indices (FSS, -1.42; FAS, -7.49), relevant to each measure.

While Table 7.5 lists the size of the change data for each of the 39 participants for whom data was available, it is not easy to appreciate from Table 7.5 the relatively persistent nature of post-MTBI fatigue. That is, while a significant positive change over time was found for post-MTBI fatigue severity there is a large percentage of the whole sample who either made no reliable clinically significant change or actually deteriorated. Table 7.6 presents the RCSC data summarised into three groups: no significant change, significant deterioration and significant improvement. RCSC is specific to both measure and time period although there is a general pattern evident.

Over half the sample made no reliable clinically significant change over the six months, supporting the common perception that post-MTBI fatigue is a persistent symptom. Up to a third of the participants showed improvement in post-MTBI fatigue by the end of the study period and a small proportion exhibited increased post-MTBI fatigue (see Table 7.6).

Table 7.5

Change Scores for the FSS and FAS Measures at 3 and 6 Months Post Baseline

ID	FSS Change scores		FAS Change scores	
	Baseline - 3 mths	Baseline - 6 mths	Baseline - 3 mths	Baseline - 6 mths
c	.00	-1.11	.00	-20.00**
2	1.22	.44	.00	-6.00
3	1.44	1.44	5.00	5.00
4	.67	-1.11	-4.00	-1.00
5	1.67	-.56	-8.00**	-6.00
6	-1.89*	-2.67	-12.00**	-10.00**
7		-1.00		2.00
8	-.67	-.78	-1.00	-18.78**
9	-2.03*	-1.69*	7.00	12.00
10		.11		4.00
11	1.44	-.56	11.00	8.00
12	-.61	-.11	-12.00**	-17.00**
13	-.33	.00	6.00	-1.00
14	-2.94*	-2.94*	7.00	4.00
15	-.67	-.89	-12.00**	-10.00**
16	-.89	-1.22	-9.00**	-9.00**
17	-.14	-1.58*	17.00	19.00
18	.00	-2.44*	-7.00	-9.00**
19	-.11	-.11	. 00	.00
20	-2.00*	-1.00	-27.78**	-22.78**
21	-.44	-.89	-4.00	-5.00
22	.78	1.00	-12.44**	-12.44**
23	-.67	-1.56*	-1.00	-3.00
24	.26	-1.74*	-14.00**	-14.00**
25	.22	-1.56*	1.00	-4.00
26	.33	-1.67*	-2.00	1.00
27	-.44	-.22	-8.00**	-8.00**
28	-1.33	.44	-6.00	-7.00
29	-3.56*	-2.44*	-11.00**	-8.00**
30	1.78*	-3.33*	-14.00**	-18.00**
31	.11	.22	-3.00	-4.00
32	2.00	-.89	10.00	1.00
33	-.11	-2.56*	-2.00	-10.00**
34	.89	-.11	18.00	.00
35	-1.33	-.78	-16.00**	-16.00**
36	-.56	-.89	1.00	-10.00**
37	1.11	-.56	.22	-6.44
38	-.44	-.78	-2.00	-7.00
39	-.78	.89	-1.00	9.00**

FSS = Fatigue Severity Scale, FAS = Fatigue Assessment Scale; * Change score ≤ -1.42; ** Change score ≤ -7.49

A one-way ANOVA or Chi square (as relevant) demonstrated that there was no significant difference between these three groups for time since injury, age, LOC period, accident type, work type, treatment/control group for either of the post-MTBI fatigue measures, FSS and FAS. There was a significant difference between change status and gender from baseline to three months for the post-MTBI fatigue measure

Table 7.6

Summary of the Change Status of Participants at 3 and 6 Months for the Post-MTBI Fatigue Severity Measures FSS and FAS

Condition	FSS - RCSC ± 1.42		FAS - RCSC ± 7.49	
	Baseline - 3 mths *N*(%)	Baseline - 6 mths *N*(%)	Baseline - 3 mths *N*(%)	Baseline - 6 mths *N*(%)
No RCSC	29(74)	25(64)	21(54)	19(49)
RCSC indicates deterioration	4(10)	2(5)	5(13)	4(10)
RCSC indicates improvement	6(16)	12(31)	13(33)	16(41)
Total	39(100)	39(100)	39(100)	39(100)

RCSC = Reliable Clinically Significant Change, FSS = Fatigue Severity Scale; FAS = Fatigue Assessment Scale

FAS (X^2 = (2, N = 39) = 8.74, $p < .05$) but by six months three of the males had moved into the RCSC improvement category and there was no significant difference for gender ($p > .1$).

Study One: Post-MTBI fatigue - reliable clinically significant change

Study One also employed the FSS as an outcome measure making it possible to compare the FSS change scores in the two samples from Study One and Two. The pattern for both studies was that the majority of participants exhibited no reliable clinically significant change over either period – baseline to three months and baseline

to six months. A small percentage (≤ 10%) deteriorated and less than a third of participants exhibited reliable clinically significant improvement. Comparison of FSS RCSC results from Table 7.4 with those from Study One (N = 159) showed no RCSC in post-MTBI fatigue over three months in 78.6% (74% in Study Two) of the sample, deterioration in 3.8% (10% in Study Two) and improvement in 17.6% (16% in Study Two). Similarly over the baseline to six months period there was no change in 76.1% (64% in Study Two), deterioration in 3.1% (5% in Study Two) and improvement in 20.8% (31% in Study Two). Factors such as age and gender did not discriminate between those who exhibited reliable clinically significant change in either direction and those who did not.

Effect for time - secondary outcome measures

Table 7.7 shows the means and standard deviations as well as the results of one way repeated measures ANOVAs for the secondary outcomes. There was a significant large reduction over time in postconcussion symptoms, depression and anxiety. There were also significant increases in scores for occupational activities, independent living, interpersonal relationships and psychosocial reintegration over the period of the study.

There was not a significant change in participants beliefs about whether their significant others thought them lazy. However, the mean ranged from 2.72 to 3 over the six months, that is, it was below the midpoint of the Likert scale rating (1 – 7) and, less than a third (30%) of the whole sample was troubled by this belief.

Table 7.7

Summary of Results of One-way Repeated Measures ANOVA for Secondary Outcome Measures

Outcome Measure	**Baseline *M*(*SD*)**	**3 months *M*(*SD*)**	**6 months *M*(*SD*)**	***F***	***df***	***p***	***partial eta squared***
RPSQ Total	35.25(10.08)	25.88(8.45)	21.53(10.20)	28.12	2,34	.001	.62
HADS Dep	7.56(3.73)	6.12(3.59)	5.34(3.83)	4.67	2,34	.016	.22
HADS Anx	9.60(4.22)	8.35(4.40)	7.36(3.61)	9.79	2,34	.001	.37
SPRS – OA	9.95(3.58)	10.84(3.32)	11.73(3.09)	10.25	2,31	.001	.40
SPRS - IR	11.62(3.01)	12.81(3.09)	13.04(3.04)	3.34	2,34	.047	.16*
SPRS – IL	13.95(2.27)	14.87(1.26)	15.19(1.36)	6.60	2,30	.004	.31
SPRS Total	35.32(7.38)	39.11(6.40)	40.21(6.30)	10.32	2,33	.001	.39
Lazy Item	2.72(2.01)	3.00(2.03)	2.64(1.61)	.72	2,34	.494	.04
Sleep Disruption	2.19(1.22)	1.95(1.33)	1.54(1.24)	5.64	2,35	.008	.24

RPSQ = Rivermead Postconcussion Symptoms Questionnaire; HADS = Hospital Anxiety and Depression Scale; Dep = Depression; Anx = Anxiety; OA = Occupational Activities; IR = Interpersonal Relationships; ILS = independent Living Skills; Lazy item - "When I am tired my family or partner thinks I am being lazy"; * power 60%;

Part 3: Post Hoc Questions Arising from Findings of Reliable Clinically Significant Change Analysis

The finding that over half of the whole sample made no reliable clinically significant change (RCSC) in fatigue over the six months of the study raised questions about whether there were differences in fatigue-related RCSC distribution between the treatment and control groups and what, if any, relationships there were between RCSC and secondary outcome measures. Question 1 looks at differences between the treatment and control groups for fatigue-related RCSC. Question 2 looks at the relationship between fatigue-related RCSC and secondary outcome measures while question 3 looks specifically at the relationship between fatigue-related RCSC and occupational activities. All results in Part 3 relate to the treatment verses control data presented in Part 1 of the results.

What other interactions were there between RCSC status and secondary outcome measures? There was a moderate to strong significant relationship between depression and RCSC for both fatigue severity and prevalence at each time period (range r = .42 to r = .78) and a weaker but significant correlation between post-MTBI fatigue RCSC and anxiety (range r = .28 to r = .42). Mixed between-within ANOVAs found a significant large interaction effect, time by group, (RCSC baseline to three months status, Table 7.4) for depression (Wilks' Lambda = .75, F(4,64) = 2.54, $p < .05$, partial eta squared = .14) with 68.6% power. There were no significant time by group interaction effects for FSS-based RCSC baseline to six months for either depression or anxiety.

On the other hand, the FAS-based RCSC showed large interaction effects for time by group for the two dependent variables depression and anxiety at all intervals, i.e., baseline to three months, baseline to six months and three to six months. Results for the interaction, RCSC baseline to three months by time, for depression was Wilks' Lambda = .70, F(4,64) = 3.10, $p < .05$, partial eta squared = .16 and for anxiety was Wilks' Lambda = .52, F(4,64) = 6.16, $p < .001$, partial eta squared = .28. The results for the interaction, RCSC baseline to six months by time, for depression was Wilks' Lambda = .65, F(4,64) = 3.81, $p < .01$, partial eta squared = .19 and for anxiety was Wilks' Lambda = .60, F(4,64) = 4.64, $p < .005$, partial eta squared = .23. SPSS results indicated power for these interactions ranged from 78.4% to 98%.

Two things stand out from these results; firstly, change in post-MTBI psychological status is consistent with change in post-MTBI fatigue status at least for the FAS measure giving support to those who argue for psychogenic rather than neurogenic

explanations for persistent postconcussion symptoms. Secondly, despite the relatively high significant correlations between the two fatigue measures FSS and FAS ($r > .5$, $p < .01$ in all cases) they often interact very differently with other variables such as depression.

Is there a relationship between RCSC status and independent variables such as occupational activities? Post-MTBI fatigue is significantly negatively correlated with occupational activities for both fatigue measures FSS ($r = -.54$ to $-.69$, $p < .005$) and FAS ($r = -.50$ to $-.63$, $p \leq .001$). There was no significant time by group effect, occupational activities by RCSC status for the FSS, however, there was a trend for a large time by group effect for occupational activities and RCSC status for the FAS with a moderate level of power (Wilks' Lambda = .743, $F(4,58) = 2.33$, $p = .07$, partial eta squared = .14, power of 64%. These finding suggest that as post-MTBI fatigue (FAS) reduces there is a reliable clinically significant trend for individuals to become more involved and satisfied with their occupation.

Chapter 7 presented Study Two, a longitudinal investigation of the effectiveness of a post-MTBI fatigue treatment programme and the results both of the controlled study and a subsequent analysis of the combined group data. This brings to an end the experimental part of the thesis and leads into Chapter 8 - a discussion of the wider project; its contribution to the literature on post-MTBI fatigue; the limitations; and, suggestions for ongoing research which could help clinicians to identify effective interventions for post-MTBI fatigue.

Chapter 8

DISCUSSION

Post-MTBI fatigue interferes with recovery, participation and quality of life for long periods of time post injury. The need for research in the area of post MTBI fatigue became apparent to the author during her clinical experience in a New Zealand Concussion Clinic. Previous studies found post-MTBI fatigue prevalence rates ranged from 22% to 59% at three months and longitudinal studies have listed post-TBI fatigue among the symptoms lingering for months and years (Hillier et al., 1997; McCullagh et al., 2001; Middleboe et al., 1992; Sundstrom et al., 2007). Studies of post-concussion symptoms in both MTBI and healthy samples have shown fatigue to be more prevalent within the MTBI population than in the healthy controls (Kashluba et al., 2004a; Stulemeijer et al., 2006; Yang et al., 2007). It is one of the three most common symptoms of mild traumatic brain injury (MTBI) (Kashluba et al., 2004b; Mittenberg et al., 2001; Mittenberg et al., 1992; Ziino & Ponsford, 2005a), yet this common postconcussion symptom has attracted little research attention to date.

Given then that post-MTBI fatigue presents a major barrier to returning to full pre-injury participation for so many people, and that there is so very little in the scientific literature to guide intervention, further investigation was clearly warranted.

The current research comprises two post-MTBI fatigue studies: Study One, which examined the prevalence of post-MTBI fatigue in a New Zealand sample; and Study Two, which examined the effectiveness of a treatment approach in reducing post-MTBI fatigue. Subsequently, the data from the Study Two treatment and control groups was combined and analysed to re-examine the hypotheses and to determine

whether there were reliable clinically significant changes in individual participant's post-MTBI fatigue over the six month period each was involved in Study Two.

Study One demonstrated that the prevalence and severity of post-MTBI fatigue in a New Zealand sample fell within the same ranges at three months and longer post injury, as reported in previous international studies (Rao et al., 2005). In the current study, fatigue was examined in the first six months after MTBI using a prospective longitudinal design whilst excluding known confounding factors such as litigation, presence of psychological or neurological disorders, and substance abuse. Importantly while previous studies used mixed TBI severity samples (Olver et al., 1996; Ziino & Ponsford, 2005a), Study One included only those who had a mild TBI thus providing specific evidence regarding the role of fatigue after *mild* head trauma. Doubt has previously been cast on the aetiology of persistent postconcussion symptoms, including post-MTBI fatigue as being attributable to injury within the brain. It has been suggested instead that baseline characteristics are more likely than mild brain injury to account for fatigue at extended periods post MTBI (de Leon, Kirsch, Maio, Tan-Schriner, Millis, Frederiksen, et al., 2009).

Litigation, a post injury characteristic has been shown to inflate symptom reporting and be a predictor of persistent postconcussion symptoms including fatigue (Belanger et al., 2005; de Leon, Kirsch, Maio, Tan-Schriner, Millis, Frederiksen, et al., 2009). Hence when the opportunity arose in 2005 to investigate the prevalence of post-MTBI fatigue in a New Zealand population where litigation has been controlled by the provision of a government sponsored, no fault, universal accident insurance, Study One was conceived. Study One prospectively examined post-MTBI fatigue prevalence

and severity, its predictors and its co-variates over the six months immediately following the MTBI. Additional baseline factors such as presence of psychological or neurological disorders and substance abuse were exclusion factors allowing a more precise measure of the prevalence and severity of post-MTBI fatigue without these confounds complicating the findings.

The results indicated that post-MTBI fatigue is a persistent postconcussion symptom, which at 26.4% is more prevalent at six months post MTBI than would be expected given the base rate (8.26%) of six month long fatigue in the general population (Evengard et al., 2005). That over a quarter of the people who present to the Emergency Department of a major New Zealand hospital with symptoms of a mild traumatic brain injury continue to report post-MTBI fatigue at six months suggests the need to look for ways to ameliorate its impact on their lives. Kay et al. (1992) noted that the frequency or prevalence of any postconcussion symptom was insufficient to distinguish those with MTBI from the normal population and suggested including severity measures when describing the presence of postconcussion symptoms. In Study One, post-MTBI fatigue severity ratings demonstrated that over a third of the sample reported clinical level post-MTBI fatigue. The generally accepted heuristic of $\geq 1SD$ above the general population mean was used to delineate the clinical level of severity. With this level of prevalence and severity it was surprising to discover that there was such a paucity of research into treatment for this symptom, regardless of whether it was psychogenic or neurogenic in origin.

Recovery from concussion or MTBI usually occurs within the first three months post injury (McCrea, 2008). While the majority of Study One participants no longer

reported significant post-MTBI fatigue at three months post injury there was still a third who were symptomatic and there was no significant change in the percentage of individuals reporting fatigue prevalence (RPSQ) or severity (FSS) in the next three month period. This finding suggested that it is important to identify those at risk of post-MTBI fatigue as early as possible to improve treatment targeting; however, this also begs the question as to date there is no proven, effective, treatment for post-MTBI fatigue. Study One results demonstrated that the immediate post injury score on a single self-report item (item 6) from the RPSQ postconcussion checklist accounted for a small (4%) percentage of the variance in fatigue severity, FSS score, at six months. However, as Kay et al (1992) recommended, symptom severity was found to be a better predictor of subsequent persistence. That is, the immediate post injury FSS score, which accounted for 24% of the variance in the six month FSS score, was more likely to identify those who are in need of a post-MTBI fatigue intervention to prevent it becoming a persistent symptom. Additionally, the severity of post-MTBI fatigue at three months was a strong predictor of fatigue problems at six months post-MTBI as it accounted for 56.7% of the variance of fatigue severity at six months.

While there was no significant change in the percentage of individuals with MTBI reporting fatigue prevalence (RPSQ) or severity (FSS) between three and six months, there was a significant increase in the percentage of those reporting depression and/or anxiety above the cutoff for mild problems at six months compared with reports at three months. This increase coincides with a levelling-off of the fatigue percentages within the sample population. A strengthening positive relationship has previously been found between perceived stress and intensity of postconcussion symptoms over time (Machulda et al., 1998). Study One examined this relationship in more detail with

respect to fatigue, anxiety and depression and found a pattern which suggests persistent symptoms are associated with increased distress as illustrated by enduring elevated fatigue, anxiety and depression scores. Also, contrary to Ziino and Ponsford's (2005a) finding, depression (but not anxiety) *was* a significant predictor of post-MTBI fatigue. When depression was held constant other factors such as pain and poor sleep did not contribute significantly to post-MTBI fatigue. The clinical implications of these findings are that both fatigue and psychological factors require treatment early to prevent symptoms becoming persistent barriers to recovery and reintegration. However, whether the increased psychological symptoms are related to fatigue, to neurological sequelae (e.g., neurotransmitter disruption within the HPA pathway) or to pre-morbid psychological conditions, remains unclear and could not be determined from the current study.

The opportunity was taken during the current study to explore the prevalence of post-MTBI fatigue sufferers being considered 'lazy', by their significant others. Such a perspective could impact both on the type of support received and the emotional health of the post-MTBI fatigue sufferer. Social support and self efficacy are important factors which facilitate recovery (Cavallo & Kay, 2005). On the other hand, critical non-supportive beliefs among family and friends could potentially slow a person's recovery from post-MTBI fatigue and exacerbate psychological reactions such as depression, anxiety or personality disorders (Ruff, 1996). If for instance, the injured individual's significant others interpret fatigue-related behaviours such as resting and loss of interest or motivation as laziness there could be a negative impact on post-MTBI fatigue recovery. Additionally, there is a heightened risk of persistent postconcussion symptoms when the individual believes that symptoms such as post-

MTBI fatigue may have serious negative consequences on their lives (Whittaker et al., 2007). This issue was briefly touched on in Study One through the addition to the FSS scale of a question about how significant others perceived fatigue-related behaviour. Approximately thirty percent of the participants in Study One endorsed the belief that their significant others perceived them as lazy when they engaged in fatigue-related behaviours. Within the whole sample there was a significant small correlation between post-MTBI fatigue and being thought lazy which increased to a large correlation at three months and then levelled out with no significant change by six months. The correlation between the belief that fatigue-related behaviours indicated laziness and depression increased from small through moderate to large over the six months. This finding gives support to Whittaker et al's (1997) contention that the individual's perceptions about their symptoms can negatively impact on their well being and recovery. The one question phrased as it was not only taps the perception of the injured individual but also begs other complementary questions about what significant others *actually* believed. Whittaker et al. wrote of not knowing how individuals' perceptions of symptoms affect outcomes and of the possibility of tailoring cognitive behavioural programmes to target illness perceptions. The correlations between being perceived as lazy, post-MTBI fatigue and depression suggest found in Study One open the door to further research into how perceptions about one's own and others' symptoms and symptom-related behaviour impact on one's recovery from MTBI. It also provides information to support development of treatment programmes which address cognitive distortions or misperceptions; for instance, through providing psychoeducation, not only to the individual with MTBI, but also to their significant others.

Study One led onto examination of treatment for post-MTBI fatigue. There has only been one treatment study specifically targeting post-(M)TBI fatigue published to date (January 2012). This was a randomised placebo controlled study of the effectiveness of Modafinil for treating fatigue in a mixed TBI-severity (25.5% MTBI) sample (Jha et al., 2008b). No clinically significant difference was found between the treatment and the placebo. Study Two set out to address this gap in the post-MTBI fatigue literature by evaluating the effectiveness of a post-MTBI fatigue treatment based on psychoeducation and aerobic exercise.

Some studies of the effectiveness of treatment for postconcussion symptoms list the results for each symptom including post-MTBI fatigue (Bell et al., 2008; Kashluba et al., 2004b; Mittenberg et al., 1996) and these provided valuable information about possible strategies, e.g., psychoeducation, to include in a post-MTBI fatigue treatment programme. Fatigue is a common symptom in other illnesses such as Chronic Fatigue Syndrome (CFS), Multiple Sclerosis (MS) and cancer and the review of that literature suggested aerobic exercise and cognitive behaviour therapy (CBT) (Fulcher & White, 1997; R Meeusen, 2005; Mostert & Kesselring, 2002; Motl & Gosney, 2008; Puetz et al., 2006; M. R. Schulz et al., 2004) combined held out the best hope of reducing subjective fatigue in the post-MTBI population. This was further supported by the reviews of post-TBI fatigue treatment literature (Fellus & Elovic, 2007; Rao et al., 2005) which depended largely upon information drawn from other illness cohorts. Fellus & Elovic's review recommended an interdisciplinary team approach, exercise, psychoeducation, pharmacology, antidepressants, gingko biloba, and ginseng as possible treatments for post-TBI fatigue. However, no *mild* TBI specific

fatigue treatments were cited. The lack of research into post-MTBI fatigue treatments motivated the author to design and evaluate a treatment for post-MTBI fatigue.

To guide the design of a post-MTBI fatigue treatment programme, earlier models of persistent postconcussion syndrome and of post-MTBI fatigue were consulted. Over the last thirty years, models of persistent postconcussion syndrome have pulled together a wide range of factors from the purely organic through psychological to environmental factors. Two models which stand out for their inclusiveness of this range of factors are the neuropsychological model of functional disability after mild traumatic brain injury (Kay et al., 1992) and the patient-oriented model (Ruff, 2005). Both take an holistic ecological approach recognising that the MTBI occurred within the individual's internal (personal) and external (environmental) context. The context has an effect on how the individual reacts to their MTBI and also influences the development of feedback loops that reinforce and exacerbate these reactions. Rao et al.'s (2005) model of post-MTBI fatigue pulled together organic and functional changes (sleep dysfunction) and psychiatric symptoms (depression and anxiety) to compose a model of post-MTBI fatigue. In the author's clinical neuropsychology practice she became aware that the model for post-MTBI fatigue needed to be broader to take in the individual's context (e.g., social, financial, relational, cultural, recreational, spiritual) within which the MTBI had occurred. Hence the ecological post-MTBI fatigue model (Figure 3.3), upon which the treatment evaluated in Study Two was based, was constructed by drawing together the Kay et al.'s and Ruff's models of postconcussion syndrome and Rao et al.'s post-MTBI fatigue model. The treatment uses psychoeducation and aerobic exercise to address the factors expressed in the model. For instance, Kozlowski's (2008) study demonstrated that aerobic

exercise helps to reduce the impact of post-MTBI on neurophysiological changes such as dysregulation of the autoregulatory system (Giza & Hovda, 2001; Leddy et al., 2007). Exercise is also a well-established component of treatment for psychological and sleep problems (Lange et al., 2005; Barbour, et al., 2007), two other factors incorporated into the proposed post-MTBI fatigue model. Psychoeducation addresses psychological factors by providing knowledge about post-MTBI fatigue, thereby both demystifying the phenomenon and providing information about how to reduce it and to avoid adopting maladaptive psychological and behavioural responses such as excessive rest, worry, fear, anger, blame, too little or too much activity, too little or too much social engagement.

Study Two was the evaluation of the effectiveness of the PERT programme in reducing post-MTBI fatigue, and other postconcussion symptoms such as depression, anxiety, sleep disorder and in increasing social reintegration. The results of the quasi-experimental pre-post-follow-up design did not find a significant time by group effect for any of the outcome measures of post-MTBI fatigue, depression, anxiety or social reintegration. Additionally, factors such as acute symptoms, mechanism of injury, time since injury and higher education levels which have been shown to be associated with post-TBI fatigue (Ouellet & Morin, 2006; Stulemeijer et al., 2006; Ziino & Ponsford, 2005a) were not found in Study Two to be significantly related to post-MTBI fatigue. Litigation, another predictor of persistent postconcussion symptoms including fatigue (Belanger et al., 2007; Binder & Rohling, 1996; Iverson, 2005), was not a relevant factor as the study was carried out with a New Zealand sample who were all covered by the government sponsored, no fault accident insurance.

During the search for explanations for the findings of no significant difference between the treatment and control groups, it was discovered that the two conditions were more similar than had been expected. A majority of the control group had engaged in physical exercise and/or had access to psychoeducation sources (psychologist or occupational therapist) beyond their initial assessment. Subsequent analysis of the combined treatment and control group data, found significant positive changes for all outcome measures – post-MTBI fatigue, depression, anxiety and social reintegration - demonstrating that, for the group data, symptoms were improving over time. The literature reports that acute post MTBI symptoms resolve quickly in 85% to 99% of MTBI patients; 7-10 days for simple, uncomplicated sports concussion and 3 and 12 months in complex, complicated (space occupying lesions or multiple MTBI) sports concussion (Carroll, Cassidy, Peloso, et al., 2004; Iverson, 2005; Katz & DeLuca, 1992; McCrea, 2008; Ruff, 2005). Hence it might not be considered surprising that the group data for Study Two found a significant positive change over time. However, even McCrea's (2008) estimate that just 1% of individuals have ongoing symptoms following an MTBI, allows for some individuals to continue to be symptomatic. Hence it made sense to examine each participant's results for information about what was happening on an individual level; for instance was there clinically significant change.

Before moving on to examination of individual data one further aspect of Study Two warrants discussion. All of the participants in the treatment group were asked to keep a daily record of their fatigue and energy levels and the length of time they spent exercising or napping.

Having the treatment group participants keep a diary of their fatigue and energy as well as their exercise and naps was valuable as it allowed monitoring of when meaningful change was occurring and when it had slowed down. It also gave an opportunity to explore beyond statistical comparison of treatment and control groups to examine the clinical significance of the changes made within the treatment group. It was hypothesized that PERT programme participants would report improvement in energy and reduction in fatigue over the course of the study. Analysis of the treatment group's daily ratings of fatigue revealed a clinically significant pattern of reduction in post-MTBI fatigue over the twelve week programme. Unfortunately the study design did not allow for gathering similar diary data from the control group thereby preventing a comparison of the daily manifestation of post-MTBI fatigue across the two samples.

The reduction in post-MTBI fatigue in the first seven weeks of the PERT programme was found to be a reliable clinically significant change. Although there was ongoing reduction in post-MTBI fatigue over the latter weeks of the programme, the change was neither reliable nor clinically significant, suggesting it had plateaued. This pattern of response to the programme raises questions about possible explanations for the slowing of improvement. In the Kozlowski (2008) study, the athletes' fitness level was assessed monthly and their exercise dose adjusted accordingly. Adding an objective fitness measure and adjustment of the exercise dose at regular intervals could help to maintain improvement. On the other hand, further observation of the natural course of improvement in post-MTBI fatigue during the PERT programme in a larger sample could show that a plateau is normal and the individual could be encouraged to continue

the effort for longer than 12 weeks. Additionally, tapering off in fatigue reduction indicates when a client is ready to exit the PERT programme.

Finding that there was no significant time by group effect but that there was a significant effect for time, led into the third section of data analysis. In this section, each participant's data was analysed to determine whether the changes in post-MTBI fatigue group means over time reflected reliable clinically significant change within individuals and also what percentage of the participants exhibited this type of meaningful change. Clinicians - psychologists, neuropsychologists, occupational therapists, medical specialists - who work with individual clients are interested in knowing whether their client's change in post-MTBI fatigue status is reliable (i.e., not due simply to measurement error) and clinically significant (i.e., there is a greater likelihood of the score being in the normative rather than dysfunctional distribution) (C. Evans et al., 1998; Jacobson et al., 1984; Jacobson & Truax, 1991; Strauss et al., 2006). The Reliable Change Index (RCI) (Christensen & Mendoza, 1986; Jacobson et al., 1984; Jacobson & Truax, 1991) is a distribution–based measure of intra-individual change over time which indicates both the reliability and clinical significance of changes in scores. Data from Study One and Two were analysed separately but the findings were similar in that over 70% of participants showed no reliable clinically significant change (RCSC) in the first three months and between 64% and 76% (FSS and FAS respectively) showed no RCSC from baseline to six months.

These results speak to the findings of several studies (Mickeviciene et al., 2002; Mittenberg et al., 1992; Ouellet & Morin, 2006; Sundstrom et al., 2007) that post-MTBI fatigue is a persistent symptom which endures for months and years post injury.

Of those who did exhibit reliable clinically significant change over the six months of the research about 5% deteriorated. Factors such as time since injury, age, LOC period, accident type and work type showed no significant relationship with post-MTBI fatigue change status over the six months in either study. Female gender has been found to correlate with prevalence of fatigue both in the general population (Kapella et al., 2006; Tiesinga et al., 1999) and in TBI samples (Cantor et al., 2008). However, the relationship between gender and recovery from post-MTBI fatigue was more tenuous. More females reported reliable clinically significant change at three months post-baseline measure but even this difference disappeared at six months when there was an increase in the number of men reporting improvement. None of the above factors were found to discriminate between those who exhibited reliable clinically significant change in either direction and those who did not. Hence there was little indication from either study of which factors might differentiate those whose post-MTBI fatigue improved over time from the rest of the sample.

A feature that stands out when reviewing fatigue and post-MTBI fatigue literature is the wide range of fatigue measures employed. Several studies (Chipchase, Lincoln, & Radford, 2003; Mead et al., 2007; Merritta, Cherian, Macaden, & John, 2010; Michielsen, De Vries, et al., 2004; Neuberger, 2003; O'Connor, 2004; Ziino & Ponsford, 2005a) report comparison of fatigue measures, usually four or five different measures, with little crossover among the measures chosen for each study. Whether all these instruments measure the same construct, fatigue, is one of the questions addressed by these studies. For instance, Michelson et al., (2004) compared four measures which when combined were found to be unidimensional for fatigue. From those four measures they constructed the Fatigue Assessment Scale which was also

found to be unidimensional for fatigue but used just 10 items. The FAS differed from the other fatigue measure, FSS, in that the latter principally measures specific types of functioning, e.g., "Fatigue interferes with carrying out certain duties and responsibilities" rather than intensity of fatigue related symptoms (Dittner, Wessely, & Brown, 2004). The FAS, on the other hand, measures a more generalised impact of fatigue on symptoms, e.g., "I have problems starting things". The results of the RCSC reported in Table 7.4 demonstrate that different fatigue scales produce different fatigue profiles. For instance double the number of participants was deemed to have reported reliable clinically significant change based on responses to the FAS compared with responses to the FSS. It is not within the scope of this thesis to examine the reasons for this discrepancy but it is important to note that any assertions made about post-MTBI fatigue could be contingent upon the measure used to collect the evidence. On the other hand, neither post-MTBI fatigue measure was significantly correlated with factors such as time since injury, loss of consciousness or GCS.

Contribution to Current Research

This thesis has made unique contributions to the MTBI and PCS literature on fatigue in a number of ways. Both studies were carried out with New Zealand samples which were free of the impact of litigation. This was significant as litigation has frequently been found to be a confound in previous international studies. Study One investigated the prevalence and severity of post-MTBI fatigue in a New Zealand sample free of the litigation confound. Study Two was only the second attempt at investigating the effect of a post-MTBI fatigue treatment programme and the first to use psychoeducation combined with exercise.

Study One had the advantage of being a prospective study meaning the early (six month) history of post-MTBI fatigue could be documented. Two important findings were that, consistent with previous literature on the history of postconcussion symptoms, post-MTBI fatigue resolved by three months in the majority of the sample. However, from that point on there was a levelling off in the percentage of individuals reporting post-MTBI fatigue, thus highlighting a possible intervention point to prevent the development of persistent post-MTBI fatigue. It could also indicate the need to start post-MTBI fatigue interventions within the first three months post injury to reduce the number of individuals still reporting fatigue difficulties beyond three months. Study One also contributed to the post-MTBI fatigue literature by employing both prevalence and severity measures, as recommended by Kay et al. (1992), and thus broadening the picture of what is going on with post-MTBI fatigue over time. Another contribution to current research on post-MTBI fatigue was made when depression was shown to be a predictor of post-MTBI fatigue and hence likely to be an important target for early post-MTBI fatigue intervention. Finally, the preliminary investigation in Study One into an aspect of social support, self efficacy and illness perceptions, being seen as lazy when exhibiting post-MTBI fatigue-related behaviours, was a unique contribution to the literature. This was the first time that this particular issue has been addressed in this context and there was a relatively high incidence, 30%, of positive responses to the question of whether the individual with post-MTBI fatigue believed they were being perceived as lazy. It has been shown that individual's perceptions about their symptoms can negatively impact on their wellbeing and recovery (Whittaker et al., 2007). The laziness question was less direct but equally poignant as it speaks to the individual's self efficacy and suggests the need to sample the significant others' perceptions directly. Additionally, the finding further supports

the need for psychoeducation for both the injured individual and their supporters regarding post-MTBI fatigue.

A further aim of the thesis was to evaluate the effectiveness of an exercise and psychoeducation based treatment specifically targeting post-MTBI fatigue. At the time Study Two was only the second attempt to find a treatment for post-MTBI fatigue, the other being a pharmacological study which did not show a positive outcome for the treatment. Although Study Two was not able to demonstrate an effective treatment for post-MTBI fatigue it highlighted an important aspect of the New Zealand community which needs to be taken into account. There is a high level of voluntary involvement in physical exercise in New Zealand and therefore there is a need to carefully control for this in research on the effectiveness of exercise as a treatment mode. On the other hand, because exercise is a common form of behaviour in the New Zealand population and given its proven therapeutic effects in other situations, it warrants further investigation in the treatment of post-MTBI fatigue.

Reporting findings for a mixed TBI severity group is likely to mask the 'real' picture for both the mild and the more severe injuries where disability is very often permanent and profound. Both current studies drew samples exclusively from the population of those who have had a *mild* traumatic brain injury adding value to the current literature by avoiding the possible confound of mixed TBI severity samples.

Clinicians work with individual clients and are interested in change within that individual. An important contribution to the post-MTBI fatigue literature resulted from the finding that the majority of the participants from Study Two did not show a

clinically significant improvement in post-MTBI fatigue. That is, it is a *persistent* postconcussion symptom and while the search for a treatment should proceed, treatment may also focus on living with post-MTBI fatigue rather than expecting to get rid of it.

Although the results of Study Two did not support the use of psychoeducation and exercise as treatments for post-MTBI fatigue, some beneficial effects were observed during the implementation of the PERT programme and on to the present day (early 2012). The explanation of post-MTBI fatigue as a consequence of neuronal regionalisation and lateralisation combined with Mendez et al.'s (2005) illustration has been enthusiastically received by the PERT programme participants and many others who have attended the Concussion Clinic in Palmerston North in recent years. This feature alone has made the concept of post-MTBI fatigue more accessible to those people who are struggling with post-MTBI fatigue and their families.

Another contribution made to current research by this thesis is the proposal of a model of post-MTBI fatigue (Figure 3.3) which added to Rao et al.'s (2005) model of post-TBI fatigue by recognizing the important contribution of maladaptive psychological and behavioural factors in maintaining post-MTBI fatigue. The proposed model also has links to previous models of PCS and Maori health by incorporating concepts and processes drawn from neuropsychological and patient-oriented models of PCS (Kay et al., 1992; Ruff, 2005) as well as from Te Whare Tapa Wha, the Maori model of health (Durie, 1984, 1994, 1998). Rao et al.'s model showed sleep disruption, post-MTBI fatigue and psychiatric symptoms as sequelae of neurophysiological changes brought about by the biomechanical forces of the blunt trauma and peri or immediate post

trauma stress. Within the Study Two sample, where all participants had been pre-selected for post-MTBI fatigue, over 70% reported sleep disturbance and/or problems with anxiety and 44% reported problems with depression. Hence the co-occurrence of these factors in a model of post-MTBI fatigue, as suggested by Rao et al., was supported by the current study.

The proposed model contains two factors, maladaptive psychological and behavioural responses, and context (including family, cultural, financial, spiritual, physical environment) gleaned from Kay et al. and Ruff's models of PCS and added to Rao et al.'s post-MTBI fatigue model. Study Two identified and addressed an example of a maladaptive behavioural response to post-MTBI fatigue; excessive daytime sleeping or naps, which was reported by a 25% of the treatment group in week 1 of the PERT programme. These participants reported napping an average of 30-90 minutes a day five days a week, a practice likely to increase de-conditioning and thereby increase the difficulty of returning to pre-injury activity level. Other maladaptive behaviours likely to be associated with post-MTBI fatigue were observed among the participants of this study. For instance, one participant went back to a full time professional position while still significantly symptomatic and became overwhelmed by fatigue, necessitating his having to stop working. His fatigue and concerns about losing his job were associated with increased anxiety and depression. His situation was one of those which supported the inclusion in the model of a feedback loop whereby maladaptive behavioural and psychological responses increase neurophysiological stress responses which in turn lead to fatigue. This example also shows the influence of contextual factors as this participant was afraid of losing his job and he was experiencing financial stress from

the reduced income he was receiving from ACC[7] so he went back to work too early in his recovery. These are just two examples of the maladaptive responses and/or contextual factors which exacerbate post-MTBI fatigue. There were many more examples within the whole sample, hence Study Two contributed to the knowledge of post-MTBI fatigue by supporting the inclusion of these two factors in the proposed model of post-MTBI fatigue.

For another two participants, who exhibited maladaptive responses such as remaining indoors and restricting activity and participation, context also played a part in maintaining their fatigue, which was initially brought on by a MTBI. The context in which the injury had occurred was one of a previous history of physical abuse which motivated them to stay indoors, thereby exposing them to de-conditioning, increased likelihood of exacerbating their post-MTBI fatigue and reduced likelihood of resuming their pre-MTBI activities. Another contextual characteristic evident during this study was reduced financial security which placed stress on several participants even when they were receiving earnings-related compensation from ACC at the rate of 80% of their pre-injury earnings. The amount they received did not enable them to meet their financial commitments which were tailored to their pre-injury income. As Ruff (2005) pointed out these types of contextual factors impact on PCS recovery. Study Two provided anecdotal information which supported inclusion of context in the model of post-MTBI fatigue. The preliminary model of post-MTBI fatigue proposed in this thesis presents a framework upon which to base future investigation into post-MTBI fatigue.

[7] ACC pays accident victims up to 80% of their pre-accident income.

Post-MTBI fatigue is one of the three most common postconcussion symptoms and has been shown to persist for years. This finding was also supported by Study Two as at the end of the study, that is an average of 12 months post injury, 75% of the sample continued to report post-MTBI fatigue, at least at the mild level (RPSQ Item 6 ≥ 2), despite reporting improvement in severity over that time.

During the review of fatigue literature it was noted there were contradictory findings on the relationship between post-TBI fatigue and gender (Borgaro et al., 2005; Cantor et al., 2008; Ziino & Ponsford, 2005a). There was no significant difference between the males and females for post-MTBI fatigue prevalence or severity throughout the six months of either Study One or Two. Female gender was not related to post-MTBI fatigue, which is at odds with Cantor et al.'s (2008) review of correlates of post-TBI fatigue. They reported that gender was the only demographic or injury variable related to post-TBI fatigue. The current studies' finding re gender and post-MTBI fatigue was consistent with the other two TBI-fatigue studies cited. However, fatigue in general has been found to correlate with female gender in a number of different health-related populations (Kapella et al., 2006; Tiesinga et al., 1999). Another possibility for the discrepancy in findings re gender is differences between measures of fatigue. Ziino and Ponsford used the same measure, Fatigue Severity Scale, which was used in both current studies but Borgaro et al. used the Barrow Neurological Institute Fatigue Scale (Borgaro et al., 2004) which they had designed and Cantor used the Global Fatigue Index (Belza, 1995; Belza, Henke, Yelin, Epstein, & Gilliss, 1993; Borman, Shively, Smith, & Gifford, 2001).

Rather than comparing fatigue prevalence and severity for gender, it was possible to look at the difference gender might make on a measure of recovery via reliable clinically significant change. The contribution made by the analysis of the Study Two combined group sample to the debate about the influence of gender was that female gender was an advantage during the first three months of the study but thereafter there was no gender effect in the second six months. That is in the longer term, gender was not a significant factor in whether reliable clinically significant changes were observed.

In summary, this research has made unique contributions to the post-MTBI fatigue literature by investigating post-MTBI fatigue in a New Zealand populations where the effect of litigation as a confound was countered by the no-fault accident insurance covering all participants. Post-MTBI fatigue severity as well as prevalence was measured in both studies. Depression was shown to be a significant predictor of post-MTBI fatigue while anxiety and sleep dysfunction were not significant predictors. Misperception of fatigue related behaviour as laziness is present and needs further investigation to clarify its role in post-MTBI fatigue recovery and available significant other support. Reliable and clinically significant change in post-MTBI fatigue over time was less common than expected and research into the natural history and treatment of post-MTBI fatigue needs to take this into account. This became apparent when the issue of gender and post-MTBI fatigue was explored and it was found that not only was there no relationship over time, but only a short term relationship between gender and reliable clinically significant change.

Limitations

Study One was presented as a published paper and limitations are discussed on pages 96–98 above. In summary, one limitation common to both studies was that the Hospital Anxiety and Depression Scale like all other depression scales contains items, e.g. “I feel as if I am slowed down”, which are common to both depression and post-MTBI fatigue. Additionally, there is minimal research on the HADS validity and reliability following MTBI. Hence the HADS scales must be interpreted with caution (Bailey et al., 2009; Schönberger & Ponsford, 2010).

Another limitation of Study One was that there was no systematic attempt to measure pre-injury fatigue status. However, many clinicians and researchers are of the belief that the individual’s perception of their pre-injury status is not reliable. It is likely to be coloured by their post-injury status and other issues such as personal resilience and secondary gain factors such as financial or emotional support (Davis, 2002).

A limitation of Study One was the lack of available information about treatments provided to the participants after their head injury. This confounds the findings related to the effect of time on fatigue as treatment effects are likely to be influencing the findings.

For Study Two the most significant limitation arose from the fact that the majority of the control group participants reported doing exercise during their recovery period. This was a major confound to one of the primary elements of the treatment programme which was based on using aerobic exercise to reverse the physiological effects of MTBI. In 2006, the New Zealand Guidelines Group, an ACC sponsored team of

experts, published "Traumatic brain injury: Diagnosis, acute management and rehabilitation" (New Zealand Guidelines Group, 2006) which contained no fatigue-specific rehabilitation recommendations. There was the recommendation to provide reassurance and information on strategies to manage the postconcussion symptoms listed. Fatigue was on that list but no detail regarding strategies was provided. Similarly there were no specific guidelines in the ACC Concussion Clinic contract document regarding the treatment of post-MTBI fatigue. Hence there was no official information from which predictions about any post-MTBI fatigue rehabilitation strategies the control group might be provided with. Ethically it is not possible to set up a control group that does not receive any treatment for their postconcussion symptoms and in this vein it was not considered ethical practice to prevent the control group participants from engaging in exercise.

A second key limitation of Study Two was the small number of participants in each group (treatment $N = 16$; control $N = 21$). As a result the study lacked power. Apart from attrition which is a factor in any longitudinal design, there were other elements which interfered with obtaining the sample size intended i.e. $N \geq 26$ in each group. One reason for reduced treatment group numbers was that recruitment was passed to other psychologists for a period of six months due to staff shortages in other parts of the clinic. As a result the principal researcher was notified of fewer candidates during that time. Similarly, in one of the clinics from which control participants were being recruited, the Concussion Clinic psychologist position was vacated twice during the recruitment period. These changes were not directly communicated to the principal researcher hence there were periods when no control candidates were being recruited. Another reason for the small numbers in the groups was that the online questionnaires

were not always completed fully and there was no inbuilt monitor which could have notified respondents of missing information in their forms. It would have been preferable to build this in so as to prompt participants. At the same time, participants were advised they could decline all, or any, of the items – perhaps the missing responses were in fact intentional. Prompts for missing responses would have to be constructed in such a way that participants could still choose not to respond after being reminded once. Another mechanism could be to provide a "Don't Know" option for each item. This poses the risk of too many "Don't Know" responses. Also the respondents had a history of brain injury which is often associated with decision-making difficulty, and adding another option ("Don't Know") to each item could exacerbate this difficulty. Manual checking by the principal investigator was done some time after the questionnaire was completed and it was not always practical to ask the respondent to reconsider their missed responses - nor was it appropriate given that they could chose whether or not to answer.

Taking treatment participants from one clinic and control participants from two other clinics could potentially impact on the findings as there could be a number of factors which differed across the clinics, including environment, rural verses urban living, access to therapy where there is minimal public transport, experience and knowledge of therapists.

One of the issues, which arises when exercise is used in treatment, is setting the duration and intensity of that exercise, i.e., the dose (Rimmer, Chen, McCubbin, Drum, & Peterson, 2010). A limitation of Study Two was the use of an ad hoc method for determining dose on an individual basis. Kozlowski (2008) addressed the issue by

individualising the duration of the treatment exercise session based on the duration of the exercise test carried out to establish each individual's VO_2 max, or onset of postconcussion symptoms whichever came first. That is, the duration was tailored to the concussed individual's fitness level using an evidence based approach. Study Two lacked this type of technology-based systematic approach to dose setting. The PERT programme was deliberately designed to be independent of technology as much as possible in order to increase its accessibility and decrease the expenses associated with delivering the programme. However, under the new Concussion Service model introduced in July 2010, there is the possibility of involving a physiotherapist in providing or monitoring an exercised-based treatment programme enabling access to the type of equipment which would allow systematic dose setting and fitness monitoring without additional cost.

"Seeing is believing" is a common phrase and one of the features of the PERT manual was a progress chart where treatment participants could enter their daily fatigue and energy ratings. Charting is a valuable feature of exercise programmes (Ferney & Marshall, 2006), hence its use should be encouraged in as many ways as possible. The chart in the PERT manual was included to provide feedback on progress as a motivational tool to encourage participants to engage in behavioural change, i.e. to engage in the exercise programme. A limitation of this study was that charting of fatigue and energy ratings was not universally used by participants, nor universally monitored by the therapists involved. Several changes to the delivery of the programme could improve compliance in this area. A revised manual would have the chart at the front, probably on the inside front page so that it was noticed more often by both participant and therapist. If online data entry was used then the chart could be updated automatically every time the participant entered their diary data. Therapists

could also be encouraged to be more consistent in their monitoring of the graph during the weekly diary discussion. Another method for ensuring compliance would be the placement of a prompt on the diary record page (weekly ratings) in the manual. The prompt could direct the participant and therapist to record the data in the chart. Alternatively, and more simply, the diary table could be eliminated and all ratings recorded in chart form. Anecdotal evidence of charting's reward and motivational roles was clear from the smiles on the faces and comments of some participants when they saw their charts showing progress towards the goals of reduced fatigue and increased energy.

Another area where this study could have been strengthened was in seeking information about significant others' attitudes to fatigue-related behaviour. The one question "When I am tired my family or partner thinks I am being lazy" was insufficient to obtain a well-rounded understanding of the reaction of significant others to post-MTBI fatigue. The question as asked was somewhat complex and reminiscent of circular questioning (systemic therapy). An answer of agreement does not mean the family is unsupportive but only that the fatigued individual *believes* they are regarded as lazy. Sampling both the participants' and their significant others' responses through complementary questions would have added to the picture of how post-MTBI fatigue is perceived. Knowledge of the actual perceptions could inform the therapist of needs such as education being extended to the significant others.

There was likely to be variability in the way the three therapists, two occupational therapists and one clinical psychologist delivered the programme. Possible sources of variability would be firstly that the psychologist providing the therapy had developed

the programme and therefore had a more in-depth understanding of the theory and more investment in the outcomes, i.e. researcher objectivity could have potentially been compromised to some extent. Secondly, each professional provided additional rehabilitation therapy such as graduated return to work or anxiety therapy as it pertained to individual participants and their expertise. That is, they interacted with each participant in individualistic ways which potentially impacted on the uniformity with which the PERT programme was delivered, despite it being a manualised programme.

A classic problem with carrying out treatment trials in real life clinical situations is that it is almost impossible to identify a sample whose only problem is the one being investigated. The statistical solution is to use as large a sample as possible, a solution which frequently calls for extensive resources involving multiple sites or very large centres of population. Several members of the treatment group had other health difficulties that were likely to have interfered with the effectiveness of the programme. Winter illness increased fatigue, reduced motivation and perhaps, ability to engage in physical exercise. One participant was found, months after completion of his programme, to have evidence of very early stage Multiple Sclerosis, a condition which could potentially have contributed along with the head injuries to his feeling of fatigue. Another individual who completed the programme and demonstrated improvement in fatigue and psychological symptoms, was subsequently withdrawn from the statistical analysis because the diagnosis was revised and depression related to significant psychosocial factors was seen as the primary diagnosis. The presence of these undetected conditions and/or winter illness muddies the picture for both assessment and treatment of post-MTBI fatigue.

Conclusions

Although subjective fatigue is one of the most commonly reported and long lasting postconcussion symptoms, research into prevalence and treatment of post-MTBI fatigue is relatively sparse. Study One examined post-MTBI fatigue in a non-litigious population and found that not only does it persist for at least six months post-injury, but also that it does not improve significantly after about three months. As the fatigue becomes more persistent, psychological factors such as anxiety and depression tend to worsen. These findings are useful in guiding interventions for post-MTBI fatigue. The second study was designed to evaluate the effectiveness of a post-MTBI fatigue treatment employing a combination of psychoeducation and aerobic exercise. While post-MTBI fatigue reduced over time, the lack of a significant difference between the treatment and control groups means there is still no known effective treatment for persistent fatigue after MTBI. From a clinical perspective, it was found that the majority of participants did not exhibit reliable clinically significant change over time. There is still a need to conduct research into effective treatment for post-MTBI fatigue. Since the current studies were carried out, anecdotal information about another trial of treatment for post-MTBI fatigue being conducted in Auckland has become available. Although the treatment is once again based on psychoeducation and aerobic exercise with the research design allowing for each group of participants to receive only one of these treatments and for both treatment groups to be compared to a control group over time. So the search for an effective way to help people with post-MTBI fatigue continues.

Some further suggestions for improving the investigation for a post-MTBI fatigue treatment include:

1. Having a more structured dose-setting protocol for the exercise component, with a built in review period
2. Surveying significant others as well as the those with MTBI-fatigue when asking about issues such as how fatigue behaviour is perceived
3. Placing the progress chart inside the front cover of the manual
4. Incorporating a monitoring device in online questionnaire webpages to encourage completion of all items of a questionnaire while allowing for intentional gaps
5. Providing the psychoeducation material in video/audio format as well as written
6. Eliminating the wide range in time since injury
7. Qualitatively investigating the experience of post-MTBI fatigue
8. Investigating the factors which differentiate those who, after completing an exercise/education programme, exhibit reliable clinically significant change from those who do not. These factors could be contextual (e.g., environmental, cultural) or dynamic (e.g., emotional intelligence, locus of control, coping styles and attribution, self-efficacy, extraneous psychosocial issues, sense of entitlement, pain) or static (e.g., pre-morbid posttraumatic stress history, previous TBI).

As can be seen from this list, the field is wide open to researchers interested in discovering "best practice" methods for reducing post-MTBI fatigue and promoting rehabilitation.

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APPENDICES

Appendix A

Information Sheet - Treatment Group

Massey University
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Energy Crisis: Post-Mild Traumatic Brain Injury Fatigue

INFORMATION SHEET

Introduction

We invite you to take part in a project to evaluate the effectiveness of a rehabilitation programme for fatigue after concussion or mild traumatic brain injury (post-MTBI fatigue).

The purpose of the project is to find out whether the rehabilitation programme reduces the severity and impact of post-MTBI fatigue. The study is being carried out by Joan Norrie, Clinical Psychologist and Principal Investigator, as part of her dissertation for a Doctorate of Philosophy in psychology through Massey University.

Your participation in this study is entirely voluntary (your choice). You do not have to take part and, if you choose not to, you will receive the usual treatment/care provided by the Concussion Clinic you went to after your mild head injury.

If you do agree to take part you are free to withdraw at any time from the study, without having to give a reason and again, this will in no way affect your future health care. If you do not wish to be contacted further regarding this study please indicate this to the principal investigator, Joan Norrie (email: J.M.Norrie@massey.ac.nz) or phone the Psychology Clinic receptionist (06 350 5196).

The project

The study involves comparing the results for two groups of people with post-MTBI fatigue. The rehabilitation therapy will be provided to one group with post-MTBI fatigue and the usual treatment will be provided to the other group. You will be referred to a therapist in your area who will provide you with a fatigue management programme. We plan to have about thirty people in each of the groups.

How did I come to be invited to join this project?
You have been invited to enter this project because you indicated at the Concussion Clinic that you were having difficulty with fatigue and you were diagnosed with a mild traumatic brain injury. Joan Norrie will arrange an appointment to talk with you about the project, to answer any questions you may have and, to invite you to participate in the project.

What are we asking you to do?
If you decide to participate in this study we ask you to complete the consent form and post it back in the freepost envelope supplied. As soon as we receive the consent form we can enter you in the trial.

You will be asked to confirm the information about your injury and contact details and to answer some questionnaires about fatigue and other symptoms and then you will begin the 6 week fatigue management programme with your Therapist.

Part 1:

Fatigue Management Programme
You will be asked to come to the Concussion Clinic to meet with your therapist for five sessions during the twelve weeks. Your therapist will phone you during the other seven weeks of the programme to talk with you about your progress.

Before you begin the programme you will be asked to complete some questionnaires about fatigue, mood and participation on the study website. A paper copy of the questionnaires will be available if you do not have access to a computer. During the programme your therapist will explain about post-MTBI fatigue and other postconcussion symptoms. Your therapist will also make suggestions about pacing your return to work, school or home activities. You will be asked to do 20 – 30 minutes of aerobic (moderate) exercise (walking, biking, swimming or similar) five times a week. If you feel unfit you can build up to this time over the first week or two. You will be asked to record your exercise in your programme on the website or in your handbook. You will also record your fatigue and energy levels as well. We think this will take only 1-2 minutes to enter each time.

We will ask you to answer the fatigue, mood and participation questionnaires on the study website (or paper copy) at the end of the 12 week programme and then again at 24 weeks and one and two years after you begin the programme. We will get in touch with you before each of these follow-up times to remind you and send you the website address or the questionnaires. This will help you and us to track the success of the programme.

Part 2:

Follow-up
Because post-MTBI fatigue sometimes lasts for months or years we want to monitor the effect of the programme for two years after the end of the programme. We would like to contact you at six months, one and two years after the beginning of your fatigue management programme to see how you are getting along. We would ask you to complete the same questionnaires on each of these occasions. We expect that this will involve no more than thirty minutes each time.

Is there a cost involved?
There will be no cost to you for the fatigue management programme. Travel costs for anyone travelling from out of town will be met in the usual way under ACC travel policy.

Why should you participate?
Post-MTBI fatigue is one of the most common symptoms following brain injury and even after a mild brain injury it can interfere with people's lives for months or years. There is very little knowledge about what is the most effective treatment for post-MTBI fatigue. It is also associated with other postconcussion symptoms such as irritability, depression and anxiety which frequently disrupt family and relationships when someone in the family has had a mild traumatic brain injury. Joan Norrie, through her reading and discussion with MTBI experts has designed a fatigue management programme which she believes will greatly reduce the severity of fatigue and will help people to get back to their normal lives.

What will happen to the information you give us?

The information will be stored on the Principal Investigator's computer at Massey University on a secure site. All paper records will be stored in a locked cabinet. At the end of the project all records will be kept in locked storage for ten years under the care of the Psychology Clinic Director, Massey University Palmerston North. After ten years the records will be destroyed as per clinic policy.

All results of the project will be written up and published anonymously as group data. Individual Concussion Clinic treatment reports will be prepared by the Therapist at the end of the fatigue management programme and sent to ACC as is the normal protocol for Concussion Clinic interventions. These reports will not be stored with the project data but in the usual client file locked storage facility.

When will the results be available?
You will be provided with information about your individual results by the Therapist at the end of your programme**.** The fatigue management will be provided throughout 2009 and we expect Part 1 results to be available mid 2010. However, writing up the project is not expected to be complete until the end of 2010. The results of Part 2 will be available in late 2011. A brief summary of the results will be available on the project website and if requested we can email you a copy when the results of each part of the project have been written up.

Are there any risks?
There are no risks associated with this project.

Participant's Rights

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- *decline to answer any particular question;*
- *withdraw from the study (specify timeframe);*
- *ask any questions about the study at any time during participation;*
- *provide information on the understanding that your name will not be used unless you give permission to the researcher;*
- *Be given access to a summary of the project findings when it is concluded.*
- *Ask for the recorder to be turned off at any time during the interview.*

Compensation for Injury

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, contact your nearest ACC office or the investigator.

Joan Norrie, BA, MA DipClinPsych **Registered Clinical Psychologist** **Principal Investigator** **Ph 06 356 9099 ext 2080** **J.M.Norrie@massey.ac.nz** **Psychology Clinic** **Massey University** **PB 11 222**	**Prof. Janet Leathem, PhD** **Registered Clinical Psychologist** **First PhD Supervisor** **Ph 06 356 9099 ext 62035** **J.M.Leathem@massey.ac.nz**

Palmerston North	
Ross Flett, PhD **Senior Lecturer, School of Psychology** **Second PhD Supervisor** **Ph 06 356 9099 ext 2051** R.A.Flett@massey.ac.nz	

This study has received ethical approval from the Central Districts Ethics Committee

You are welcome to contact the Principal Researcher or the Supervisors if you have any questions about the project.

Appendix B

Information Sheet - Control

Massey University
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T 64 6 356 9099 extn 2040
F 64 6 350 5673
www.massey.ac.nz
http://psychology.massey.ac.nz

Energy Crisis: Post-Mild Traumatic Brain Injury Fatigue

INFORMATION SHEET

Introduction

We invite you to take part in a project to evaluate the effectiveness of a rehabilitation programme for fatigue after concussion or mild traumatic brain injury (post-MTBI fatigue).

The purpose of the project is to find out whether the rehabilitation programme reduces the severity and impact of post-MTBI fatigue. We hope that it will help those who have post-MTBI fatigue to get back to their pre-injury lifestyle as soon as possible. The study is being carried out by Joan Norrie, Clinical Psychologist and Principle Investigator, as part of her dissertation for a Doctorate of Philosophy in psychology through Massey University.

Your participation in this study is entirely voluntary (your choice). You do not have to take part, and, if you choose not to, you will receive the usual treatment/care provided by the Concussion Clinic you went to after your mild head injury.

If you do agree to take part you are free to withdraw at any time from the study, without having to give a reason and this will in no way affect your future health care. If you do not wish to be contacted further regarding this study please indicate this to the principal investigator, Joan Norrie (email: J.M.Norrie@massey.ac.nz) or phone the Psychology Clinic receptionist (06 350 5196).

The project

The study involves comparing the results for two groups of people with post-MTBI fatigue. Your group will be provided with the usual rehabilitation treatment for post-MTBI fatigue. You will be referred to a therapist in your area who will provide you with a fatigue management programme. We plan to have about thirty people in each of the groups.

How did I come to be invited to join this project?
You have been invited to take part in this project because you indicated at the Concussion Clinic that you were having difficulty with fatigue and you were diagnosed with a mild traumatic brain injury. Joan Norrie will arrange to phone you to talk with you about the project, to answer any questions you may have and, to invite you to participate in the project. Whether you decide to take part in the research project or not you will be referred for fatigue management to an Occupational Therapist in your local area. We plan to have at least thirty people taking part is this phase of the study.

Part 1:

You will be asked to confirm the information about your injury and contact details and to answer

some questionnaires about fatigue and other symptoms and then you will begin a fatigue management programme with your Occupational Therapist or Physiotherapist. The questionnaires will take 20 - 30 minutes to complete. We will ask you to answer the same questionnaires at 12 and 24 weeks after you begin the programme.

These questionnaires can be answered on our website or we can send you a booklet of the questionnaires, which you can post back to us.

Part 2:

Follow-up
Because post-MTBI fatigue sometimes lasts for months or years we want to monitor the effect of the programme for two years. We would like to contact you one and two years after the beginning of your fatigue management programme to see how you are getting along. We would ask you to complete the same questionnaires on each of these occasions. We expect that this will involve no more than thirty minutes each time.

Is there a cost involved?
There will be no cost to you for the fatigue management programme. Travel costs for anyone traveling from out of town will be met in the usual way under ACC travel policy.

Why should you participate?
Post-MTBI fatigue is one of the most common symptoms following brain injury and even after a mild brain injury it can interfere with people's lives for months or years. There is very little knowledge about what is the most effective treatment for post-MTBI fatigue. It is also associated with other postconcussion symptoms such as irritability, depression and anxiety which frequently disrupt family and relationships when someone in the family has had a mild traumatic brain injury. Joan Norrie, through her reading and discussion with other MTBI experts has designed a fatigue management programme which she believes will greatly reduce the severity of fatigue and will help people to get back to their normal lives. In order to show that the new programme works we need to compare it with the treatment that is currently being provided. You will be helping by taking part in the control group.

What will happen to the information you give us?
The information will be stored on the Principal Investigator's computer at Massey University on a secure site. All paper records will be stored in a locked cabinet. At the end of the project all records will be kept in locked storage for ten years under the care of the Psychology Clinic Director, Massey University Palmerston North. After ten years the records will be destroyed as per clinic policy.

All results of the project will be written up and published anonymously as group data. Individual Concussion Clinic treatment reports will be prepared by the Occupational Therapist at the end of the fatigue management programme and sent to ACC as is the normal protocol for Concussion Clinic interventions. These reports will not be stored with the project data but in the usual client file locked storage facility.

When will the results be available?
You will be provided with information about your individual results by the Occupational Therapist at the end of your programme**.** The fatigue management will be provided throughout 2009 and we expect Part 1 results to be available mid 2010. However, writing up the project is not expected to be complete until the end of 2010. The results of Part 2 will be available in late 2011. A brief summary of the results will be available on the project website and if requested we can email you a copy when the results of each part of the project have been written up.

Are there any risks?
There are no risks associated with this project.

Participant's Rights

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- *decline to answer any particular question;*
- *withdraw from the study (specify timeframe);*
- *ask any questions about the study at any time during participation;*
- *provide information on the understanding that your name will not be used unless you give permission to the researcher;*
- *be given access to a summary of the project findings when it is concluded.*
- *ask for the recorder to be turned off at any time during the interview.*

Compensation for Injury

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, contact your nearest ACC office or the investigator.

Joan Norrie, BA, MA DipClinPsych **Registered Clinical Psychologist** **Principal Investigator** **Ph 06 356 9099 ext 2080** **J.M.Norrie@massey.ac.nz** **Psychology Clinic** **Massey University** **PB 11 222** **Palmerston North**	**Prof. Janet Leathem, PhD** **Registered Clinical Psychologist** **First PhD Supervisor** **Ph 06 356 9099 ext 62035** **J.M.Leathem@massey.ac.nz**
Ross Flett, PhD **Senior Lecturer, School of Psychology** **Second PhD Supervisor** **Ph 06 356 9099 ext 2051** R.A.Flett@massey.ac.nz	

You are welcome to contact the Principal Researcher or the Supervisors if you have any questions about the project.

Appendix C

Consent to Be Contacted

Massey University
COLLEGE OF HUMANITIES AND SOCIAL SCIENCES
Te Kura Pükenga Tangata

SCHOOL OF PSYCHOLOGY
Te Kura Hinengaro Tangata
Private Bag 11 222
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Energy Crisis: Post-Mild Traumatic Brain Injury Fatigue

CONSENT TO BE CONTACTED BY PRINCIPAL INVESTIGATOR

This consent form will be held for a period of five (5) years

I consent to the Concussion Clinic psychologist passing on my contact details to Joan Norrie, Principal Investigator.

I understand that Joan Norrie will phone me and explain the research in detail. I have been given the information pack to read at home.

Signature: ..... **Date:** .....

Full Name - printed

Postal Address

Phone Numbers **Day:** **Cellphone:**

Email Address .....

Joan Norrie, BA, MA DipClinPsych
Registered Clinical Psychologist
Principal Investigator

Ph 06 356 9099 ext 2080
J.M.Norrie@massey.ac.nz
Psychology Clinic
Massey University
PB 11 222
Palmerston North

Prof. Janet Leathem, PhD
Registered Clinical Psychologist
First PhD Supervisor

Ph 06 356 9099 ext 62035
J.M.Leathem@massey.ac.nz

REQUEST FOR INTERPRETER
(to be included on all consent forms)

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
	Other languages to be added following consultation with relevant communities.		

Appendix D

Participant Consent Form

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Energy Crisis: Post-Mild Traumatic Brain Injury Fatigue

PARTICIPANT CONSENT FORM

This consent form will be held for a period of five (5) years

I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time

I agree/do not agree to the interview being image and/or sound recorded.

I wish/do not wish to have data placed in an official archive.

I agree to participate in this study under the conditions set out in the Information Sheet.

Signature: ..... **Date:** .....

Full Name - printed .....

REQUEST FOR INTERPRETER

(To be included on all consent forms)

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
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Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
	Other languages to be added following consultation with relevant communities.		

Appendix E

Structured Interview Form

Energy Crisis: Post- Mild Traumatic Brain Injury Fatigue

Click and either type in an answer or choose from the menu

Participant Number
DOB: Age
Date of Injury
Gender
Years of Education
Injury details
PTA minutes
GCS
Cause of Injury
Did you get knocked out
How long were you knocked out for
How long were you confused for hours
Did you remember the accident
What was your last memory before the accident
Approximately how long was that before the accident
Do you have persistent pain other than headache
Where is your pain
On a scale of 0 to 10, how bad is your pain (0 = no pain and 10 = really really bad pain)
Apart from seeing a doctor before coming to the Concussion Clinic what other treatment have you had since your head injury Details of other treatment
Head Injury history
Have you been knocked unconscious before
How many times What was the longest time you were knocked out for before this accident
Did you have time off work or school after any of those accidents
Medical and Psychiatric history
Have you had any serious illness like, diabetes, epilepsy, asthma
Which illnesses
Have you ever been to a doctor, psychologist, counsellor for depression anxiety panic attacks more serious mental illness
Have you ever been prescribed medication for any of these difficulties
What was the medication
How long did you take it for
Fatigue and Sleep
Did you have problems with fatigue before this accident
What sort of fatigue problems did you have

How many hours per night did you sleep before the accident hours
Did you have sleep problems before this accident
When you go to bed, how long does it take you to get to sleep now minutes
How often do you wake in the night
School, Polytech, University Students
Student
How many hours per week are you normally studying
Have you returned to study/school since the accident
How many hours per week are you currently at study/school since the accident
Work or other daily activity
What kind of work do you usually do
How many hours per week do you normally work
Have you returned to work or normal activity since the accident
How many hours per week are you currently working since the accident
Drugs and Alcohol
Alcohol
Cannabis
Other recreational drugs
Computer Access
Do you own a computer with internet access
If not, can you get easy access to a computer

Appendix F

Online Information Sheet

Postconcussion Energy Recovery Training (PERT) Programme

INFORMATION SHEET

Welcome

If you are reading this page then you have already agreed to be a participant in the project which is looking at whether the PERT rehabilitation programme reduces the severity and impact of post-Mild Traumatic Brain Injury (post-MTBI) fatigue. The study is being carried out by Joan Norrie, Clinical Psychologist (Neuropsychology) and Principal Investigator, as part of her dissertation for a Doctorate of Philosophy (PhD) in psychology through Massey University. The research is being supervised by Dr Janet Leathem, Professor of Neuropsychology, and Dr Ross Flett, Senior Lecturer, Massey University. You will also have already met your therapist who will guide you through this site and through the PERT programme.

What do I have to do?

Energy Crisis Project: Part 1

Week 1

ALL PARTICIPANTS:
The **first time you log into the website**, you will answer the questions in the concussion, fatigue, depression and anxiety questionnaires as linked. They are called the Rivermead Postconcussion Symptoms Questionnaire, Fatigue Assessment Instrument, Fatigue Assessment Scale, Hospital Anxiety and Depression Scale and the Sydney Participation Reintegration Scale.

Palmerston North Concussion Clinic participants ONLY:
During the Week 1, please rate your fatigue and energy each weekday and keep a record of any exercise you do and any naps you have on those days. Remember do not change your routine this week. Please enter these ratings into the diary on this website.

A link to the online diary for data entry purposes will be provided by your therapist.

Week 2 – 11

Palmerston North Concussion Clinic participants ONLY:
For weeks 2 – 11 Your therapist will help you plan the exercise you are doing during this time. Please enter your fatigue and energy ratings, the exercise you do and any naps you take. You can enter these ratings everyday or once a week before your next appointment with your therapist.

Week 12

ALL PARTICIPANTS:
Please do the questionnaires you did at the beginning of the PERT programme. The Rivermead Postconcussion Symptoms Questionnaire, Fatigue Assessment Instrument, Fatigue Assessment Scale, Hospital Anxiety and Depression Scale and the Sydney Participation Reintegration Scale.

Palmerston North Concussion Clinic participants ONLY:
This is the last week of the PERT programme. As usual please enter your fatigue and energy ratings, the exercise you do and any naps you take.

Week 24

ALL PARTICIPANTS:
Welcome back, we hope you are well. Please do the questionnaires you did at the beginning of the PERT programme. The Rivermead Postconcussion Symptoms Questionnaire, Fatigue Assessment Instrument,

Fatigue Assessment Scale, Hospital Anxiety and Depression Scale and the Sydney Participation Reintegration Scale. This is the end of data collection for Joan Norrie's PhD dissertation but...as we discussed at the beginning of this project we really want you to stay with the project so that we can look at the longer term picture of post-MTBI fatigue.

If you are having fatigue or other postconcussion difficulties please tell your ACC Case Manager who can refer you for further intervention.

Energy Crisis Project: Part 2

Week 52 (Year 1)

ALL PARTICIPANTS:
Thank you very much for continuing to be a part of this project. Welcome back, we hope you are well. Please do the questionnaires you did at the beginning of the PERT programme. The Rivermead Postconcussion Symptoms Questionnaire, Fatigue Assessment Instrument, Fatigue Assessment Scale, Hospital Anxiety and Depression Scale and the Sydney Participation Reintegration Scale.

If you are having fatigue or other postconcussion difficulties please tell your ACC Case Manager who can refer you for further intervention.

Week 104 (Year 2)

ALL PARTICIPANTS:
Thank you very much, once again, for continuing to be a part of this project. This is the last time we will ask you to complete the questionnaires. Please fill in your responses to the questionnaires. The Rivermead Postconcussion Symptoms Questionnaire, Fatigue Assessment Instrument, Fatigue Assessment Scale, Hospital Anxiety and Depression Scale and the Sydney Participation Reintegration Scale.

If you are having fatigue or other postconcussion difficulties please tell your ACC Case Manager who can refer you for further intervention.

The following is an extract from the Information Sheet you were given at the beginning of your involvement in the Energy Crisis Project.

What will happen to the information you give us?

The information will be stored on the Principal Investigator's computer at Massey University on a secure site. All paper records will be stored in a locked cabinet. At the end of the project all records will be kept in locked storage for ten years under the care of the Psychology Clinic Director, Massey University Palmerston North. After ten years the records will be destroyed as per clinic policy.

All results of the project will be written up and published anonymously as group data. Individual Concussion Clinic treatment reports will be prepared by the Therapist at the end of the PERT programme and sent to ACC as is the normal protocol for Concussion Clinic interventions. These reports will not be stored with the project data but in the usual client file locked storage facility.

When will the results be available?

You will be provided with information about your individual results by the therapist during and at the end of your programme. The PERT programme will be provided throughout 2009 and we expect Part 1 results to be available mid 2010. However, writing up the project is not expected to be complete until the end of 2010. The results of Part 2 will be available in late 2011. A brief summary of the results will be available on the project website and if requested we can email you a copy when the results of each part of the project have been written up.

Participant's Rights

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- *decline to answer any particular question;*
- *withdraw from the study (specify timeframe);*
- *ask any questions about the study at any time during participation;*
- *provide information on the understanding that your name will not be used unless you give permission to the researcher;*

- *be given access to a summary of the project findings when it is concluded.*
- *ask for the recorder to be turned off at any time during the interview.*

Researcher:	Supervisor:
Joan Norrie School of Psychology Turitea Campus Massey University New Zealand	Professor Janet Leathem School of Psychology Wellington Campus Massey University New Zealand
Telephone: 3569-099 Ext 2080 Email: J.M.Norrie@massey.ac.nz	Telephone: 04 801 5799, Ext 62035 Email: J.M.Leathem@massey.ac.nz

This project has been approved by the
Central Regional Ethics Committee, Ministry of Health:
Application CEN/09/02/02.

If you have any questions or concerns about your rights as a participant in this study, you can contact an independent health and disability advocate.
This is a free service provided under the Health and Disability Commissioner Act.
Telephone: (NZ Wide) 0800 555-050
Free Fax (NZ Wide) 0800 2787-7678 (0800 2 SUPPORT)
Email (NZ Wide): advocate@hdc.org.nz

Appendix G

Online Questionnaires

Postconcussion Energy Recovery Training (PERT) Programme

All going well, you have been directed here from the preceding information sheet about this survey.

Instructions

Thank you for participating in this study. There are four questionnaires and they require roughly 10 – 15 minutes to do, each time.

You have entered your own code and your responses will be viewed only by Joan Norrie, Principal Investigator and your therapist (if you are attending the Concussion Clinic in Palmerston North). They will be held in a secure file at Massey University, Palmerston North.

The information you provide will enable increased understanding of the nature of post-MTBI fatigue over a long time (2 years) and whether the treatment programme being tried in Palmerston North is an effective way of treating this common postconcussion symptom. If you are not in Palmerston North you will receive post-MTBI fatigue treatment as it is usually provided in your centre.

Please complete all the questions below if possible. You have the right to decline to answer any particular question.

PLEASE NOTE:
If at any stage you would like to check your previous answers to any questions please scroll up and down the document. Do not use the back-button on your tool bar, as this will take you out of this survey without saving your answers.

Many thanks for your assistance with this survey.

Rivermead Postconcussion Symptoms Questionnaire

Rivermead Rehabilitation Centre, Abingdon Road, Oxford, OX1 4XD,

Client code
Please enter your Initials and birthdate (XXDDMMYY) in the box to the right
(as provided for confidentiality of answers)

After a head injury or accident some people experience symptoms which can cause worry or nuisance. We would like to know if you now suffer any of the symptoms given below. As many of these symptoms occur normally, we would like you to compare yourself with before the accident.

For each one please click the number closest to your answer.

0	1	2	3	4

	not experienced at all	no more of a problem	a mild problem	a moderate problem	a severe problem

	Compared with before the accident, do you now (i.e., over the last 2 weeks) suffer from:	0	1	2	3	4
R1	Headaches	○	○	○	○	○
R2	Feelings of dizziness	○	○	○	○	○
R3	Nausea and/or vomiting	○	○	○	○	○
R4	Noise sensitivity, easily upset by loud noise	○	○	○	○	○
R5	Sleep disturbance	○	○	○	○	○
R6	Fatigue, tiring more easily	○	○	○	○	○
R7	Being irritable, easily angered	○	○	○	○	○
R8	Feeling depressed or tearful	○	○	○	○	○
R9	Feeling frustrated or impatient	○	○	○	○	○
R10	Forgetfulness, poor memory	○	○	○	○	○
R11	Poor concentration	○	○	○	○	○
R12	Taking longer to think	○	○	○	○	○
R13	Blurred vision	○	○	○	○	○
R14	Light sensitivity, easily upset by bright light	○	○	○	○	○
R15	Double vision	○	○	○	○	○
R16	Restlessness	○	○	○	○	○
	Are you experiencing any other difficulties? *Please specify, and rate as above:*	0	1	2	3	4
R17		○	○	○	○	○
R18		○	○	○	○	○

Fatigue Assessment Scale

The following ten statements refer to how you usually feel. For each statement you can choose one out of five answer categories, varying from Never to Always.

(Please use key below)

1	2	3	4	5
Never	Sometimes	Regularly	Often	Always

		1	2	3	4	5
F1	I am bothered by fatigue	○	○	○	○	○
F2	I get tired very quickly	○	○	○	○	○

F3	I don't do much during the day	○	○	○	○	○
F4	I haven't enough energy for everyday life	○	○	○	○	○
F5	Physically, I feel exhausted	○	○	○	○	○
F6	I have problems starting things	○	○	○	○	○
F7	I have problems thinking clearly	○	○	○	○	○
F8	I feel no desire to do anything	○	○	○	○	○
F9	Mentally, I feel exhausted	○	○	○	○	○
F10	When I am doing something, I can concentrate quite well	○	○	○	○	○

The Fatigue Assessment Instrument (adapted)

Below are a series of statements regarding your Fatigue. By Fatigue we mean a sense of tiredness, lack of energy or total body give-out.

Please read each statement and choose a number from 1 to 7, where #1 indicates you completely disagree with the statement and #7 indicates you completely agree.

Please answer these questions as they apply to you in the **past TWO WEEKS**.

	Rating scale :- 1= completely disagree to 7 = completely agree	1	2	3	4	5	6	7
1	I feel drowsy when I am fatigued	○	○	○	○	○	○	○
2	When I am fatigued, I lose my patience	○	○	○	○	○	○	○
3	My motivation is lower when I am fatigued	○	○	○	○	○	○	○
4	When I am fatigued, I have difficulty concentrating	○	○	○	○	○	○	○
5	Exercise brings on my fatigue	○	○	○	○	○	○	○
6	Heat brings on my fatigue	○	○	○	○	○	○	○
7	Long periods of inactivity bring on my fatigue	○	○	○	○	○	○	○
8	Stress brings on my fatigue	○	○	○	○	○	○	○
9	Depression brings on my fatigue	○	○	○	○	○	○	○
10	Work brings on my fatigue	○	○	○	○	○	○	○
11	My fatigue is worse in the afternoon	○	○	○	○	○	○	○
12	My fatigue is worse in the morning	○	○	○	○	○	○	○
13	Performance of routine daily activities increased my fatigue	○	○	○	○	○	○	○
14	Resting lessens my fatigue	○	○	○	○	○	○	○
15	Sleeping lessens my fatigue	○	○	○	○	○	○	○

	Rating scale :- 1= completely disagree to 7 = completely agree	1	2	3	4	5	6	7
16	Cool temperatures lessen my fatigue	○	○	○	○	○	○	○
17	Positive experiences lessen my fatigue	○	○	○	○	○	○	○
18	I am easily fatigued	○	○	○	○	○	○	○
19	Fatigue interferes with my physical functioning	○	○	○	○	○	○	○
20	Fatigue causes frequent problems for me	○	○	○	○	○	○	○
21	My fatigue prevents sustained physical functioning	○	○	○	○	○	○	○
22	Fatigue interferes with carrying out certain duties and responsibilities	○	○	○	○	○	○	○
23	Fatigue predated other symptoms of my head injury	○	○	○	○	○	○	○
24	Fatigue is my most disabling symptom	○	○	○	○	○	○	○
25	Fatigue is among my 3 most disabling symptoms	○	○	○	○	○	○	○
26	Fatigue interferes with my work, family or social life	○	○	○	○	○	○	○
27	Fatigue makes other symptoms worse	○	○	○	○	○	○	○
28	Fatigue that I now experience is different in quality or severity than the fatigue I experienced before my head injury	○	○	○	○	○	○	○
29	I experienced prolonged fatigue after exercise	○	○	○	○	○	○	○
30	When I am tired my family or partner thinks I am being lazy	○	○	○	○	○	○	○

Hospital Anxiety & Depression Scale (HADS)

Clinicians are aware that emotions play an important part in most illnesses.
If you clinician knows about these feelings he or she will be able to help you more.

	Please answer these questions as they apply to you in last 7 days	***Please click on the most appropriate option***
H1	I feel tense or 'wound up'	○ Most of the time ○ A lot of the time ○ From time to time, occasionally ○ Not at all

H2	I still enjoy the things I used to enjoy	Definitely as much Not quite as much Only a little Hardly at all
H3	I get a sort of frightened feelings as if something awful is about to happen	Very definitely and quite badly Yes, but not too badly A little, but it doesn't worry me Not at all
H4	I can laugh and see the funny side of things	As much as I always could Not quite as much now Definitely not so much now Not at all
H5	Worrying thoughts go through my mind	A great deal of the time A lot of the time Not too often Very little
H6	I feel cheerful	Never Not often Sometimes Most of the time
H7	I can sit at ease and feel relaxed	Definitely Usually Not often Not at all
H8	I feel as if I am slowed down	Nearly all the time Very often Sometimes Not at all
H9	I get a sort of frightened feeling like 'butterflies' in my stomach	Not at all Occasionally Quite often Very often
H10	I have lost interest in my appearance	Definitely I don't take as much care as I should I may not take quite as much care I take as much case as ever
H11	I feel restless as if I have to be on the move	Very much indeed Quite a lot Not very much Not at all
H12	I look forward with enjoyment to things	As much as I ever did Rather less than I used to Definiltely less than I used to Hardly at all

H13	I get sudden feelings of panic	○ Very often indeed ○ Quite often ○ Not very often ○ Not at all
H14	I can enjoy a good book or radio or television programme	○ Often ○ Sometimes ○ Not often ○ Very seldom

SYDNEY PSYCHOSOCIAL REINTEGRATION SCALE (SPRS)

ROBYN L TATE
DEVELOPED IN ASSOCIATION WITH
ADELINE HODGKINSON, AHAMED VEERABANGSA, ANNE PFAFF AND GRAHAME SIMPSON
BRAIN INJURY REHABILITATION UNIT AT LIVERPOOL HOSPTIAL, SYDNEY

Work and Leisure

S1	**Current work: HOW DO YOU RATE YOUR WORK (OR STUDY), OR THE TYPE OF WORK (STUDY)?** (If you are a student, answer the questions in this section in terms of changes in studies)		
		○ Very good	
		○ A little difficulty	Work (studies) less than average hours per week, OR work duties (studies) are easy/light ones
		○ Definite difficulty	Work casually, OR has some help from others in doing some work (study)
		○ A lot of difficulty	Unemployed, OR in rehabilitation, OR in a supported work program, OR do volunteer work, OR receives remedial assistance in studies
		○ Very poor	Unable to work (study) at present
S2	**Work skills: HOW DO YOU RATE YOUR WORK (STUDY) SKILLS?**		
		○ Very good	
		○ A little difficulty	For example, I have to put in a lot of effort to get good results, get tired easily, lose concentration
		○ Definite difficulty	For example, sometimes make mistakes
		○ A lot of difficulty	For example, I am slow, work is of poor quality
		○ Very poor	For example, I need need constant supervision and/or reminders
S3	**Leisure: HOW DO YOU RATE THE NUMBER OR TYPE OF LEISURE ACTIVITIES OR INTERESTS YOU DO?**		
		○ Very good	
		○ A little difficulty	I have leisure activities and interests, but do not do them often
		○ Definite difficulty	Definite difficulties in developing and doing leisure activities and interests
		○ A lot of difficulty	I have a lot of difficulty developing and doing leisure activities and interests

H13	I get sudden feelings of panic	○ Very often indeed ○ Quite often ○ Not very often ○ Not at all
H14	I can enjoy a good book or radio or television programme	○ Often ○ Sometimes ○ Not often ○ Very seldom

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		○ Definite difficulty	Definite difficulties in developing and doing leisure activities and interests
		○ A lot of difficulty	I have a lot of difficulty developing and doing leisure activities and interests

	○ Very poor	I do not have any leisure activities or interests at present

S4	**Organising activities: HOW DO YOU RATE THE WAY YOU ORGANISE WORK AND LEISURE ACTIVITIES?**

○ Very good	
○ A little difficulty	For example, I need prompts or supports from others
○ Definite difficulty	I am fairly dependent on other people to organise activities, e.g. others suggest what to do and how to go about it
○ A lot of difficulty	I needs other people to do the organising, e.g. making arrangements, providing transport
○ Very poor	I am dependent on other people to suggest and organise activities at present

Relationships

S5	**Spouse or partner: DO YOU HAVE A PARTNER OR SPOUSE?**

a) IF YES, HOW DO YOU RATE THE RELATIONSHIP?

○ Very good	
○ A little difficulty	Not good, but still able to get along together, and if it broke down I have the skills to form new relationship
○ Definite difficulty	Definite difficulties, but I have the skills to form and also probably maintain a new relationship
○ A lot of difficulty	Might have the skills to form a new relationship
○ Very poor	Relationship is extremely limited (e.g., partner is a primary caretaker) and I do not have the skills to form a new relationship

b) IF NO, HOW DO YOU RATE YOUR ABILITY TO FORM AND MAINTAIN SUCH A RELATIONSHIP?

○ Very good	
○ A little difficulty	I have the skills to form and maintain a new relationship
○ Definite difficulty	I have the skills to form and also probably maintain a new relationship
○ A lot of difficulty	Might have the skills to form a new relationship
○ Very poor	Do not have the skills to form a new relationship

S6	**Family: HOW DO YOU RATE YOUR RELATIONSHIPS WITH OTHER FAMILY MEMBERS?**

○ Very good	
○ A little difficulty	Not good, but still able to get along together
○ Definite difficulty	Definite difficulties, but still see family
○ A lot of difficulty	A lot of difficulties getting along with some family members
○ Very poor	Relationship is extremely limited and there has been breakdown

S7	**Leisure: HOW DO YOU RATE THE NUMBER OR TYPE OF LEISURE ACTIVITIES OR INTERESTS?**

○ Very good	

	○ A little difficulty	Not good, but have close friends, make new friends, and get along with work mates and neighbours
	○ Definite difficulty	Definite difficulties, but still see some friends once a month or more and can make new friends
	○ A lot of difficulty	Only see a few friends (or other people outside family), and do not make new friends easily
	○ Very poor	Do not see any friends (or other people outside the family)
S8	**Communication: HOW DO YOU RATE YOUR COMMUNICATION SKILLS (THAT IS, TALK WITH OTHER PEOPLE AND UNDERSTAND WHAT OTHERS SAY)?**	
	○ Very good	
	○ A little difficulty	For example, I ramble and get off the point, talk is sometimes inappropriate, have some trouble finding the words to express myself
	○ Definite difficulty	For example, difficulties thinking of things to say, joining in talk with groups of people, only talk about myself
	○ A lot of difficulty	For example, I have trouble understanding what people say
	○ Very poor	Communication is almost impossible

Living Skills

S9	**Social Skills: HOW DO YOU RATE YOUR SOCIAL SKILLS AND BEHAVIOUR IN PUBLIC?**	
	○ Very good	
	○ A little difficulty	For example, I am awkward with other people, do not worry about what other people think or want
	○ Definite difficulty	For example, can act in a silly way, am not as tactful or sensitive to other people's needs
	○ A lot of difficulty	For example, am dependent on other people, am socially withdrawn, have difficulty interacting appropriately with other people
	○ Very poor	For example, have temper outbursts in public, require supervision when with other people
S10	**Personal habits: HOW DO YOU RATE YOUR PERSONAL HABITS (E.G. HIS/HER CARE IN CLEANLINESS, DRESSING AND TIDINESS)?**	
	○ Very good	
	○ A little difficulty	For example, do not take much care
	○ Definite difficulty	Attend to own hygiene, dress and tidiness, but have definite difficulties in this area; need supervision
	○ A lot of difficulty	Need prompts, reminders or advice from others, but respond to these; need stand-by assistance
	○ Very poor	Need prompts, reminders or advice from others, but unwilling to respond to these; need hands-on assistance
S11	**Community travel: HOW DO YOU RATE YOUR USE OF TRANSPORT AND TRAVEL AROUND THE COMMUNITY?** *NOTE: Do not include the driver of transport, or other passengers using such transport, in rating whether you can travel "on your own".*	
	○ Very good	

	A little difficulty	Unable to use some forms of transport (e.g. driving a car) but can still get around in the community by using other forms of transport without help
	Definite difficulty	Definite difficulty using transport, but after training can travel around the community on my own
	A lot of difficulty	Need assistance to plan use of transport, but with such help can travel around the community on my own
	Very poor	Unable to go out into the community on my own
S12	**Accommodation: HOW DO YOU RATE YOUR LIVING SITUATION?**	
	Very good	
	A little difficulty	Live in the community, but with emotional or social supports provided by other people, such as family, friends or neighbours. Could not be left alone without supports for a two-week period
	Definite difficulty	Live in the community, but could not be left alone for a weekend unless someone checked that everything was OK
	A lot of difficulty	Live in the community but in supported accommodation, such as a group home, boarding house,transitional living unit, in family home but I require daily supervision or assistance
	Very poor	Need care, which may be at home requiring extensive, daily supervision or other care OR in a facility, e.g., a nursing home, residential service, rehabilitation unit

To submit your results, please click on the ***Submit this information*** button.

If you wish to wipe your answers, click on the ***Clear your answers*** button.
With submission of your answers, you imply consent to participate in this study.

Submit this information | Clear your answers.

Thank you for taking the time in complete these questionnaires!

Your help is appreciated.

Thank You!

This project has been approved by the
Central Regional Ethics Committee, Ministry of Health:
Application CEN/09/02/02.

If you have any questions or concerns about your rights as a participant in this study, you can contact an independent health and disability advocate.
This is a free service provided under the Health and Disability Commissioner Act.
Telephone: (NZ Wide) 0800 555-050
Free Fax (NZ Wide) 0800 2787-7678 (0800 2 SUPPORT)
Email (NZ Wide): advocate@hdc.org.nz

The Fatigue Severity Scale (FSS) is embedded in the Fatigue Assessment Inventory above, pp 256 – 257. A copy of the specific questions in the FSS appears below on page 262.

Fatigue Severity Scale

INSTRUCTIONS: ***Date.....***

Below are a series of statements regarding your Fatigue. By Fatigue we mean a sense of tiredness, lack of energy or total body give-out. Please read each statement and choose a number from 1 to 7, where #1 indicates you completely disagree with the statement and #7 indicates you completely agree. Please answer these questions as they apply to you in the **past TWO WEEKS**.

Circle the appropriate number

		Completely disagree						Completely agree
3*.	My motivation is lower when I am fatigued	1	2	3	4	5	6	7
5*.	Exercise brings on my fatigue	1	2	3	4	5	6	7
18*.	I am easily fatigued	1	2	3	4	5	6	7
19*.	Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
20*.	Fatigue causes frequent problems for me	1	2	3	4	5	6	7
21*.	My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
22*.	Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
25*.	Fatigue is among my 3 most disabling symptoms	1	2	3	4	5	6	7
26*.	Fatigue interferes with my work, family or social life	1	2	3	4	5	6	7

Appendix H

Online Diary Data Entry

Postconcussion Energy Recovery Training (PERT) Programme

Palmerston North Concussion Clinic participants ONLY:
During the Weeks 1 - 12, please rate your fatigue and energy each weekday and keep a record of any exercise you do and any naps you have on those days. Remember do not change your routine in the first week of the programme. Please enter these ratings into the diary on this website.

The link to this online diary for data entry purposes will have been provided by your therapist.

Instructions

You and your therapist will use the diary to keep track of how you are doing on the PERT programme. Also, the data, without your name will be used to judge how well the programme works to reduce post-MTBI fatigue.

You can enter the information into your workbook and at the end of the week enter it into the diary on this page. If you miss a day of exercise, put a zero in the exercise column. You can still rate your fatigue and energy and record nap minutes as usual

Please enter your data into the diary BEFORE your appointment with your therapist each week. Your therapist prefers you to enter the data a day before your appointment so she can look at it before she talks with you.

You have entered your own code and your responses will be viewed only by Joan Norrie, Principal Investigator and your therapist. They will be held in a secure file at Massey University, Palmerston North.

Please complete the diary for each day if possible. You have the right to decline to answer any particular question.

PLEASE NOTE:
If at any stage you would like to check your previous answers to any questions please scroll up and down the document.
Do not use the back-button on your tool bar, as this will take you out of this survey without saving your answers.

Many thanks for your assistance with this survey.

Fatigue and Energy Ratings Diary

Client code ***Please enter your Initials and birthdate (XXDDMMYY) in the box to the right*** *(as provided for confidentiality of answers)*	

Date of day 1 of this diary (dd/mm/yy)	

Please enter the number of **minutes** of exercise and naps for each day.
Rate your Fatigue and Energy level for each day as per the 1-10 scale provided at the same time of day and enter into the diary below.

0—1—2—3—4—5—6—7—8—9—10
No Fatigue/Tireness **Exhausted**

0—1—2—3—4—5—6—7—8—9—10
No energy **Full of Energy**

	Exercise (minutes)	Nap (minutes)	Fatigue	Energy
Day 1			Rating	Rating
Day 2			Rating	Rating
Day 3			Rating	Rating
Day 4			Rating	Rating
Day 5			Rating	Rating

To submit your results, please click on the ***Submit this information*** button.

If you wish to wipe your answers, click on the ***Clear your answers*** button.
With submission of your answers, you imply consent to participate in this study.

Submit this information | Clear your answers.

Thank you for taking the time in complete these diaries!

Your help is appreciated.

Thank You!

This project has been approved by the
Central Regional Ethics Committee, Ministry of Health:
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If you have any questions or concerns about your rights as a participant in this study, you can contact an independent health and disability advocate.
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Telephone: (NZ Wide) 0800 555-050
Free Fax (NZ Wide) 0800 2787-7678 (0800 2 SUPPORT)
Email (NZ Wide): advocate@hdc.org.nz

Appendix I

PERT Programme – Therapist Manual

from Fatigue

to Energy

THERAPIST MANUAL

CONTENTS

WEBSITE ADDRESS: http://psych-research.massey.ac.nz/fatigue/

Postconcussion Energy Recovery Training (PERT)

Introduction

- The Postconcussion Energy Recovery Training (PERT) programme was designed specifically to promote recovery from post-MTBI fatigue. It consists of education about post-MTBI fatigue, aerobic exercise, and guidelines for managing energy and fatigue related factors.

- The rationale for the programme is included in the education section of Session 1 of the manual. To date the most effective treatment for postconcussion syndrome (PCS) has been provision of education about concussion and its sequelae early in the recovery period. Recently, aerobic exercise has been shown to be effective in reducing the length of postconcussion recovery time. The PERT programme is designed to combine these two rehabilitation approaches and evaluate their effectiveness in treating post-MTBI fatigue, one of the most common and persistent postconcussion symptoms.

- PERT is currently in the trial stage of its development. The objective is to gather evidence about its effectiveness in treating post-MTBI fatigue.

- The exercise programme is planned by the client and the therapist to suit individual fitness levels while exercising within the aerobic range.

- Clients are expected to exercise five times a week for 30 minutes and to record their exercise, fatigue and energy ratings each day.

- Each client receives manual containing information about post-MTBI fatigue, the exercise programme, diary and monitoring questionnaires.

- The therapist manual contains the client manual and guidelines for session protocol.

- The programme has a website at http://psych-research.massey.ac.nz/fatigue/ for gathering of data which can be entered daily, weekly and at baseline and follow-up intervals.

- The clients record their plan for the week and their actual exercise, along with their fatigue and energy levels. This data is entered into the website.

- There are five face to face sessions and seven phone sessions during the twelve weeks of the programme. The first session is expected to be up to 90 minutes long, other face-to-face sessions will be 60 minutes and phone calls 30 – 60 minutes long.

It is imperative that the therapist follows the programme as it is set out below so that the research conclusions can be based on the design protocol. Divergence from this protocol will contaminate the findings.

Guide to Implementation of Postconcussion Energy Recovery Training

The PERT programme combines information about post-MTBI fatigue with regular aerobic exercise. It is delivered over five fact-to-face sessions and seven phone sessions and can be either clinic or home-based.

This programme is designed to be delivered by a therapist who specialises in traumatic brain injury rehabilitation. Therapists are most likely to be clinical psychologists or occupational therapists.

PROGRAMME SCHEDULE

Week 1 starts from the day on which the first appointment with the Client occurs.

Sessions (Weeks) 2 and 3: face-to-face 60 minutes.

Sessions (Weeks) 4 – 7: phone 15 - 30 minutes.

Session (Week) 8: face-to-face 60 minutes.

Sessions (Weeks) 9 – 11: phone 15 - 30 minutes.

Session (Week) 12: face-to-face 60 minutes.

Table 1: Postconcussion Energy Recovery Programme Schedule

Week	1	2	3	4	5	6	7	8	9	10	11	12
Concussion Clinic	X	X	X					X				X
Phone				X	X	X	X		X	X	X	
Record Energy and fatigue ratings	X	X	X	X	X	X	X	X	X	X	X	X

PLEASE FILL IN THE DEMOGRAPHIC AND ACCIDENT DETAILS QUESTIONNAIRE AS MUCH AS POSSIBLE

Participant ID (Initials DOB (dd/mm/yy)
DOB:
Age
Gender
Years of Education
Injury details
Date of Injury
PTA minutes
GCS
Cause of Injury
Did you get knocked out?
How long were you knocked out for?
How long were you confused for? hours
Did you remember the accident?
What was your last memory before the accident?
Approximately how long was that before the accident?
Do you have persistent pain other than headache?
Where is your pain?
On a scale of 0 to 10, how bad is your pain (0 = no pain and 10 = really really bad pain)
Apart from seeing a doctor before coming to the Concussion Clinic what other treatment have you had since your head injury? Details of other treatment
Head Injury history
Have you been knocked unconscious before?
How many times? What was the longest time you were knocked out for before this accident?
Did you have time off work or school after any of those accidents?
Medical and Psychiatric history
Have you had any serious illness like, diabetes, epilepsy, asthma?
Which illnesses?
Have you ever been to a doctor, psychologist, counsellor for depression ❑ anxiety ❑ panic attacks ❑ other mental illness?
Have you ever been prescribed medication for any of these difficulties?
What was the medication?
How long did you take it for?
What medications are you currently taking?
What other treatments are you currently having or taking to help you with fatigue?
Fatigue and Sleep
Did you have problems with fatigue before this accident?

What sort of fatigue problems did you have?
How many hours per night did you sleep before the accident? hours
Did you have sleep problems before this accident?
When you go to bed, how long does it take you to get to sleep now? minutes
How often do you wake in the night?
School, Polytech, University Students
Student at School ❑ Polytech ❑ University ❑ Other❑
How many hours per week did you normally study before the accident?
Have you returned to study/school since the accident?
How many hours per week are you currently at study/school since the accident?
Work or other daily activity
What kind of work do you usually d?
How many hours per week do you normally work?
Have you returned to work or normal activity since the accident?
How many hours per week are you currently working since the accident?
Drugs and Alcohol
Alcohol, how much do you drink now? Before the injury?
Cannabis? Yes ❑ No ❑
Other recreational drugs? Yes ❑ No ❑
Computer Access
Do you own a computer with internet access? Yes ❑ No ❑
If not, can you get easy access to a computer? Yes ❑ No ❑ if no we will supply you with copies of the questionnaires we would like you to do

The Assessment Instruments

Copies of these instruments are available at the end of this manual.

Rivermead Postconcussion Symptoms Questionnaire (RPSQ): A 16-item self-report checklist of presence and severity of PCS symptoms (King et al., 1995) in the previous 24 hours. In the current study the clients are asked to rate the extent to which these symptoms have been any more of a problem over the previous two weeks compared with pre-accident levels, using a rating scale with values of 0-4. The alteration in period was made because the baseline data is taken from people who may be from a few days to many months post-concussion. Additionally another study carried out by the principal investigator used this adaptation and to maintain consistency the interval was set at the previous two weeks. The RPSQ has good discriminant validity differentiating MTBI from healthy controls, ($p<0.0001$) (Chan, 2001) and high test-retest (0.91) and inter-rater (0.87) reliability (King et al., 1995). A score ≥ 2 on item 6 (fatigue) at initial Concussion Clinic assessment is the criteria for invitation to take part in the PERT evaluation trial.

Fatigue Assessment Instrument (FAI): is a 29 item measure of global fatigue severity, situation-related fatigue, the impact of fatigue on daily functioning (Kleinman et al., 2000; Schwartz et al., 1993). It has a seven point Likert scale ranging from "1 = Completely disagree" to 7 "Completely agree". It has a four factor solution, global fatigue severity (GFS), situation specific (SS), consequences (Con) and response to rest/sleep (RS) with subscale internal consistency ranging from 0.70 to 0.94 respectively. Schwartz et al reported FAI has discriminant validity for patients and controls for a variety of illnesses. One item "When I am tired my family, or partner, thinks I am being lazy" was added to the end of the FAI to assess significant other attitude towards fatigue. The *Fatigue Severity Scale (FSS):* (Krupp et al., 1989) is an earlier fatigue measure developed by the same team and correlated highly with the GFS ($r = .976$, $n=235$). FSS internal consistency was 0.94 and test-retest reliability was 0.82 (Kleinman et al., 2000). The FSS mean for a normal healthy population was 3.35 (1.11) (Ziino & Ponsford, 2005a) and 2.3 (Krupp et al., 1989). The latter study also report FSS means for systemic lupus erythematosus 4.7 and multiple sclerosis 4.8 while it was 4.36 (SD=1.52) for a group of mixed severity TBI at a mean of six months (M=241.67 days) post injury. A large variety of fatigue studies have used FSS as the primary fatigue measure and few report the GFS subscale of FAI. It is calculated from FAI items so requires no further input from clients completing these instruments. Also the FSS includes a "motivation" question while the GFS does not. There is a very high incidence of prefrontal lobe injury, i.e., involving motivation disruption, so it was considered important to have this item included in the fatigue measure.

Hospital Anxiety and Depression Scale (HADS): A 14 item measure of generalised anxiety and depression (Zigmond & Snaith, 1983). Items are rated 0-3. Two scales anxiety and depression each rated mild 8-10, moderate 11 – 13, and severe ≥ 14 total. Both clinically and in research, it is a widely used instrument (Bjelland et al., 2002) found to be reliable and valid by (Herrmann, 1997) whose literature review reported Cronbach's alphas for anxiety, 0.80 and depression, 0.81. Bjelland et al's (2002) review noted Cronbach's alphas ranged from .68 to .93 (mean = 0.83) for anxiety and from .67 to .90 (mean = .82) for depression. Both reviews found a two factor solution, anxiety and depression, although up to four factors have been found in studies reviewed in 1997 and 2002. Bjelland et al (2002) reported a cut-off score of ≥ 8 gave 0.80 sensitivity and specificity respectively. Internal consistency of the English version is acceptable as is two week retest reliability ($r>0.8$). Over time the test re-test reliability reduces suggesting HADS is a suitable measure of change. The two factors, anxiety and depression, explain 50% of the variance, remain stable across subgroups, correlate highly with the corresponding subscales ($r>0.9$) (Herrmann, 1997).

One major advantage of the HADS is that it was designed to exclude somatic symptoms such as insomnia, anergia and fatigue (Martin, 2005) making it a suitable instrument to use while exploring fatigue in an MTBI population. However, clinically, the Principal Investigator has observed that the depression score can be inflated by an item referring to feeling "slowed down"; a feeling which could also be contingent upon MTBI-related slowed information processing speed as it is a common postconcussion cognitive symptom.

Sydney Participation Rating Scale: (Tate et al., 1999): A 12 item scale which assess community integration across three domains (occupational activities, interpersonal relationships and independent living skills commonly disrupted after TBI. It has high levels of internal consistency (alpha = .90) and reliability (r = .90), convergent and discriminant construct validity and sensitivity (Tate et al., 1999). It has both self and other (therapist or relative) forms.

Session Format

After the first session, each session starts with a **review of the previous week's exercise, fatigue and energy ratings.**

Discuss with the client their experience of the programme and how their fatigue and energy has been for the week.

Check the participant has entered their fatigue and energy ratings into personal graphs in their manual.

Celebrate good progress and review difficulties.

If greater fatigue or less energy than expected, enquire about any novel events, during the week, which might explain these changes.

Discuss ways to manage difficulties and barriers to improvement.

Set goals for the coming week and get Client to record these in their manual.

Each session contains an education section.
Present the ideas contained in the education informally using the manual script to guide the discussion. Avoid reading the manual verbatim but suggest the Client reads it over during the week.

Session 1: face-to-face at Concussion Clinic, 60 - 90 minutes

Objective:
Meet with the client in the Concussion Clinic to

- explain the programme,
- introduce the manual
- present information about post-MTBI fatigue as per the manual,
- describe rationale for the aerobic exercise component programme and emphasize its central role in the programme
- ask about current exercise participation,
- set goals for the week,
- discuss any individual barriers to exercise and ways to overcome them
- take baseline measurements using web-based tests

Begin by establishing a good working relationship with the client. Create an expectation of success. Say "*Exercise and information have helped many people to get over excessive fatigue in other illnesses such as Multiple Sclerosis and I expect that with your commitment to this programme you will see improvements in your energy and reduction in your fatigue. Let's have a look at what this programme can do for you. Firstly I want to quickly go over the Concussion Clinic report to check its accuracy and ask how things have changed since you first came to the Concussion Clinic"*

Confirm clinical history from CARR and enquire about current functioning.

Explain the rationale for the programme beginning with "**Getting Started – Becoming Energised**" and going through to "**Postconcussion Energy Recovery Training**".

Client Manual P4

Getting Started - Becoming Energised

What this programme can do for me?

The programme aims to give you information about concussion, mild traumatic brain injury (MTBI) and one particularly bothersome postconcussion symptom – Fatigue. It aims to help you regain your Energy through activity and pacing. Your family can also be involved in the programme as it helps if they understand why you are so tired and how they can help you make it better.

Why me?

At the Concussion Clinic you were asked to do a short questionnaire in the waiting room. You circled a number between 2 and 4 for the question "Fatigue, tiring easily" in the two weeks before coming to the clinic. ACC agreed with our recommendation that you attend the programme to help you to get over the concussion and get back to your normal lifestyle.

Who will guide me through the programme?

The **Postconcussion Energy Recovery Training** will be provided to you by a Clinical Psychologist or an Occupational Therapist, familiar with traumatic brain injury

Fatigue stops you from doing the things you want to do. It interferes with concentration, attention, memory and feeling good about yourself. It can make your grumpy, snap at your friends and stop you enjoying life. **Energy** is the power which lets you do things. It is the fuel we use to do things like think, walk, feel and relate to our family and friends.

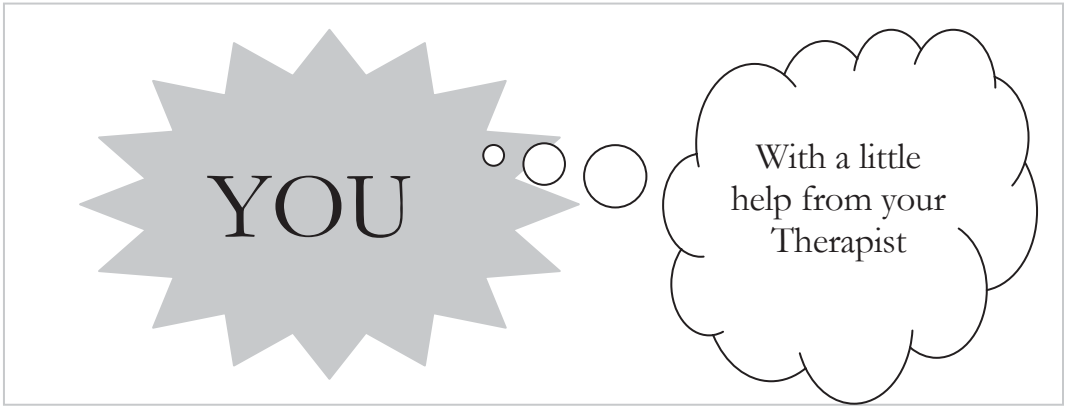
The "GOOD NEWS" is....

There are ways to help the brain

- **recover from the effects of MTBI,**
- **build up ENERGY**
- **reduce POST-MTBI FATIGUE**

The "BAD NEWS" is....

The ways to increase your ENERGY and reduce your POST-MTBI FATIGUE are up to ...



All it needs is YOUR commitment to making a difference

Postconcussion Energy Recovery Training

The programme involves five sessions with a therapist (Clinical Psychologist or Occupational Therapist) and seven shorter phone sessions with your therapist. Additionally you will be doing up to 30 minutes moderate exercise 5 times a week.

Your therapist will go through the information about post-mild traumatic brain injury fatigue, (post-MTBI fatigue) in this manual. This will help you to understand why you are feeling so tired and how you and your therapist can work to improve it.

People vary in the amount of time that post-MTBI fatigue is a problem and they vary in the amount of time and effort it takes to reduce it. We believe that by following the plan, you and the therapist set up, you will feel more energetic.

Energy won't happen overnight but it WILL happen…

What is post-MTBI fatigue?

Fatigue is feeling tired. You can feel tired mentally, physically, emotionally and/or spiritually (hinengaru, tinana, wairua).

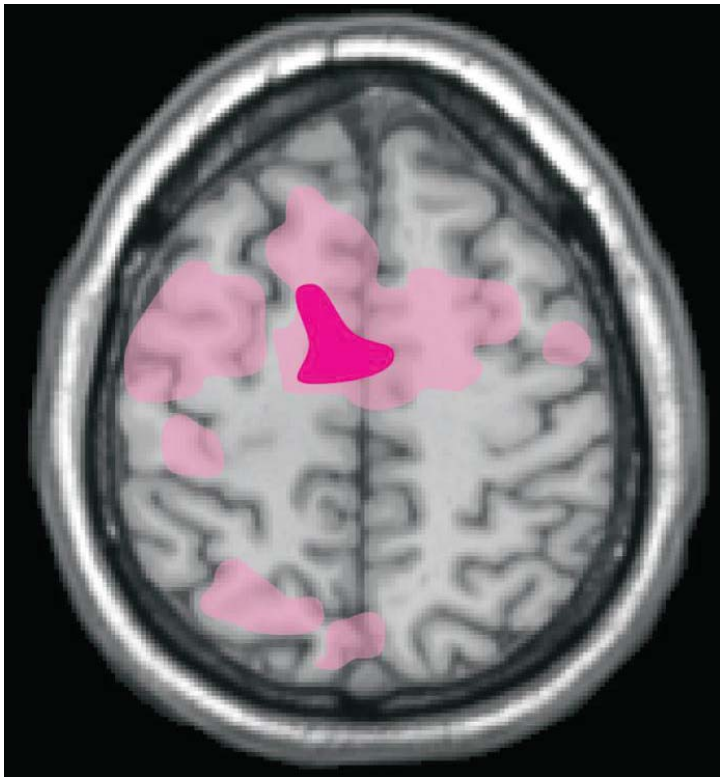
Post-MTBI fatigue is the feeling of tiredness which comes after a Concussion or MTBI. People, who have post-MTBI fatigue, talk about suddenly becoming tired, running out of energy, feeling exhausted. They say they "can't be bothered" doing the things they know they should be doing. They get very tired even when they have only done a small amount of mental or physical work. They feel like they have no energy.

We will show you that doing physical activity or aerobic exercise can chase away mental fatigue. Physical activity may seem like a funny thing to do when you are feeling tired but it can revive your mental energy.

What causes post-MTBI fatigue? More brain cells called neurons, on the job

Neuroscientists think post-MTBI fatigue is caused by your brain needing more energy than usual to do the jobs it has to do. We know that after a mild brain injury the brain uses more brain cells, called neurons, to do the same job it did before the injury so it is reasonable to think it needs more fuel (oxygen and glucose).

We use different parts of our brain to perform roles such as thinking, speaking, remembering, seeing, walking, shaking hands and so on. These roles involve certain parts of the brain while the rest of the brain is relatively inactive. After an MTBI, the brain uses a larger area of brain cells by recruiting nearby cells or uses cells from other areas of the brain in order to perform these roles. More energy is needed to fuel the extra cells and this makes the injured brain tire more easily.



Most mild brain injury is closed head injury, that is, the skull is not broken. The brain can shake around inside the skull which is not smooth on the inside. As is shown in Figure 2 on the next page, brain cells have a long tail called an **axon**, and this can be twisted, stretched and/or torn during the incident or accident.

Figure 1: This picture of the brain shows a small darker coloured area used by the healthy brain and the much larger pale areas used by the injured brain to do the same task. Adapted from Mendez et al. (2005) p.300.

The brain uses electrical impulses to transmit messages to and from the body and within the brain itself. The messages travel along the axons through the cell body to the next neuron jumping over the gaps between neurons using chemicals called neurotransmitters. If the axon is damaged or the neurotransmitters are disrupted the message does not get sent as efficiently as it usually is. Until the neuron's axon recovers it does not work properly and other neurons are needed to assist in the roles of thinking, concentrating, remembering, talking, walking, seeing and so on and you get tired, fatigued.

The pattern of damaged brain cells can randomly spread out throughout the brain in a diffuse pattern, a bit like a banana cake speckle. This diffuse axonal injury means there may be many damaged individual neurons spread out in various parts of the brain. One of the effects is slower thinking.

People who have a motor vehicle accident, a fall, bike accident or are assaulted are especially likely to have this type of injury because their head gets shaken and twisted during the accident or incident. We think that post-MTBI fatigue is partly caused by diffuse axonal injury in the brain areas that control the sleep/wake cycle,

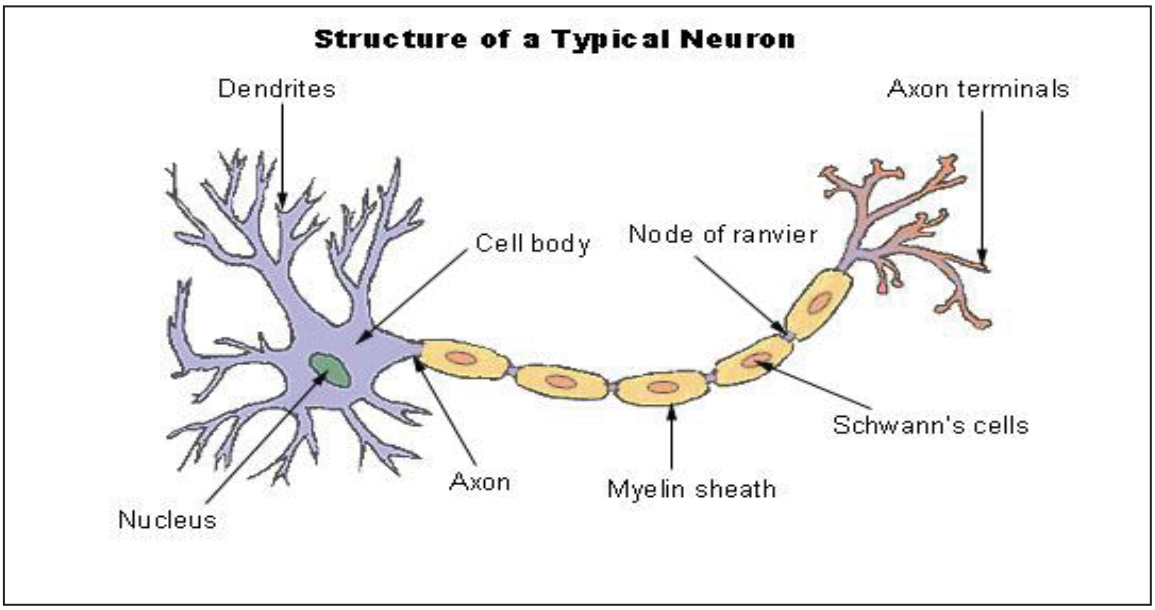


Figure 2: Structure of a typical neuron. Reprinted from Wikipedia under GFDL

general brain activation and motivation. Injury in those areas explains why many people who have post-MTBI fatigue often also have sleep problems, taking a long time to go to sleep and/or waking frequently during the night. It also explains why when you are feeling fatigued you can not be bothered doing the things you want to do, or think you should do.

Aerobic exercise helps the brain heal

by promoting the substances which stimulate neuronal repair and regrowth. Neuroplasticity is the technical term for the process of neuronal repair and regrowth.

Aerobic exercise also improves mood

Sometimes after a concussion people find themselves being more depressed, tearful or worried than usual and this can be the result of post-MTBI fatigue or interruption to the neurotransmitter systems. The chemicals which help the messages get through from one neuron to the next. Some of these neurotransmitters help to keep us happy, they reward us with good feelings. Serotonin, Dopamine, and Norepinephrine are neurotransmitters which make a difference to how we feel and they can be improved by aerobic, that is moderate, exercise.

Remember the **"Good News… Bad News"**?
Well…

The Good News is that there is a way to help with post-MTBI fatigue. The Bad News …well there is no need for Bad News… the Good News is that if you follow the programme you will feel better over the next twelve weeks

Aerobic exercise is one of the best ways that has been found to help people with mental fatigue to increase their energy and feelings of wellbeing. Health scientists found that regular moderate intensity exercise helped reduce fatigue in people suffering from Multiple Sclerosis, Chronic Fatigue or Depression. A team of psychologists, medical specialists and physiotherapists in America[8] have shown that aerobic exercise helps athletes recover from postconcussion symptoms. We believe that aerobic exercise will help you overcome the mental fatigue which has bothered you since your concussion.

We already know that spending too much time resting or watching TV can make you feel stale, tired and/or bored. Avoiding physical activity can cause you to lose the fitness you had before the accident so part of the programme is to do aerobic exercise five times a week. You can build up the length of time you exercise at moderate intensity in the early weeks of the programme. In Session 2 we will show you how to judge whether you are exercising at moderate intensity, that is staying in the aerobic zone.

Introduce the Assessment Protocol to the Client

- Explain the need to get a starting point (baseline) from which to measure changes in fatigue and energy over the course of the training. Suggested statement…
  Say… "*So that you and I can track the changes in your post-MTBI fatigue and energy over the course of your participation in PERT, I will be asking you to fill in some questionnaires about postconcussion symptoms, fatigue, depression, anxiety and participation in work and home activities. We have put these questionnaires on to a PERT website to make it easier to collect the information for the research we are doing. If you do not have computer access you can fill in the questionnaires at the end of your booklet and I will collect them from you OR you can Freepost them to me. We call this first time you fill in the questionnaires the BASELINE as it is the beginning against which we look for change over the programme. Only the Principal Investigator, Joan Norrie, (and your therapist) will see your answers. They will be anonymously combined with other people's answers, when the research questions are being looked at.*"
- Show the Client that there are printed copies of the questionnaires at the back of their manual, page 40 client's manual.
- Demonstrate how to log onto the website. Let the Client do the action under direction from you so that they have a better opportunity of remembering the procedure.
- Ask the Client to complete the baseline questionnaires in the session. Explain that we will also use the first week to obtain a BASELINE of

[8] Kozlowski, K. F., Willer, B., Leddy, J., Chevalier, N., & Scarsaletta, S. (2006)

exercise, naps, fatigue and energy. Direct the client to look at the table designed to gather this information either in their manual or on the website.

- WEEK 1: Tell the client that during this week they are asked to carry on as they have been doing since the concussion. "**Do not change your naps, activity or exercise".**
- Ask the Client to keep a record of their fatigue and energy levels, naps and exercise in the table on this page. Nil exercise is recorded if applicable.
- Ask the Client to go to the website at the end of the week and enter the information they have recorded. They can enter the data each day if they want to. Review the procedure with the Client in this first session.

✍ **Record date and time of next appointment. Same day and time**

Week 1 – Plan and Diary

- Firstly we need to measure your fatigue and mood and so we will log on to the website http://psych-research.massey.ac.nz/fatigue/ and complete the questionnaires.
- Then during this week you are asked to carry on as you have been doing since the concussion. **Do not change your activity or exercise.**
- Keep a record of your fatigue and energy levels, naps and exercise (even if you are not doing much) in the table on this page.
- At the end of the week go to the website and enter the information you have recorded. Your therapist will go through this with you the first time.
- For printed copies of the questionnaires Go to page 40.

My Plan for Week 1 is to record my fatigue, energy, exercise, naps or rest on 5 days of this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2……3……4……5……6……7……..8……..9…..10

No fatigue/tiredness **Exhausted**

0……1……..2……3……4……5……6……7……..8……..9…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 2: face-to-face 60 minutes.

BEFORE you meet with the Client REVIEW their data online to see if they have been recording the fatigue, energy, exercise and nap information.

Start with a review of the previous week's training. Check chart of exercise, fatigue and energy ratings. If these are not being entered into the website, review and demonstrate procedure. Allow the Client to find the website and enter data, do not do it for them.

Introduce the fatigue and energy ratings graph at the end of the manual and explain how graphing the ratings will help with motivation to keep up the training. Enter data from Week 1.

Review the rationale for aerobic exercise plus information as ways of reducing post-MTBI fatigue.

Set goals for the coming week and get Client to record these in their manual.

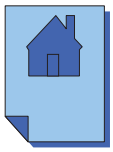
Information section.
Present the ideas contained in the information section, informally, using the manual script to guide the discussion. You may need to do this in sections if the Client has memory or attention difficulties. Avoid reading the manual verbatim but suggest the Client reads it over during the ensuing week. Use **Verification** to confirm that the Client has understood the information provided.

Verification: Ask the Client to repeat the gist of the information in their own words. OR Encourage the Client to ask for clarification if they do not understand

Record date and time of next appointment. Same day and time

Client Manual P12

Week 2 – Step out for energy



My Concussion Clinic appointment with ……. is at ……am/pm on……

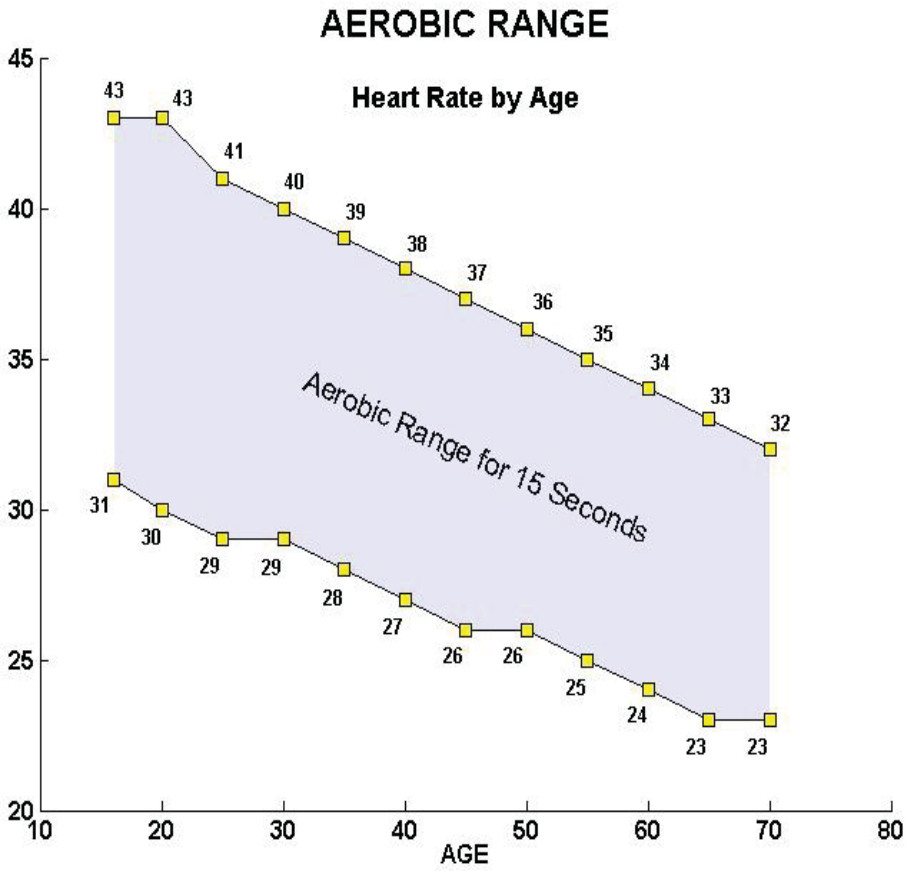
Review of diary: You wrote down your current exercise level and we are going to use that to plan an activity programme with you.

the Aerobic Zone

We talked about moderate or aerobic exercise last week. To judge whether you are exercising at the correct intensity use one of the following ways.

1. The Talk Test - if you can talk in brief sentences while you are exercising but you can not sing (because of shortness of breath) then you are exercising in the aerobic zone.

2. You may feel slightly sweaty, breathe faster than usual and have some strain in your muscles when you are in the aerobic zone.
3. Counting your heartbeat while you are exercising is another way to judge the "aerobic zone". There are many websites which do the calculations. Or you can refer to the chart below.



Are you experiencing any postconcussion symptoms like headache or dizziness when you exercise? If you are then reduce the intensity a bit until you can exercise without headache.

Week 2: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 3: face-to-face 60 minutes

BEFORE you meet the Client REVIEW their data online to see if they have been recording the fatigue, energy, exercise and nap information.

Start with a review of the previous week's training. Check chart of exercise, fatigue and energy ratings. If these are not being entered into the website, review and demonstrate procedure. Allow the Client to find the website and enter data, do not do it for them.

Enter fatigue and energy ratings into graph at the end of the manual and discuss any changes between Week 1 and Week 2.

Review the rationale for aerobic exercise and ways to check the Client is exercising within that zone.

Set goals for the coming week and get Client to record these in their manual.

Information section.
Present the ideas contained in the information section,

Ask the Client to **Verify** by giving you a brief summary of the information. Remember you may need to do this in sections if the Client has memory or attention difficulties.

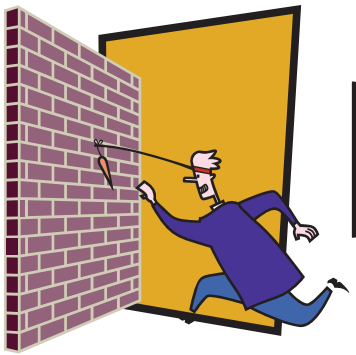
Record date and time of next appointment.

Client Manual P14

Week 3

My Concussion Clinic appointment with ……..
is at ……am/pm on……

Review of diary: How was your second week on the programme?



BARRIERS TO EXERCISE

"once you identify your specific barriers to exercise, and realize that these are simply problems to be solved, you can begin and sustain a life changing programme for health" (Hansen, 2008). Denise Hansen is living with brain injury

and has some great ideas from her struggle with fatigue. You will read more about Denise Hansen's journey later in the programme.

Meanwhile here are some frequently raised barriers to exercise and ways to get around them

I'm too tired to exercise. Do your regular exercise at the same time of the day, when you have a good supply of energy. Morning exercise is best because then it is done for the day and it builds up energy for your day. Get up early and eat then exercise if you are slow waking up.

I don't have time to exercise. Make exercise a regular part of your day just like brushing your teeth.

I don't have the right clothes to wear. Wear anything comfortable. Walkers need a good pair of walking shoes and comfortable socks. If biking you need a helmet, and clothes that will not catch in the wheel. Try swimming with a snorkel.

It is too hot, too cold, too wet outside. Walk in a mall. Dress for the climate warm coat, hat and gloves for the cold and cool cottons and a hat for the heat. You will only be out there 30 minutes. Plan a nice drink hot or cold for your return.

I get too sore when I start to exercise. Exercise within your aerobic range. Start at the bottom of your range and increase the intensity slowly over the weeks of this programme. Warm up and stretch before and after exercise and cool down slowly.

Walking, swimming, biking … which should I choose? Choose the one you like the most? Avoid exercise that hurts. You can do different types of exercise throughout the week.

Exercise makes my postconcussion symptoms (headache, dizziness) worse. If you are getting headache or other postconcussion symptoms when you exercise then you are exercising too hard. Work out the exercise level which you can maintain without pain, preferably in your aerobic zone, and exercise at that level. Talk to your therapist about this problem and work out a solution together.

Exercise is boring… Choose the least boring type of exercise. Some people love the treadmill and others find it very boring. Listen to music or a talking book. Take an interest in your surroundings, look at the gardens or houses or other things that you are walking past. Think about your friends and family, plan your day, and think over a particular problem. Notice the landmarks that tell you how far through the exercise session you are. Walk different routes on different days.

I can't motivate myself to start the exercise session: Do your exercise at the same time every day. Get your gear ready beforehand, e.g., before you go to bed. Tell yourself you have committed to the programme and really want to succeed and get better. Your brain injury may be part of the motivation problem and a way to help your brain heal is to use exercise to encourage new growth, neuroplasticity.

Week 3: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 4: phone call 15 - 30 minutes

BEFORE you meet the Client REVIEW their data online to see if they have been recording the fatigue, energy, exercise and nap information.

Start with a review of the previous week's training. Check chart of exercise, fatigue and energy ratings.

Enter fatigue and energy ratings into graph at the end of the manual and discuss any changes between Week 2 and Week 3. Celebrate positive changes and if no change or negative changes enquire about 1. frequency and consistency of exercise 2. non-brain injury related events which could be causing stress. If there are barriers to exercise problem solve these with the Client.

PROBLEM SOLVING MODEL

1. Define the problem
2. Generate as many possible solutions as can be thought up, write all of these down without evaluating them. Accept 'silly' ones as well as 'sensible' ones because the 'silly' ones sometimes turn out to be able to be adapted to useful solutions.
3. Eliminate unsuitable or impossible solutions. Prioritize preferred solutions.
4. Choose one solution and plan how to implement it.
5. Try the solution
6. Evaluate its effectiveness and refine or repeat some of the steps if necessary to find a new solution.

Review ways the Client can check they are exercising within the aerobic zone.

Set goals for the coming week and get Client to record these in their manual.

Information section.
Present the ideas contained in the information section. Say *"Today we are going to look at Planning and Pacing activity during your day so that you can manage your fatigue and energy. You can get things done without burning yourself out and having extra fatigue for several days following a busy day"*

Ask the Client to **Verify** by giving you a brief summary of the information. Remember you may need to do this in sections if the Client has memory or attention difficulties.

✍ Record date and time of next meeting in next weeks section.

Client Manual P17

Week 4

My phone appointment with ……..
is at ……am/pm on……

Review of diary: How was your third week on the programme. What did you enjoy most? What did you find hardest?

Now lets look at ways to save Energy and prevent Fatigue

Planning & Pacing

First rule of prevention is to PLAN ahead. If you know that there are jobs which have to be done but you also know you will get tired, plan the amount of time you are going to spend on the job. For instance, PLAN to spend between 10 minutes and 30 minutes on the job and PLAN to stop or change your activity to something completely different.

DO NOT work until you are tired.

STOP before you are tired.

Your Occupational Therapist can help you plan your return to work. You may start by going back part-time and building up to your normal number of hours over a few weeks.

Many people go back to work TOO SOON, they go through a BOOM and BUST cycle. The BOOM is going back to full activity and the BUST is having to give up because they are too tired, are making too many mistakes or are not able to manage.

Even at home some people do a lot one day then spend a day or more recovering. To avoid fatigue and keep an energy balance you need to begin with shorter periods of activity with rest or change of activity in between. Build up your stamina by gradually extending the time you spend on activities.

Changing your activity …

- ***If you have been doing mental activity then change to physical***
- ***If you have been doing physical activity then change to mental activity***

Your therapist can help you plan your work or home activity to fit your energy supply as it grows.

Week 4: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2……3……4……5……6……7……..8……..9…..10

No fatigue/tiredness **Exhausted**

0……1……..2……3……4……5……6……7……..8……..9…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 5: phone call 15 - 30 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph. Celebrate positive changes. Say** *"Wow look how your fatigue is going down and your energy is coming up. Keep doing what you are doing and you will soon be on top of the fatigue."*
- **Discuss progress and troubleshoot difficulties collaboratively.** Ask about non-MTBI events which are causing stress and difficulties. Explain how regular exercise helps build stamina to manage stress. Predict dip in motivation and need to meet that challenge and continue with the exercise.
- **Specific aerobic zone for the Client – review the aerobic range, p12 client manual.**
- **Set goals for coming week and record in manual**
- **Provide information and discuss with Client.** Remember you may need to do this in sections if the Client has memory or attention difficulties. Say *"You and your partner and/or family may have noticed you are having problems 'holding it together' since your head injury. We are going to talk about the types of emotional problems that are typical after a head injury especially if you have been hit on the front of your head"*
- **Verify information.**

Record date and time of next meeting in next weeks section.

Client Manual P19

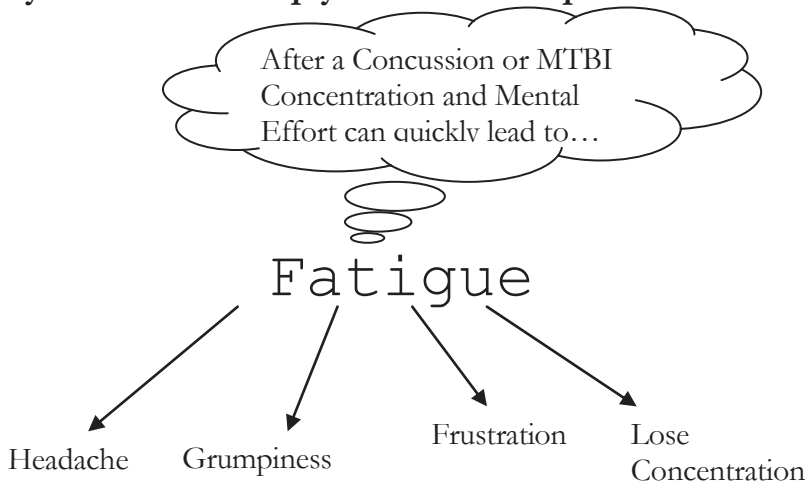
Week 5

My phone appointment with ……..
is at ……am/pm on……

Review of diary: How was your fourth week on the programme. What did you enjoy most? What did you find hardest?

Problems that come with Fatigue and low Energy

It is normal to feel tired after a day's work but post-MTBI fatigue comes on more quickly and can mess up your relationships at work and home.



RECOGNISE you are getting tired and your energy is getting low before it creates a mess.

If you are feeling low in energy, STOP AND TAKE A BREAK OR A WALK.

If you are feeling FRUSTRATED that is a strong signal that fatigue is telling you to take a break.

If you feel grumpy…LOOK AT YOURSELF FIRST…It is easy to blame others, yell at them, or cry in anger… when your energy is low

SAY "Sorry, I feel grumpy right now…I am going to take a break and get my energy back up".

GO AWAY from the situation for about 20 minutes, have a non-alcoholic drink and a small snack, and/or go for a walk

COME BACK and talk about the problem, if there is one

Week 5: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 6: phone call 15 - 30 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph.**
- **Discuss progress and troubleshoot difficulties collaboratively.** Ask about non-MTBI events which are causing stress and difficulties. Explain how regular exercise helps build stamina to manage stress.
- **Specific aerobic zone for the Client**
- **Set goals for coming week and record in manual**
- **Provide information and discuss with Client.** Remember you may need to do this in sections if the Client has memory or attention difficulties.
- **Verify information and exercise programme**

✍ Record date and time of next meeting in next weeks section.

Client Manual P21

Week 6

My phone appointment with ……..
is at ……am/pm on……

Review of diary: You should be well into the routine of the programme by now. If you are having problems keeping to the programme lets talk about how to deal with them.

Another way to save Energy and prevent Fatigue is to …

say 'No'

…OR

...ask for help

if it all seems too much to cope with.

You can say "No" to other people's requests if you are feeling too tired or think the activity will be too stressful. Explain that you are getting over a concussion and need to pace yourself. If it is something you really want or need to do then PLAN it into your activity schedule. If your children need your attention and you are feeling tired sit with them for a quiet time, read a story to them or talk with them.

You can delegate tasks to other people at home or at work.

The Occupational Therapist is there to help you talk with your employer about light duties and a gradual return to your work.

Your therapist can meet with you and your family/whanau to talk about the effects of post-MTBI fatigue and explain your need to spend shorter times doing activities and to find a quiet place for a little while to "recharge your battery", after which, you can rejoin the whanau/family.

Week 6: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 7: phone call 15 - 30 minutes

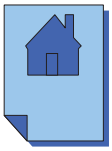
REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph.**
- **Discuss progress and troubleshoot difficulties collaboratively.** Ask about non-MTBI events which are causing stress and difficulties. Explain how regular exercise helps build stamina to manage stress. Predict dip in motivation and need to meet that challenge and continue with the exercise.
- **Specific aerobic zone for the Client**
- **Set goals for coming week and record in manual**
- **Provide information and discuss with Client.** Say *"One of the things you may have noticed since your head injury is that your sleep pattern has changed. This can be caused by injury to the part of your brain which manages your sleep/wake cycle or it could be caused by changes in your daily routine which mean you are resting much more during the day and are not tired at night. If you have been doing the exercise routine fairly consistently you are probably finding your sleep pattern is settling back into what it used to be. I am going to talk with you about useful hints to ensure you get a healthy amount of sleep each 24 hours."*
- **Verify information and exercise programme with the Client**

Record date and time of next meeting in next weeks section.

Client Manual P23

Week 7 A Good Night's Sleep



My appointment with ……..
is at the Concussion Clinic on……

Review of diary: Half way Can You Believe It! What has the sixth week been like?

SL…E…E…P…

In the beginning of this manual we talked about the parts of the brain which control the sleep/wake cycle, that is the Midbrain and parts of the Frontal Lobe.

Sleep Timing Problems

Just over a third of people who have had an MTBI have sleep trouble after their head injury. They take longer to fall asleep and/or they wake up a lot during the night.

We know that mild head injury can upset the sleep/wake cycle, the Circadian Rhythm.

Problems like this can be worrying and also cause more daytime tiredness and fatigue. Getting a bad night's sleep can make post-MTBI fatigue worse.

In the first week or two after your MTBI you may need a nap every day.

After that we suggest you reduce the number of naps you take in a week and replace them with rest, being in a quiet place and aerobic exercise.

The therapist can help you PLAN your sleep routine so that you can reset your internal clock, your circadian rhythm back to what is normal for you. Most people need 8 hours good sleep a night to recharge their energy and firm up their memories.

On the next page are some helpful hints for improving your sleep pattern.

Also there are lots of great websites with guidelines for good sleep, sleep hygiene
For instance, http://www.helpguide.org/life/sleep_tips.htm; http://www.ualberta.ca/~uscs/sleep_hints.htm
Here are some tips on how you can improve your sleep hygiene. They come from
http://www.sleepeducation.com/Hygiene.aspx downloaded on 23.10.2008.

1. **Go to bed when you are sleepy, not before.** If you are not sleepy at bedtime, then do something else. Read a book, listen to soft music or browse through a magazine. Find something relaxing, but not stimulating, to take your mind off worries about sleep. This will relax your body and distract your mind.

2. **If you are not asleep after 20 minutes, then get out of the bed.** Find something else to do that will make you feel relaxed. Do this in another room. Your bedroom should be where you go to sleep. It is not a place to go when you are bored. Once you feel sleepy again, go back to bed.

3. **Begin rituals that help you relax each night before bed.** This can include such things as a warm bath, light snack or a few minutes of reading.

4. **Get up at the same time every morning.** Do this even on weekends and holidays.

5. **Get a full night's sleep on a regular basis.** Get enough sleep so that you feel well-rested nearly every day.

6. **Avoid taking naps if you can.** If you must take a nap, try to keep it short (less than one hour) or have a short rest. Never take a nap after 3 p.m. Do something active if you are feeling sleepy, walk or prepare the vegetables for dinner, weed a garden.

7. **Keep a regular schedule.** Regular times for meals, medications, chores, and other activities help keep the inner body clock running smoothly.

8. **Bed is for sleeping and sex do your other activities, like watching TV, in another room.**

9. **Keep your caffeine drinks to the morning before lunch.** That is avoid coffee, tea, "V". Red Bull etc after lunchtime.

10. **Have at least six hours between having a beer, a glass of wine, or any other alcohol and your bedtime.**

11. **Cigarettes or any other source of nicotine should be avoided before bedtime. Nicotine is a stimulant, it wakes your brain up.**

12. **Do not go to bed hungry, eat a small snack, not a big meal, near bedtime.**

13. **Only gentle exercise within six hours of your bedtime.** You should exercise on a regular basis, but do it earlier in the day.

14. **Sleeping pills should be avoided, or** prescribe sleeping pills for periods of more ☐ **used cautiously.** Most doctors do not than three weeks.

15. **Take 30 minutes to think about your worries before you go to bed.** Your bed is a place to rest, not a place to worry. When you have thought about your worries tell yourself you are going to sleep and that you can not do anything about your worries now.

16. **Make your bedroom quiet, and dark.** The dark will help your brain to produce the chemical (melatonin) which tells it to sleep. Cover your eyes with a sleep mask if you can't keep the light out.

Week 7: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7.....…..8...…..9…..10
No fatigue/tiredness **Exhausted**
0…….1……..2..……3..……4..……5..……6..……7.....…..8...…..9…..10
No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 8: face-to-face at Concussion Clinic, 60 minutes

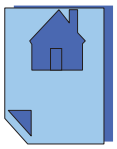
REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph.**
- **Discuss progress and troubleshoot difficulties collaboratively.**
- **Go over the "**useful hints to keep energy up and fatigue down" **section with client**
- **Begin to anticipate the end of the PERT programme and plan for post PERT activity.**
- **Ask about social supports and social activities.** Encourage participation to pre-injury levels.

Record date and time of next meeting in next weeks section.

Client Manual P26

Week 8



My Concussion Clinic appointment with ……..
is at ……am/pm on……

Review of diary: How was your week on the programme.

Beat Fatigue – Slowly but Surely

Ken Jelinek, OTR/L, ATP, Outpatient Therapist at UWMC[9]

Physical and mental fatigue are serious issues that can be addressed with planning and assistance from professionals and caregivers alike. This article will provide background information and practical tips to help gradually increase your endurance. Fatigue can undermine concentration, attention, memory, communication, and physical activity. Abnormal fatigue is often described as an excessive tiredness and lack of energy unrelated to exertion and not helped by rest. Problems with abnormal fatigue can occur independent of depression and younger people and those with milder injuries tend to report greater fatigue. Does it get better? Physical and mental fatigue usually diminishes over time; it should be greatly improved within 6 months after a serious brain injury. Does it go away completely? For many, it appears that it does not; two years after brain injury at least 50% identify fatigue as one of their biggest problems. For a variety of reasons, fatigue is often not systematically addressed. Fortunately, there is much you can do to reduce fatigue if you or your caregivers can prepare for and follow a program. Did you know that adding a well designed exercise program can help your physical and mental endurance? It may seem counterintuitive, but exercise can boost your overall reserves. Adding activity slowly and incrementally is often the answer for newer and older injuries. For instance, an hour of morning activity may be all you can handle. From there, you slowly and incrementally add activity followed by rest breaks; closely monitor your fatigue levels until you reach an acceptable level that you can tolerate. Avoid extreme fatigue!

What can you do for fatigue?
Preparations:

[9] *TBI Updates, 4*(1), *4*

- Consult your physician
- Start a diary to understand patterns and triggers
- Plan proper nutrition
- Follow a sleep schedule and reduce disruptions
- Use stress management and relaxation techniques
- Educate caregivers and include them in the goals
- Get help to become and stay organized
- Consult an Occupational Therapist for energy conservation techniques and devices
- Consult a physiotherapist for an exercise program

Practical steps:

- Do strenuous activities when energy is normally highest and rest when energy is normally lowest
- Take scheduled naps and rest breaks, but be increasingly active in-between
- Simplify tasks whenever possible - conserve your energy
- Add tasks only as you can tolerate them; slowly and incrementally
- Set a cut-off time for ending daily activities
- Be positive about your ability to manage the symptoms!

Resources:

• www.tbiguide.com/fatigue.html
• www.bcftbi.org/resources.html
• www.biausa.org/
• Do an internet search using the words: brain injury fatigue

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useful hints to keep energy up and fatigue down

- ❖ Prioritize tasks. Figure out which things have to be done and which can be
- ❖ Plan ahead (schedule strenuous tasks throughout the week, not all at once)
- ❖ Perform the most strenuous task during the part of the day when you have the most energy
- ❖ Pace yourself. Plan the length of time you are going to spend on the task and stop when the time is up. Rest and plan the length of the next period of effort and stop when the time is up, not when you are too tired to go on.
- ❖ Use labour-saving techniques, like making one trip upstairs for several tasks not lots of trips for lots of different tasks.
- ❖ Write everything down: diaries, loose-leaf organizers, and hand-held computer/organizers are helpful.
- ❖ Have a particular place for everything and always put things back where they belong; encourage others to do the same.
- ❖ Repeat things that need to be remembered. And write them down.
- ❖ Try not to get hung up on recalling a word. People are often happy to chime in with the right one. Let them.
- ❖ Take your time. Plan your work and don't be rushed by anyone.
- ❖ If you find mental problems crop up at a particular time of day, reorganize activities so you have the more demanding things done before that time.

Week 8: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2……3……4……5……6……7……..8……..9…..10

No fatigue/tiredness **Exhausted**

0…….1……..2……3……4……5……6……7……..8……..9…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 9: phone call 15 - 30 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph. Discuss progress and celebrate or problem solve as appropriate.**
- **Discuss progress and troubleshoot difficulties collaboratively.** Remember to ask about non-MTBI events which could be causing stress and difficulties.
- **Specific aerobic zone for the Client**
- **Set goals for coming week and record in manual**
- **Provide information and discuss with Client.** Remember you may need to do this in sections if the Client has memory or attention difficulties.
- **Ask your client to Verify information and exercise programme**

Record date and time of next appointment.

Client Manual P29

Week 9

My phone appointment with ……..
is at ……am/pm on……

Review of diary:

We looked at some of the problems that come when you are low in Energy and high in Fatigue.

After an MTBI you may find yourself crying at small things and then feeling embarrassed. Sometimes you snap at your partner or family over little things.

The most common part of the brain to be injured in a mild head injury is the front (frontal lobes). One of the jobs this part of the brain does is to regulate how we express our emotions, it puts on the brakes. It enables us to choose not to cry or snap about little things. When it is injured it is like having slipping brakes, you find it harder to stop yourself and you do things you regret or feel embarrassed about.

The GOOD NEWS is

YOU ARE NOT GOING CRAZY
You can do something to help it.

- **RECOGNISE when you are getting tired.**
- **TAKE A BREAK or change your activity.**
- **LEAVE STRESSFUL DISCUSSION to a time when you are feeling fresh.**
- **CUDDLE with partner or family or your pet**
- **It is OK TO CRY**
- **GO FOR A WALK or other exercise**
- **TALK TO YOUR Occupational Therapist OR ACC Case Manager. They can arrange for you to talk with a Clinical Psychologist who is trained to help with the strong feelings that go with accidents, assaults and brain injury.**

Bad Dreams ...

Scary accidents or being assaulted can give some people BAD DREAMS. Usually these go away after a short time but if you are still having lots of bad dreams, or FLASHBACKS (when you are awake), you might be experiencing posttraumatic stress.

Another sign of posttraumatic stress is AVOIDING thinking about or going near the place where your injury happened. Not driving because you feel afraid or nervous. Feeling too scared to ride your bike or go outside your home.

The third sign of posttraumatic stress is HYPERVIGILANCE, being very watchful, extra careful as you go about your ordinary life. Sometimes this is good. When the accident or assault happened because you were not careful; like walking out onto the road without looking or getting very drunk and going home alone. But sometimes you just had an accident or were assaulted because you were unlucky and in the wrong place at the wrong time and now your feel afraid in your own environment.

If you are having these types of problems then your ACC Case Manager can refer you to the Concussion Clinic Clinical Psychologist who is trained to help. Better to get help sooner than later so you get back your normal confidence as soon as possible.

Week 9: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2……3……4……5……6……7……..8……..9…..10

No fatigue/tiredness **Exhausted**

0…….1……..2……3……4……5……6……7……..8……..9…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 10: phone call 15 - 30 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph.**
- **Discuss progress and troubleshoot difficulties collaboratively. Plan for post PERT.**
- **Set goals for coming week and record in manual**
- **Provide information and discuss with Client. Say** *"This week we will look at Part 1 of Denise Hansen's tale of exercise after MTBI."*
- **Ask your Client to Verify information and exercise programme**

Record date and time of next appointment.

Client Manual P32

Week 10

My phone appointment with ……..
is at ……am/pm on……

Review of diary:

Denise Hansen's story...

about her experience of exercise after brain injury

Importance of Exercise After TBI, Part I
By Denise Hansen[10]

Nearly 8 years ago, on a round trip bike ride from Seattle to Edmonds, I crashed. In 15 years of bike racing I never had a close call. But that day, 5 miles from home, anxious to beat a red light, my luck expired. In the seconds it took for my tire to jam in a groove, my life changed forever, and my motivation for exercise lay on the road alongside layers of skin from my face, legs and shoulders. The momentum of 25 mph catapulted me and the bike over 40 yards and across 4 lanes of traffic. Finally stopping underneath a minivan, I suffered numerous fractures and complications from severe muscle trauma and nerve injuries. The impact crushed my helmet and my brain suffered injury as well. Despite surgeries to repair bone, years of rehab, and the best treatment options available, I continue to endure relentless, debilitating chronic pain that refuses to back off. My goal of returning to competitive cycling has faded as I come to terms with the body which betrayed me with its stubborn refusal to heal. The cognitive dysfunctions of a brain injury plague me and I am followed by a nameless cloud of fear. Biking rattles me and cognitive confusion renders me unable to make the quick decisions one needs to ride safely. Never to physically recover enough to allow me to compete or enjoy the rush of speed and endurance challenges, my fragile identity remains at question. You see, although exercise provides numerous health benefits (more on that later), disease prevention was never my motivation to endure lunatic training levels. I was motivated by personal challenge, vanity, and closeted bragging rights. I trained 200 miles per week to spare my fragile ego the self imposed humiliation of failing to be first to reach a summit or worse, to be dropped from the pack when

[10] Hansen, D. (2006a). Importance of exercise after TBI: Part 1. *TBI Updates, 4*(1), 3.

racing. I felt subtle physical superiority when remarks were made on the size of my quads and muscle definition in my calves. Sadly, exercise preserved a longstanding misconception that nothing else about me was remarkable. Exercise shored up a wobbly self image and lack of confidence. Unfortunately, following my accident, as the size of my thighs began to shrink, and my strength diminished, so did the motivation I had for exercise. I struggle to find the point of an hour of rowing or a slow paced bike ride on the Burke Gilman. The all or nothing attitude which served my past identity, allowed me to just do it. The challenge to create form around the amoeba like identity of today, leads me into daily negotiations with the excuses of pain, fatigue and disorganization and often turns into I just can't do it. Fortunately, although I have lost something once essential, I have not lost myself. I reach deep into my competitive spirit, and realize I must find within me the desire to do my best. So, with new motivations and improving attitudes, I keep score under the new uninvited rules. Since an hour of exercise is more difficult now than an 80 mile training ride ever was, I get more points. It all comes down to the degree of difficulty. In the next issue, I will discuss why exercise is important for someone with a TBI. The barriers may seem insurmountable, but within yourself, you can find the motivation to succeed.

Week 10: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

Session 11: phone call 15 - 30 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph.**
- **Discuss progress and troubleshoot difficulties collaboratively.**
- **Set goals for NEXT TWO WEEKS and record in manual. Say** *"Next week is the last week of the programme and so we will make our appointment nearer to the end of that week. This will allow you to get the maximum benefit from the exercise training before you fill in the same questionnaires you answered at the beginning of the PERT programme. We will plan your exercise for the next two weeks and write it into the plan"*
- **Provide information and discuss with Client.** Say *"Let's look at part 2 of Denise Hansen's tale about the importance of exercise after TBI."*
- **Verify information and exercise programme for NEXT TWO WEEKS.**

Record date and time of next appointment.

Client Manual P34

Week 11

My phone appointment with ……..
is at ……am/pm on……

Review of diary: Second to last session of the programme

Importance of Exercise After TBI, Part II
By Denise Hansen[11]

Last issue, I introduced a series on the benefits of exercise following TBI. For a moment, I contemplated writing from the perspective of an Exercise Physiologist; providing a list of the benefits and describing the basics of an exercise program. In the past, this would have brought me satisfaction. I might have flaunted my academic credentials to legitimize the trite information I spewed to captive audiences and I wrongly believed that loading people with facts would inspire a life of joyful exercise. Worse, the competitive and vanity driven motives I had for exercise, those which allowed me to just do it, led me to critically judge those who didn't. Lacking empathy for those with barriers, I could offer no solutions. As I struggled with writing, I was confronted with the irony that since my accident, all of my knowledge fails to motivate even myself. How can I encourage anyone else when, for days at a time, pain or a night without sleep intrudes on my rowing schedule? Feelings of guilt urge me to confess that I am proof positive that knowledge does not equal behaviour change. Those academic credentials are in fact weak, unimpressive, and in the end, add nothing to persuade a sophisticated TBI audience that exercise is crucial to ones emotional and physical health. Instead, that which allows me to be convincing is that because of a freak bicycling accident - I share in the unpredictable daily challenges and join in the defiant battle to not allow the injuries to define life. There is no choice but to courageously adapt. So, as I proceed to the didactic information regarding the benefits of exercise, it is with the understanding that I cannot do so without eventually exploring the significant barriers and the strategies one needs to negotiate these obstacles. For individuals with TBI, we would expect to find the same general health benefits from aerobic exercise as seen in healthy individuals. These include reduced risk for diseases such as

[11] Hansen, D. (2006b). Importance of exercise after TBI: Part 11. *TBI Updates, 4*(1), 3.

diabetes, heart attack and stroke. Calorie expenditure and increased muscle mass contribute to increased metabolism, weight loss and successful weight management. Exercise can prevent osteoporosis and guard joints from the dysfunction of arthritis. These are important, of course, but what may be most compelling for those with TBI is the contribution exercise may make in improving cognitive function and lowering levels of depression. Although little research exists to confirm or deny this, preliminary evidence suggests that the benefits include the following: Fewer physical, emotional and cognitive complaints, such as sleep, irritability, and better memory and organization skills. As a result of the chemicals released during aerobic workouts, TBI survivors may experience less depression and improved self esteem. Although I make no attempt to ascribe meaning to exercise beyond my own, the latter has become the benefit I most often use as motivation to overcome my impulse to avoid an exercise session. It is no longer about the size of muscles, the competition or the bike (which I finally sold). I daily renew my commitment to some sort of activity, even if it is not what I had planned. I consider the limitations of that day and focus on what I can do rather than on what I can't do. I like the feeling when I'm done more than the feeling I will have if I do nothing. If this has not yet inspired a visit to the gym, I will not be surprised since it still is an attempt to provide information. In no way does it tackle the issues of motivation or how to overcome the harsh realities of the obstacles to exercise.

Week 11: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No fatigue/tiredness **Exhausted**

0…….1……..2..……3..……4..……5..……6..……7....…..8...…..9.…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

MAKE NEXT APPOINTMENT FOR THE **END** OF THE 12th WEEK AND MAKE THE EXERCISE PLAN THE SAME AS FOR WEEK 11.

Session 12: face-to-face 60 minutes

REVIEW

- **Client's data online**
- **Previous week's training**
- **Enter fatigue and energy ratings into graph. Discuss changes over the training programme. Plan for future – maintain exercise programme, need for further intervention**

END OF TRAINING

- **Remind Client of the baseline questionnaires they filled in at the beginning of the training. Ask them to go to the website in this session and complete the questionnaires again.**
- **Explain that they will be asked to do these questionnaires again in 12 weeks time. Identify the exact date and time and suggest they record this in a diary or cellphone. Tell them they will receive an email and/or phone reminder at that time.**
- **Remind them that they will also be asked to do the questionnaires at one and two years following the start of the training. Identify the dates and write them down. Tell them they will be sent email or postal reminders two weeks before the due date. Explain that post-MTBI fatigue sometimes lingers for years and we want to monitor how they are getting along over the next two years to make sure the gains are maintained.**
- **Thank the Client for agreeing to continue to provide data to the study.**

CLIENTS WHO CONTINUE TO REPORT POST-MTBI FATIGUE

- **Reassure Client. Review Clients pre-accident factors, current lifestyle and stressors**
- **Recommend to ACC Case Manager, a psychological assessment to identify factors contributing to ongoing postconcussion symptoms or other condition.**

✍ Record date and time of appointment for follow-up email and questionnaires.

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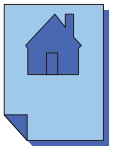
Week 12



My Concussion Clinic appointment with ……..
is at ……am/pm on……

Review of diary:

☺ Alert: At the end of this week your therapist will contact you and ask you to complete the same questionnaires you filled in at the beginning of the programme.

Does Fatigue Really Strike TBI Survivors?
By Kelly Gilliam[12]

I can still remember my exact thoughts when first reading that fatigue commonly occurs in people who suffered a head injury: "Fatigue? No way! Maybe in someone else, but not to me!" I continued to log onto numerous TBI (traumatic brain injury) websites and fatigue surprisingly always popped up. Still, I chose not to believe this would happen as long as I followed the discharge instructions by the Harborview Medical Centre Rehab Team experts. And yet, over time, mental fatigue crept up on me. How could this be? Right up until my mountain bike accident, I had worked 115-125 hours per week in Alaska and still made time for bicycle riding and playing volleyball. I had energy and endurance. And then I am instructed, after three weeks in the hospital: (1) I can not return to my Alaska job, (2) do not return to my California job for at least two months, and (3) slowly build up to working 40 hours per week. Why, I felt like my energy was back to normal, however, my speech pathologist and vocational counsellor were quite stern about this. And like many other of the instructions, I followed it against my will. After slowly working up to 40 hours a week, I finally realized the importance of why not to rush back to full time. I began to experience mental fatigue. From working 115-125 hours per week with left over energy, to 40 hours and experiencing fatigue, was very odd and frustrating. By the time I finished working an eight hour day, my brain would be exhausted. Like many other TBI cognitive deficits, I learned though great resources, to accept and compensate by doing certain things to avoid getting mental fatigue:

- **Try to sleep for at least eight hours per night**
- **Take a mid-day fifteen minute nap (which I despise doing, but it works) on a busy work day**
- **Exercise during lunch break**
- **Eat healthier foods and on a fairly structured routine (i.e., 7am, 12pm, and 5pm)**
- **Cross-word puzzles**

The most important tool I use, aside from sleep, is exercising. Since I followed my physical discharge order of not bicycling for two months and took one year off from high velocity sports (i.e., triathlons), I avoided physical fatigue. It took my body at least six months to rebuild the muscle and endurance. Four years have now gone by since the accident and I have more endurance and energy than before. However, when I allow about two days to go by without any exercise, I can sometimes sense mental fatigue in the early evening. The mental fatigue strongly reduces my problem solving skills and takes a lot longer for my mind to make decisions.

Medication and Fatigue

Although fatigue is a common complaint after TBI, there is little research that helps to define what causes fatigue or how to treat it. It is likely that fatigue is caused by many factors. Sleep problems and depression can often cause fatigue. Many medications such as anti-seizure or anxiety medications have a possible side effect of fatigue. A lack of physical fitness can contribute to a sense of fatigue. In addition, it is likely that the mental effort required for those people with slowed abilities to process information or shift their attention from one task to another is also a factor in the feeling of fatigue. The patient and physician should make a thorough search for factors that may cause fatigue and try to eliminate them by improving sleep, maintaining an exercise program, or minimizing drug intake. If fatigue continues to be an issue, there are a number of possible drugs that may improve fatigue.

[12] Gilliam, K (2004). Does fatigue really strike TBI survivors? TBI Updates, 2(4).

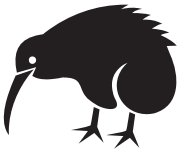
***Caffeine**, a widely available drug (especially in Seattle), has long been used by college students and night workers to enhance alertness for a short period of time. There is often, however, a rebound effect after the caffeine wears off.*

***Amantadine** is a medication that has been used in multiple sclerosis (MS) to combat fatigue.*

***Methylphenidate** (Ritalin) is another drug that has been used to treat attention disorders in children that has a neurostimulant effect when used as prescribed.*

***Dextroamphetamine** also is a neurostimulant that can be useful to treat fatigue. Both methylphenidate and Dextroamphetamine is controlled substances and has a reputation for being abused by certain populations. Both may cause seizures in a small percentage of people as well.*

***Modafinil** (Provigil) is a newer stimulant used to treat narcolepsy and some types of sleep apnoea. It has been used clinically both in TBI and for MS although very little research has been done on its effects. It has all the side effects one might see with other neurostimulants but hasn't been linked to seizures. It is very expensive.*



Note: In New Zealand it is very unusual to prescribe medication for fatigue following MILD TBI. As Kelly Gillam points out, regular EXERCISE is what makes the difference.

Week 12: My Plan is to ……..for …minutes on 5 days this week

Rate your Fatigue and Energy level each day at the same time of day and write into the chart below.

0……..1……..2……3……4……5……6……7……..8……..9…..10

No fatigue/tiredness **Exhausted**

0……..1……..2……3……4……5……6……7……..8……..9…..10

No Energy **Full of Energy**

Date dd/mm/yy	Exercise Minutes	Nap	Fatigue	Energy
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
	Total			

Data entered into website on (Date)……

At the end of Week 12 we will ask you to complete the questionnaires on the website for the second time. They questionnaires are also reprinted below.

WEBSITE ADDRESS: http://psych-research.massey.ac.nz/fatigue/

Printed Questionnaires page 40 Client manual

Tracking Your Progress

Put an **X** in the box which shows the level of fatigue for the day. Put a **0** in the box which shows the level of energy for the day. Join **X** to **X** and **0** to **0** to track your fatigue and energy over the course of the PERT programme.

Levels of fatigue and energy over 12 weeks of the PERT programme

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
Fatigue X----X																																																																		
Energy O----O																																																																				

10
9
8
7
6
5
4
3
2
1
0

Day number

Fatigue Severity Scale

consists of the 9 items from the Fatigue Assessment Inventory (see Appendix G).

INSTRUCTIONS: ***Date.....***

Below are a series of statements regarding your Fatigue. By Fatigue we mean a sense of tiredness, lack of energy or total body give-out. Please read each statement and choose a number from 1 to 7, where #1 indicates you completely disagree with the statement and #7 indicates you completely agree. Please answer these questions as they apply to you in the **past TWO WEEKS**. ***Circle the appropriate number***

		Completely disagree						Completely agree
3*.	My motivation is lower when I am fatigued	1	2	3	4	5	6	7
5*.	Exercise brings on my fatigue	1	2	3	4	5	6	7
18*.	I am easily fatigued	1	2	3	4	5	6	7
19*.	Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
20*.	Fatigue causes frequent problems for me	1	2	3	4	5	6	7
21*.	My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
22*.	Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
25*.	Fatigue is among my 3 most disabling symptoms	1	2	3	4	5	6	7
26*.	Fatigue interferes with my work, family or social life	1	2	3	4	5	6	7

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Parking
Gate Code is 4567#
Client Car Park numbers are 45, 46, 47, 48, 49, 50 opposite the Psychology Clinic entrance

Appendix J

Publications and Conference Presentations

Norrie, J. (2005, August). *"Hitting the wall": Fatigue and traumatic brain injury.* Paper presented at the TBI Functional Rehabilitation Conference: 'Get Real' Top Ten Challenges in TBI Rehabilitation.

Abstract

Fatigue is a commonly identified sequelae of mild traumatic brain injury (MTBI) which has a wide reaching impact on everyday functioning, recovery and mood.

TBI related fatigue is qualitatively different to everyday fatigue where there is a gradual slowing down of energy. Instead, after TBI energy is lost suddenly, performance falters and the person with TBI can look like they have "hit a wall". Problems of depression and pain, also common after TBI, have different presentations and can be discriminated from TBI related fatigue.

The paucity of data currently available about the nature, extent and guidelines for treatment of TBI related fatigue coupled with a need for an effective intervention for such problems by people with concussion and MTBI attending a Concussion Clinic provided the impetus for the study to be outlined here.

This presentation will report on the first stages of the study, beginning with an exploration of the epidemiology and nature of TBI related fatigue, the impact that it has on the direction and progress of recovery and a review of current interventions (e.g., sleep hygiene, psycho-education). This will be followed by discussion of a research programme aimed at development, implementation and evaluation of an intervention aimed at reducing the negative impact of fatigue for this group.

Norrie, J.M. (2005, November) Fatigue and Mild Traumatic Brain Injury. Paper presented at the Rehabilitation: Challenges of Participation and Reintegration Conference, New Zealand Rehabilitation Association, Auckland, New Zealand.

Abstract

Fatigue following Mild Traumatic Brain Injury (MTBI) is a significant challenge to rehabilitation and prevents individuals from being able to participate in daily work and home activities for extended periods following their mild traumatic brain injury. Post-MTBI fatigue qualitatively different to everyday fatigue where there is a gradual slowing down of energy. After MTBI, fatigue is experienced as a sudden loss of energy, cognitive and/or physical performance falters and the person with MTBI can look like they have "hit a wall". Although there is an extensive body of literature about fatigue associated with other medical conditions, such as cancer, multiple sclerosis and chronic fatigue syndrome, there is a paucity of data available about the many aspects of post-MTBI fatigue.

This presentation contains current information about the nature and epidemiology of post-MTBI fatigue predictors of severity and lifestyle impact, such as level of education and time since injury and factors such as depression and pain which confound identification and assessment of post-MTBI fatigue. The discussion will include associated relevant issues such as post-MTBI sleep disturbance, fatigability, personality, lifestyle and current rehabilitation interventions which are largely under-evaluated. In addition, a study will be outlined which will explore, within a New Zealand population, the epidemiology and nature of post-MTBI fatigue and the impact that post-MTBI has on the direction and progress of recovery and develop an effective rehabilitation intervention with a population of people with MTBI attending a Concussion Clinic.

Norrie, J., Heitger, M., Leathem, J., Anderson, T. & Jones, R. (2006, September). *Fatigue and post-concussion syndrome following mild traumatic brain injury: A preliminary report from a New Zealand sample*. Paper presented at the Joint Conference of the Australian Psychological Society and New Zealand Psychological Society, Auckland, New Zealand.

Abstract

Although fatigue is a common sequelae of mild traumatic brain injury (MTBI) both in the post-acute phase and at 6 months post injury (McCullagh, Ouchterlony, Protzner et al., 2001), very few studies have examined post-MTBI fatigue in detail. This is in spite of post-MTBI fatigue being identified as the most important single factor inhibiting return to work after MTBI (Wrightson & Gronwall, 1999). Without a robust theory of post-MTBI fatigue development of guidelines for assessment and treatment of post-MTBI fatigue is severely hampered.

This paper will build on recent results of a study of a TBI sample of mixed severity (Ziino & Ponsford ,2005), which found just two predictors of post-TBI fatigue - years of education and time since injury.

The preliminary findings are reported of a study of post-MTBI fatigue characteristics being investigated as part of a larger (n=500) Christchurch based study into prediction of outcome following MTBI being conducted by Heitger, Anderson & Jones. The Fatigue Assessment Instrument (FAI), Rivermead Postconcussion Symptoms Questionnaire, Hospital Anxiety and Depression Scale, SF36 version 2 subscales and a demographic questionnaire were administered at approximately 1 week, 3 months and 6 months post injury. The results of this study will inform clinical/neuropsychological practice in Concussion Clinics and contribute to the development of both a theory of post-MTBI fatigue and guidelines for prevention or reduction of its impact on the MTBI population.

Norrie, J. M., Heitger, M.H., Leathem, J.M., Anderson, T.J., Jones, R.D. . (2007, August). *Fatigue following mild traumatic brain injury: Early results from a longitudinal prospective study*. . Paper presented at the TBI Functional Rehabilitation Conference: Seize the Moment: Opportunities for intervention in everyday life, Christchurch, New Zealand

Abstract

This study is investigating the prevalence, severity and likely predictors of subjective fatigue following mild traumatic brain injury (MTBI) one of the most frequently reported symptoms in both the acute and post acute stages of MTBI. Participants are a New Zealand cohort aged 16-70, 48 female, 88 male, with MTBI, who were covered by a no-fault, government-sponsored accident insurance (Accident Compensation Corporation). Measures of fatigue, postconcussion symptoms, depression, anxiety and general health were administered at one week (n=136), three months (n=107) and six months (n=83) post-injury as part of a larger study investigating outcome after MTBI. Predictors of post-MTBI fatigue were explored using linear regression. At 6 months, 25.3% of participants reported problems with persistent fatigue as indicated by a Global Fatigue Severity score > 4 (range 1 – 7). There was no significant relationship between fatigue at six months and gender, age, education, TBI history, injury cause, injury severity (initial GCS, PTA length), or time since injury. Fatigue severity at 1 week (r = .43) and 3 months (r = .64) were significantly related to fatigue severity at 6 months ($p \leq .001$). Fatigue or low energy is among the criteria for diagnosis of depression in both the DSM-IV and ICD-10. Hence, the relationship between depression and post-MTBI fatigue was included in the current data analysis. Depression at three months accounted for 44% of the variance in fatigue at 6 months. After controlling for the influence of depression, fatigue severity at 3 months continued to make a unique contribution (beta= .56, $p \leq .001$) to fatigue severity at 6 months. There was a negative correlation between hours of work and post-MTBI fatigue ($r = -.24$, $p \leq .05$) at 6 months. For a small sample of participants (n = 9), fatigue problems only became apparent at 3 or 6 months post MTBI. That is, their Global Fatigue Severity score at 1 week was ≤ 4 but had increased to > 4 at one or more of the later measurement times. Conclusions: Persistent post-MTBI fatigue is related to early fatigue symptoms but can also develop over time. Early targeting of fatigue

management and depression is recommended to prevent persisting fatigue-related disability and consequent slowing of return to pre-accident functional levels. Investigation of predictive factors within the first three months is underway. The next phase of the research will examine the effectiveness of a multidisciplinary approach to management and alleviation of post-MTBI fatigue.

Norrie, J. M., Heitger, M.H., Leathem, J.M., Anderson, T.J., Jones, R.D. (2007, June). *Mild traumatic brain injury and Fatigue: Preliminary findings from a longitudinal prospective study*. Poster presented at the 5th Annual Conference of the American Academy of Clinical Neuropsychology.

Abstract

Aim: This study investigated the prevalence, severity and likely predictors of subjective fatigue following mild traumatic brain injury (MTBI), one of the most frequently reported symptoms in both the acute and post acute stages post MTBI.

Method: Participants were a New Zealand cohort aged 16-70, 44 female, 73 male, with MTBI, who were covered by a no-fault, government-sponsored accident insurance. Measures of fatigue, postconcussion symptoms, depression, anxiety and general health were administered at one week (n=117), three (n=96) and six months (n=66) post-injury as part of a larger study investigating outcome after MTBI. Predictors of post-MTBI fatigue were explored using linear regression.

Results: At 6 months, 19% of participants reported problems with persistent fatigue. There was no significant relationship between fatigue at six months and gender, age, education, TBI history, injury cause, injury severity (initial GCS, PTA length), or time since injury. Fatigue severity at 1 week ($r = .48$) and 3 months ($r = .71$) were related to fatigue severity at 6 months ($p \leq .001$). Depression at three months accounted for 22% of the variance in fatigue at 6 months. After controlling for the influence of depression, fatigue severity at 3 months continued to make a unique contribution (beta=.629, $p \leq .001$) to fatigue severity at 6 months. There was a negative correlation between hours of work and fatigue ($r = -.25$, $p \leq .05$) at 6 months. For five participants, fatigue problems only became apparent at 3 or 6 months post MTBI.

Conclusions: Persistent post-MTBI fatigue is related to early fatigue symptoms but can also develop over time. Early targeting of fatigue management and depression is recommended to prevent persisting disability. Investigation of predictive factors within the first three months is underway.

Mild traumatic brain injury and fatigue

Preliminary findings from a longitudinal prospective study

NORRIE, J.*, HEITGER, M.**, LEATHEM, J.*, ANDERSON, T.** & JONES, R.**

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Te Kunenga ki Pūrehuroa

Introduction

Fatigue is one of the three most common subjective symptoms reported following mild traumatic brain injury (MTBI). Kashluba, Paniak, Blake et al. (2004) reported that 59% of those with MTBI and 36% of non-injured controls reported fatigue but by three months post-injury only the MTBI group listed fatigue in their top ten symptoms. Rao, Rollings & Spiro's (2005) literature review found prevalence rates of 22% to 37% at three months while other studies found persistent post-MTBI fatigue at six to 12 months (Kay, Cavallo, Ezrachi, 1988; Trahan, Ross & Trahan, 1999; McCullagh, Ouchterlony, Protzner, Blair & Feinstein, 2001). Masson, Maurette, Salmi et al (1996) found 35.1% reported post-MTBI fatigue five years after injury. Recovery occurs within three months of the injury for 85% of MTBI population (Kay, Newman, Cavallo, Ezrachi, & Resnick, 1992; Ruff, Camenzuil & Mueller, 1996) but 15%, the "Miserable Minority" (Ruff et al 1996; Wood, 2004) may require three to five years to resolve sequelae. Most studies of fatigue and TBI to date used mixed samples of severity and/or etiology of brain injury and litigation was a confounding factor. The current study explored prevalence, severity and predictors of fatigue in a sample of MTBI patients who were covered by New Zealand government sponsored no fault insurance.

Method

Participants: were 111 people with MTBI (40 females, 71 males), aged between 16-69 years, recruited from a pool of people admitted to the Emergency Department, Christchurch Hospital, New Zealand (the principal hospital for a regional population of over 400,000). MTBI fatigue severity was studied in the context of a major prospective longitudinal study of outcome prediction following closed head injury (see www.vanderveer.org.nz for details). Mean Glasgow Coma Scale score was 14.82 ±0.43, length of Posttraumatic Amnesia was 52.2 ±118.7 minutes and years of education 14.3 ±2.8. Over one quarter (27.9%) had a history of traumatic brain injury. Follow-up data was obtained from 91 participants at three months and 64 participants at six months.

Measures: Fatigue Assessment Instrument (FAI), Rivermead Post Concussion Questionnaire, Rivermead Head Injury Follow-up Questionnaire, Hospital Anxiety and Depression Scale, SF-36 Health Survey Version 2. Fatigue severity was defined as a Global Fatigue Severity (GFS; subscale of FAI) z score >1. Personal and injury information was obtained from hospital records and through interview.

Procedure: At 1 week post-injury participants were interviewed, underwent oculomotor assessment (see Heitger et al, 2007 for procedure details) and completed the questionnaires. At three and six months the questionnaires were posted out with a follow-up phone call where necessary. Ethical approval and informed consent was obtained and withdrawal at any stage was an option. The project is expected to continue until approximately March 2008.

Results

Prevalence of post-MTBI fatigue at each time period during the first year of data collection is shown below

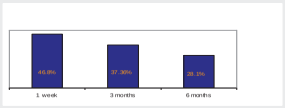

Figure 1: Percentage of MTBI patients with Global Fatigue Severity z score >1 (i.e., GFS = 3.5; Swartz, Jandorf and Krupp, 1993).

Overall GFS at one week was a stronger predictor of fatigue severity at three months than at six months as the change over time became less after three months (Table 1).

Table1: Correlation between Global Fatigue Severity scores at 1 week, 3 months and 6 months .

GFS	1 wk	3 mth	6 mth
** p=.0005			
1 wk		0.64** N=85	0.47** N=60
3 mth			0.71** N=63

There was a negative correlation between hours of work and fatigue (Table 2) at each time period.

Table 2: Correlation between Global Fatigue Severity and hours of work at 1 week, 3 months and 6 months.

	GFS 1 week	3 mth	6 mth
Hours of work			
1 week	-.28*		
3 mth		-.25*	
6 mth			-.25*

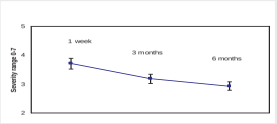

Figure 2: Comparison of mean Global Fatigue Severity scores for each time period.

A one-way repeated measures ANOVA was conducted to compare scores on the Global Fatigue Severity subscale at 1 week, 3 months and 6 months. Table 3 lists means and standard deviations. There was a small significant effect for time [Wilks' Lambda = .83, F(2,57)=4.67, p=.05, multivariate partial eta squared = .17].

Table 3: Descriptive Statistics for Global Fatigue Severity subscale Test Scores for 1 week, 3 months and 6 months.

Time Period	N	Mean	Standard deviation
1 week (6.8±3 days)	59	3.51	1.7
3 months (93.1±15.8 days)	59	3.25	1.6
6 months (181±17.4 days)	59	2.89	1.45

There was no significant relationship between fatigue severity (GFS) at six months and gender, age, education, TBI history, injury cause, injury severity (initial GCS, PTA length), or time since injury.

In five cases, problems with fatigue severity only became apparent at three or six months.

Discussion

Fatigue is as one of the most frequently reported post-MTBI symptoms. This prospective longitudinal study was carried out in a population whose medical and rehabilitation costs were covered by a no fault accident insurance thus ruling out litigation as a confounding factor. Fatigue severity, not just symptomatology, was measured.

Findings were consistent with earlier MTBI literature on fatigue. Prevalence of fatigue severity (Global Fatigue Scale z score >1) was 46.8% at 1 week, 37.36% at 3 months and 28.1% at 6 months. Fatigue severity was comparatively stable over time (time related effect size = 0.17, p= .05) among the 59 participants for whom data was available at all three measurement periods. Fatigue at three months is more strongly correlated with fatigue at six months (r = .71) than fatigue at one week is related to the six month level (.47). This suggests the possibility of a *window of opportunity* between one week and three months post closed head injury when a fatigue-focused intervention would be most likely to reduce subjective fatigue severity. It could also reduce the likelihood of fatigue becoming a persistent barrier to resumption of pre-injury activity at work or home. Early intervention for postconcussion syndrome is effective (Mittenberg, Canyock, Condit, & Patton, 2001) and the next stage of the current research project is to investigate the effectiveness of a fatigue targeted cognitive behavioural intervention.

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I thank Marcus Heitger, Tim Anderson and Richard Jones of the University of Otago and the Van der Veer Institute (www.vanderveer.org.nz) for giving me the opportunity to combine this project with data from the closed head injury outcome study; Janet Leathem and Ross Flett my PhD supervisors for their advice and encouragement; Massey University, Psychology Department for funding to support the project and Education New Zealand for travel funding.

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Presented to the 5th Annual Conference of the American Academy of Clinical Neuropsychology, Denver, Colorado, 7-9 June 2007

Norrie, J., Fatimath Rifshana, Andrews, P., Seemann, R., Harvey, S., & Stephens, C. (2009). *Concussion Clinics: Access and Evaluation - A Case Study (Technical Report to Accident Compensation Corporation)*. Palmerston North, NZ: Turitea Psychology Clinic.

Executive Summary

Palmerston North Concussion Clinic, Massey University, is one of 19 locations in New Zealand where Concussion Clinics provide assessment and treatment to those who have received a mild traumatic brain injury. This research was initiated out of concern that some sections of the community appeared to be were underrepresented among the Concussion Clinic clientele. Members of the Palmerston North Concussion Clinic were also interested in investigating the effectiveness of service delivery in facilitating recovery from a mild traumatic brain injury. These two concerns led to two studies. Study One investigated access to the Concussion Clinic and Study Two measured the effectiveness of the Concussion Clinic intervention using an independent samples methodology.

Participants for both studies were recruited from the Emergency Department, Palmerston North Hospital and the Concussion Clinic, Massey University. Data for Study One were collected using a file audit to gather demographic information about patients who presented following accidents with symptoms suggestive of concussion or MTBI. Those recorded as experiencing a possible MTBI had received a Glasgow Coma Scale score of 13 or 14, described a loss of consciousness, met the criteria for MTBI, and reported a past history of head injury. Analysis of these data indicated that of those with possible MTBI, only 6.6% were referred to the Concussion Clinic (9 of 136). The small sample of referrals meant statistical analysis was not possible. Visual inspection, particularly of the non-referred group, showed that factors which might have been expected to trigger referrals such as Glasgow Coma Scale score of 13 or 14, loss of consciousness, meeting the criteria for MTBI, and past history of head injury did not do so. For instance, the youngest and oldest age groups were not referred and females being more likely than males to be referred.

Study Two results indicated a clinical advantage was found for those attending the Concussion Clinic across postconcussion symptoms, anxiety, depression and

psychosocial functioning. Statistically significant changes for anxiety and depression were found between the groups over time. These findings suggest the Concussion Clinic is successful in promoting recovery from MTBI. A small sample size could have hindered the clarity of findings and combining results from non-referred and referred non-attenders into a non-intervention group may have produced statistically equivocal results. These two groups could be very different and aggregating their scores was likely to have masked the differences expected among these and the intervention group. These results highlight the need for accurate identification of mild traumatic brain injury, as the effectiveness of the service is likely to be severely compromised by the low referral rate, and it carries significant implications for review and/or revision of referral pathways. In spite of the small sample size, results from this research suggest those who are able to attend the Concussion Clinic indeed fare better than those who do not, lending support to the efficacy of treatment received through the Concussion Clinic.

Norrie, J., Heitger, M., Leathem, J., Anderson, T., Jones, R., & Flett, R. (2010). Mild traumatic brain injury and fatigue: A prospective longitudinal study. *Brain Injury, 24*(13-14), 1528-1538. doi:10.3109/02699052.2010.531687

See Chapter 4

Appendix K

Statement of Contribution to Doctoral Thesis Containing Publications

DRC 16

MASSEY UNIVERSITY
GRADUATE RESEARCH SCHOOL

STATEMENT OF CONTRIBUTION
TO DOCTORAL THESIS CONTAINING PUBLICATIONS

(To appear at the end of each thesis chapter/section/appendix submitted as an article/paper or collected as an appendix at the end of the thesis)

We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: Joan Mary Norrie

Name/Title of Principal Supervisor: Prof. Janet Leathem

Name of Published Research Output and full reference:

Norrie, J., Heitger, M., Leathem, J., Anderson, T., Jones, R., & Flett, R. (2010). Mild traumatic brain injury and fatigue: A prospective longitudinal study. Brain Injury, 24 (13-14), 1528-1538. doi:10.3109/02699052.2010.531687

In which Chapter is the Published Work: Chapter 4

Please indicate either:

- The percentage of the Published Work that was contributed by the candidate: 100%

  and / or

- Describe the contribution that the candidate has made to the Published Work:

Joan Norrie — Candidate's Signature — 14.03.2012 — Date

Janet Leathem — Principal Supervisor's signature — 19.03.2012 — Date

GRS Version 3– 16 September 2011