INVESTIGATION OF A MULTIFACTORIAL MODEL FOR THE MAINTENANCE OF FATIGUE AFTER SEVERE TRAUMATIC BRAIN INJURY

and Research Portfolio

Part One

(Part two bound separately)

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July 2002

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Acknowledgements

I would like to thank Professor Tom McMillan for his support and supervision on my Major Research Project, Dr Kirsten Verity for her supervision of my Clinical Case Research Study and Dr Paul Fleming for his supervision of my Small Scale Service Evaluation Project. I would also like to thank Ms Ann Hunter, Manager, Central Scotland Brain Injury Rehabilitation Centre, Mr Ian Swann, Consultant in Accident and Emergency Medicine, Glasgow Royal Infirmary, and the co-ordinators and members of Headway who helped with the recruitment of participants for the project. Thank you also to all of my clinical supervisors, and to my family, friends and classmates for all their patience and support over the last three years.

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PART ONE (this bound copy)

CHAPTER ONE

Small Scale Service Evaluation Project

Audit of the First Nine Months of an Early Dementia Assessment and Diagnostic Service

Prepared in accordance with the instructions for presentation of a management report (see Appendix 1.1).

INTRODUCTION

The high prevalence of dementia (American Psychiatric Association, 1995), ranging from 3.0% in over 65s to over 20% in over 85s, in an increasingly aged population has led to increasing numbers of individuals presenting to National Health Services requiring assessment of memory and other cognitive difficulties. Since the creation of the first UK memory clinic in 1983, a growing number of NHS Trusts have chosen this form of service to meet the individual needs of this population, with the aims of such services found on review (Wright and Lindesay, 1995) to vary greatly across localities. The most commonly cited aims include assessment and diagnosis of dementia and the provision of a specialist treatment service, with the development of acetylcholinesterase inhibitors and a growing recognition of the high prevalence of potentially reversible conditions in community samples leading to an increased emphasis on early assessment and detection.

In 1999 the Dumfries and Galloway Primary Care NHS Trust agreed funding for such an early dementia assessment and diagnostic service (EDADS). Population estimates for the region suggested that over 65s constituted almost 20% of the total population, numbering 27400 in 1998, leading to a projected prevalence rate of dementia within the region of 2000 and an estimated annual incidence of 300. To attempt to meet the needs of this population in community settings, memory clinics were set up in 3 areas of the region, Nithsdale, Stewartry and Wigtownshire (for map see Appendix 1.2) situated in established day hospitals and health centres. Staffing time for these clinics consisted of sessions from a Consultant Older Adult Psychiatrist, Staff Grade Doctor and a community psychiatric nurse. Additional sessions for a clinical neuropsychologist were also planned for cases where unequivocal diagnosis was problematic or where further management advice was required.

Principal aims of this service were stated at the outset to include provision of accessible locality based clinics for the early assessment and diagnosis of dementia. Additional aims included the detection of preventable early dementia and other conditions masquerading as dementia, and the provision of appropriate treatment or

advice in the form of a clear management strategy for patients with early dementia (for full list of aims see Appendix 1.3). An assessment protocol was devised using clinical judgment and the results of an extensive literature search on procedures and measures available. Given the large numbers of new cases expected to appear at these clinics an emphasis on selection of brief yet sensitive measures was deemed the most appropriate means of satisfying assessment requirements. This was reflected in the final assessment protocol consisting of clinical history taking interview, physical examination and formal cognitive assessment, with the use of blood testing and neuroimaging where clinically indicated.

The cognitive assessment measures selected for this purpose were the Mini Mental State Examination (MMSE; Folstein, Folstein and McHugh, 1975) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm and Jacomb, 1989), chosen on the basis of their established reliability and validity as neuropsychological measures. The MMSE was chosen as a brief, clinician administered structured 'bedside measure' of cognitive function. Whilst once believed to be a relatively crude measure of cognitive change (see Schneider, 1997) the MMSE has since been demonstrated to successfully discriminate in clinical settings between those meeting DSM-III-R (American Psychiatric Association, 1987) criteria for dementia and non cases using advocated cut-off scores (Mulligan, Mackinnon, Jorm, Giannokopoulos and Michel, 1996), with a sensitivity of 0.76 and specificity of 0.90.

However, a number of studies (Tombaugh and McIntyre, 1992; Mackinnon and Mulligan, 1998) have argued that the MMSE is sensitive to premorbid ability levels and educational attainment and its successful completion may also be adversely affected by sensorimotor and language impairments. There is therefore a danger that it's use in isolation within brief assessment services may lead to a large number of false positives or negatives in diagnosis. It was therefore decided that an additional assessment measure, insensitive to such factors, should be selected for use in the clinics. The IQCODE was chosen for this purpose as a brief informant questionnaire which permits a quantitative rating of changes observed in the clinical

interview. An advantage of the scale is that it has been demonstrated to be unaffected by the above limitations of tests such as the MMSE, though non-cognitive factors may affect scoring.

The use of the two measures in combination within the Dumfries memory clinics was proposed as a means of overcoming limitations of each, and to therefore increase accuracy whilst still ensuring a brief assessment protocol. Whilst Jorm (1996) in a review of studies comparing informant reports with cognitive tests found no evidence for significant differences between these measures in screening for dementia, correlations between the two measures are at best moderate (Mackinnon and Mulligan, 1998), and thus the use of the two measures in combination may still provide a means of improving sensitivity. It was therefore decided that both should be used as standard practice within the memory clinics, and that scoring relative to advocated cut-offs should provide a basis for diagnosis and outcome decisions.

This service and protocol has now been in operation for nine months, and a preliminary investigation of adherence to and effectiveness of this protocol was called for to provide guidance on the future of the clinics. In the initial aims of the service, audit was cited as the basis for good clinical practice and the first descriptive stage of the audit process seemed particularly appropriate at this time, given the scope for expansion and improvement of the service offered by increased staffing time and increased staff familiarity with the protocol.

Aims

The present audit therefore aims to describe the operation of the Early Dementia Assessment and Diagnostic Service to date in relation to the stated aims of the service.

Objectives

1. To establish the demographic and diagnostic characteristics of Memory Clinic attendees to ascertain whether the target population is being seen.

2. To establish the current level of use of additional assessment and management resources.
3. To describe the use of psychometric cognitive assessment measures as diagnostic tools and predictors of outcomes within the Memory Clinics.

METHOD

Inclusion Criteria

The present audit included all patients seen at memory clinics from the period 1st August 1999 to 10th March 2000. Criteria for attendance at the memory clinic required that patients must be over the age of 65 (though in a small number of cases this age limit was waived when dementia was suspected in a younger individual), must reside within the catchment area for the service and the referral must contain a request for the assessment of memory difficulties.

Participants

68 patients met these criteria and were seen at the memory clinics during the specified time period.

Materials

The present audit utilised a database initially devised by the Clinical Audit Department, Dumfries and Galloway Primary Care NHS Trust, for use in the Memory Clinics, based on Microsoft Access software. The database was used by consultants' secretaries throughout the first nine months of the clinic to record details gathered from clinicians' paper records on patients.

Measures

The MMSE is a brief measure of cognitive ability designed as a means of screening in clinical populations for impairments in orientation, registration, attention and calculation, recall, naming, comprehension and praxis. A trained examiner, who is also responsible for scoring performance on the test, administers the test verbally. The total performance score for the test may range from 0-30, with a score of 23 or less used in the clinics as a cut-off for cognitive impairment.

The IQCODE is a 26-item informant questionnaire providing a quantitative measure of carer reports of cognitive decline. The questionnaire asks informants to rate the applicability of a statement to the individual attending for assessment, using a 5-point rating scale. The final score is then calculated by dividing the total score by 26, to give an outcome score of 0-5. A score of greater than 3 is used within the clinics as a cut-off score for cognitive decline.

Procedure

Information on attendees' demographic, problem and outcome characteristics was extracted and described. To investigate objective 3, four new groupings were devised to describe the population according to performance on formal cognitive assessment measures.

These groupings were -

Group 1 - those meeting caseness criteria for cognitive decline on both the MMSE and IQCODE (MMSE<24, IQCODE>3)

Group 2 - those meeting caseness criteria on the MMSE but not IQCODE (MMSE<24, IQCODE<3)

Group 3 - those meeting caseness criteria on the IQCODE but not MMSE (MMSE>24, IQCODE>3)

Group 4 - those failing to meet criteria for caseness on either the MMSE or IQCODE (MMSE>24, IQCODE<3).

The outcome decisions for participants were then described separately according to these groupings.

Statistical Analysis

Descriptive statistical techniques were used to describe characteristics of the total sample and to describe outcome characteristics in terms of cognitive variables.

RESULTS

Of the 68 attendees, 67 presented for assessment and 1 attended for drug review only. Given the emphasis in this audit on the assessment status of the service only those attending for assessment purposes will be considered.

Demographics

27 males and 40 females were seen, with a mean age of 74.0 years (range 54-90; sd=7.7). A principal carer (defined as a person undertaking any form of caring role) was listed for 59 (88%), with 64% of this group citing a spouse, 24% citing a son or daughter and 12% citing a friend or other relative. The area of residence of clinic attendees was recorded in all cases, with 40% of attendees resident in the Dumfries and Nithsdale area, 24% residents of Annandale and Eskdale, 22.5% residents of Wigtownshire and 13.5% residents of the Stewartry area.

Cognitive Assessment

The MMSE was administered to 52 of this group, with a mean yielded performance score of 19.7 (range 5 to 30; sd=5.6). The IQCODE was administered to 37 carers attending with patients, with a yielded mean score of 3.7 (range 1.2 to 5; sd=1.04). As no criteria are provided for cases when cognitive assessment may not be required it is assumed the inconsistent recording of scores is a result of failures to administer measures and/or record results.

Diagnosis

Of those assessed, 53 (79%) were diagnosed as having some form of dementing process. Of this group 51 were recorded as having a primary diagnosis of Dementia of the Alzheimer's Type, 1 was assigned a primary diagnosis of Lewy Body Dementia and 1 had a recorded diagnosis of mixed dementia of the Alzheimer's type and vascular dementia. Of the remaining 14 (21%) without a recorded dementia diagnosis, 1 person received a primary diagnosis of complicated grief and the remaining 13 were recorded as awaiting further investigations prior to a diagnosis being made.

Involvement of other agencies

Of the 14 not receiving a diagnosis at the clinic within the specified time period, 3 were referred to neuropsychology services for further assessment, 1 was referred to a geriatrician for further assessment and 5 were referred for neuroimaging (CT, SPECT or MRI). For the total population Figure 1 illustrates the numbers of attendees referred to other agencies for assessment or management advice, with a number of attendees receiving referrals to a number of agencies for provision of a multidisciplinary assessment and management strategy (total number of referrals=83).

INSERT FIGURE 1 HERE

Prescription of acetylcholinesterase inhibitors

Using British National Formulary criteria, 44 (66%) attendees were judged to meet requirements for prescription of acetylcholinesterase inhibitors and 41 (61%) were commenced on either Rivastigmine or Donepezil.

Monitoring decisions

Of those recorded as having a dementia diagnosis, an intention to prescribe further monitoring was recorded in 39 (58%) cases, with monitoring provided through the memory clinics, and/or by a primary care link worker, social worker or Alzheimer's Disease Society (ADS) Scotland worker.

Use of cognitive assessment measures

Scores for both the MMSE and IQCODE were recorded for 35 (52%) clinic attendees. Figure 2 illustrates the distribution and diagnostic outcomes of attendees according to criteria for cognitive impairment for these tests in combination.

INSERT FIGURE 2 HERE

The relationship between cognitive performance scores and outcomes of memory clinic attendance in terms of access gained to other assessment and support services was also examined. Other assessment services include neuropsychology, geriatrics and neuroimaging. Management and support services currently consist of a Primary Care Link Worker, Alzheimer's Disease Society Scotland worker, social worker and occupational therapist. Figure 3 illustrates the numbers of further referrals made as a result of a memory clinic attendance, according to patients' meeting or failing to meet cut-off scores for measures.

INSERT FIGURE 3 HERE

A further important outcome variable in the running of the clinics is the prescription of acetylcholinesterase inhibitors. Figure 4 illustrates the relationship between meeting assessment criteria on cognitive measures and the prescription of these drugs.

INSERT FIGURE 4 HERE

DISCUSSION

The results of this preliminary audit suggest that the memory clinics are at present meeting the brief assessment and diagnosis requirements originally proposed, with the majority of patients receiving a primary diagnosis at the clinics after one assessment visit. With respect to objective 1, the provision of locality based clinics

appears also to have met with some success in ensuring access to memory clinics for residents of each specified area within the region, though a disproportionate number of these attendees are residents of the Dumfries and Upper Nithsdale sector. However, whilst the mean age of patients attending the clinics of 74.0 years is consistent with estimates of the peak age of onset of dementia of the Alzheimer's type, the mean MMSE score of 19.7 for the population assessed does not suggest that patients are being seen in the early phases of the dementing process, where deficits on the test would be expected to fall within the milder range (scores of 23+; desRosiers, Hodges and Berios, 1998).

In addition, the under-representation of vascular and depressive pseudodementias within this population as compared to epidemiological data gathered from other areas (Livingston and Hinchliffe, 1993) suggests that the memory clinics are at present seeing a highly selected sample of patients. Whilst epidemiological research into the prevalence of the various sub-types of dementia is still in the very early stages, there is some consensus in the research literature that vascular dementia and dementia of the Alzheimer's type are the two most common forms of dementia found in community and clinical samples, accounting for 2-48% and 21-75% respectively of all dementia diagnoses (Folstein, Anthony, Parhad, Duffy and Gruenberg, 1985; O'Connor, Pollitt, Hyde, Fellows, Miller, Brook, Reiss and Roth, 1989; Livingston, Hawkins, Graham, Blizard and Mann, 1990). The low proportion of vascular dementias seen at the memory clinics may therefore suggest that these conditions are either currently neglected in health care provision or may be being detected and diagnosed by other services attending to patients following cerebrovascular or cardiovascular events.

With respect to the other stated aims of the service, including identification of reversible dementias and provision of a coherent multidisciplinary management strategy, results of the present audit are less clear. Most notably, no cases of reversible dementias were recorded for those attending within the initial nine month period, though given the relatively small numbers of patients seen it is unclear to what extent this finding may be due to a weakness of the current assessment protocol

or to the suggested low prevalence of such disorders (Freter, Bergman, Gold, Chertkow and Clarfield, 1998). With regards to the management and advice aspects of the service (objective 2), it is again unclear from the results of the present audit to what extent these aims are being met. Whilst 58% of those attending the memory clinics are recorded as having received some recommendation or referral for further monitoring, in the majority of these cases this monitoring was through a review at the memory clinics only, suggesting that the resources of the primary care link worker, social workers and ADS worker may not be being utilised most effectively at present.

The present audit also attempted to examine the use of cognitive assessment measures in the diagnostic decision making process. It was found that these measures were not used and recorded as standard within the clinics within the specified period, with only 52% of attendees having a recorded score for both the MMSE and IQCODE. In considering those for whom data on scoring for both tests was available, it was found that the majority of patients attending clinics and completing these measures met the criteria for impairment on both. Within this group, the large proportion received a diagnosis of dementia of the Alzheimer's type, suggesting a decision process for these patients which is consistent with the accumulated research literature on the measures' effectiveness in combination at differentiating dementing and non-dementing individuals in clinical settings (Mulligan et al., 1996; Mackinnon and Mulligan, 1998).

Similarly for the subgroup of two individuals for whom test information was available but where scores did not meet clinical caseness no dementia diagnosis was made, suggesting that testing within the clinics was used to provide a necessary condition for making a diagnosis. However, in a small number of cases where criteria for cognitive decline or impairment were met in one or both tests, no such diagnosis was made, suggesting that test results were not used as a sufficient basis for diagnosis. It is beyond the scope of the present audit to evaluate the effect of such irregularities on improving or decreasing diagnostic and treatment accuracy, though it is hoped that with the development of the use of cognitive assessment as

standard within the clinics the decision algorithm may be more open to scrutiny and the use of logical regression techniques to define test score use may become possible.

IMPLICATIONS

The present audit provides a first opportunity to evaluate the running of the service in terms of meeting service and protocol aims, and to offer an evidence based critique on further changes and developments indicated. The findings to date suggest that whilst the clinics have been successful in generating new referrals for assessment of memory difficulties, targets of early identification of dementia and detection of reversible dementia are not being met. Whilst this problem may be partially related to an increased waiting time for attendance at clinics due to staffing difficulties, it also seems probable that clinics are currently prevented from fulfilling these aims by the inappropriate selection of individual candidates for assessment by referral agents. Given that clinics are currently only able to offer 80 assessment appointments per year, it will not be possible for clinics to see all people who develop dementia. Therefore the appropriate selection of attendees according to service aims will be essential to promote the optimal use of the specialist assessment and management resources set up to serve a mildly cognitively impaired population and their carers. Dissemination of literature on criteria for referral to the clinics to all referral agents may help solve this problem. Development of routine recording of information on the history and duration of problems may also facilitate future evaluations of the stage in the dementing process at which people are presenting at clinics.

Results of this audit also suggest that cognitive assessment measures are not being used or recorded as standard in the current clinic practice, leading to failures to make systematic and logical use of information gained from test scores as a basis for decision making within the clinics. Failure to record the use of cognitive measures routinely also currently precludes the systematic evaluation of clinical decision-making. An additional failure to screen routinely for depression using a standardised measure such as the Geriatric Depression Scale may also mean that disabling

affective conditions comorbid with dementia may be left untreated, or that reversible causes of cognitive decline may remain undetected. Given the difficulties of differentiating dementia from depressive pseudo dementia conditions, such screening may identify individuals who require more specialised neuropsychological assessment (desRosiers et al., 1998).

Also indicated in the results of this audit is the currently limited use of non pharmacological management strategies within the clinics. If changes in referring patterns can be initiated to lead to earlier identification of dementias a need for more consistent use of services able to offer information and psychosocial support to attendees and their carers will be required. One means of assessing what sort of information is required and at what time, may be to ask the individuals attending the clinics, using a self-report measure devised for the purpose (McCormick, 1997). An evaluation of the expectations of those attending the clinics, and how the clinics are currently meeting these needs may be the next developmental task for the service, and may allow the clinics to meet their broader aims of meeting the social care needs of individuals with dementia and their carers.

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Figure 2.1 Number of recorded referrals to other services.

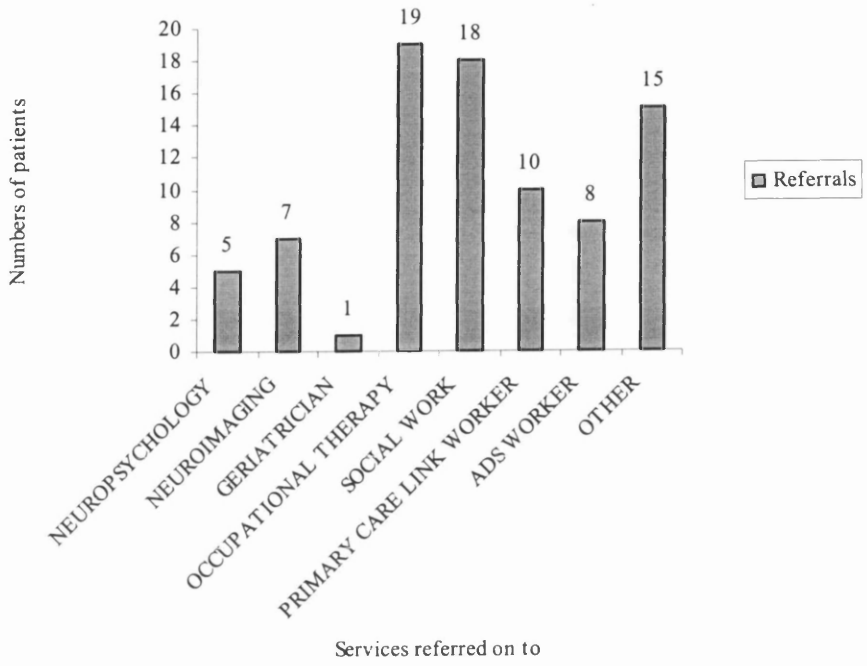


Figure 2.2 Distribution of recorded dementia diagnoses according to performance on cognitive measures.

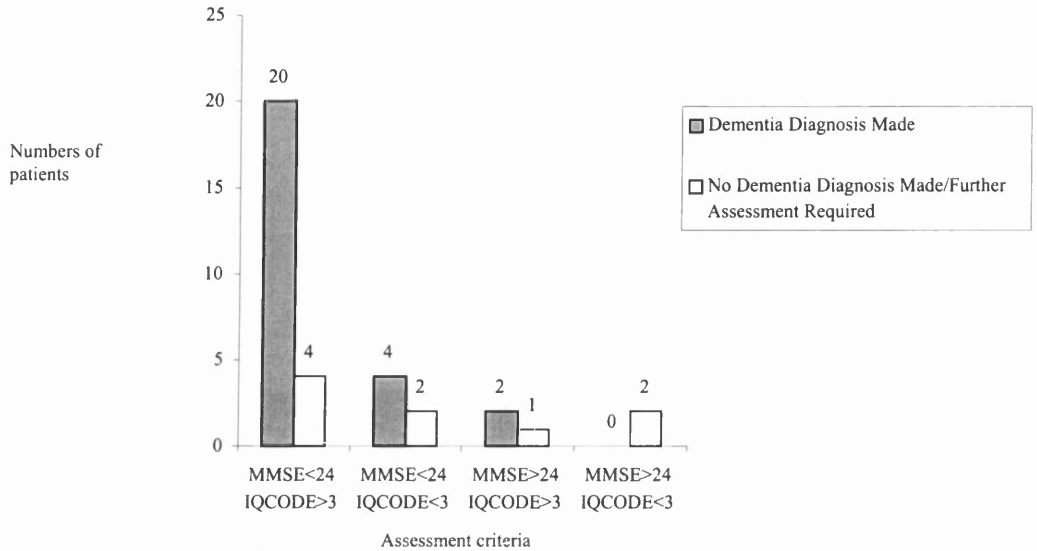


Figure 2.3 Distribution of referrals to assessment and support services according to memory clinic assessment scores.

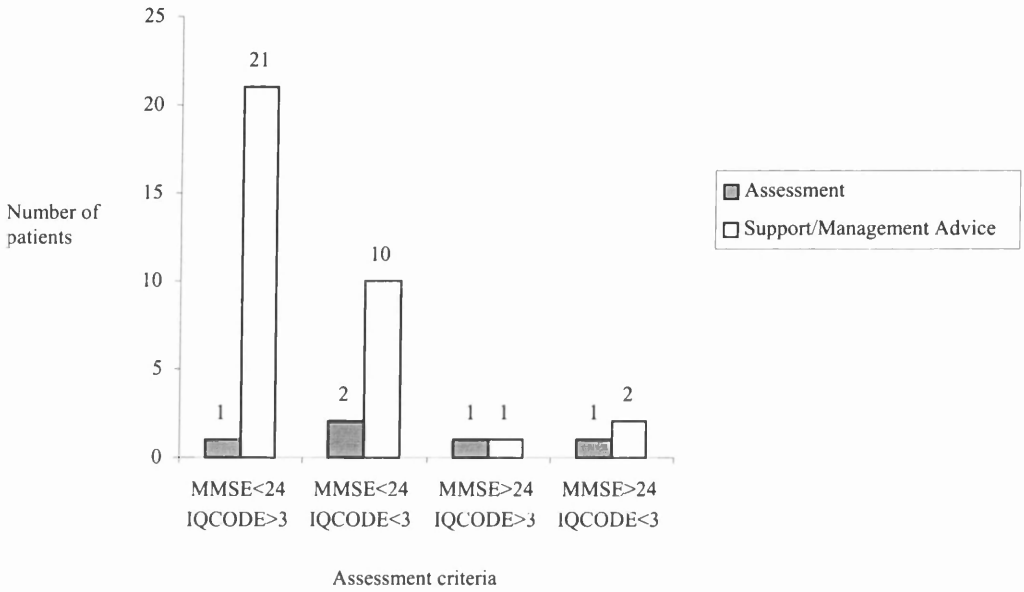
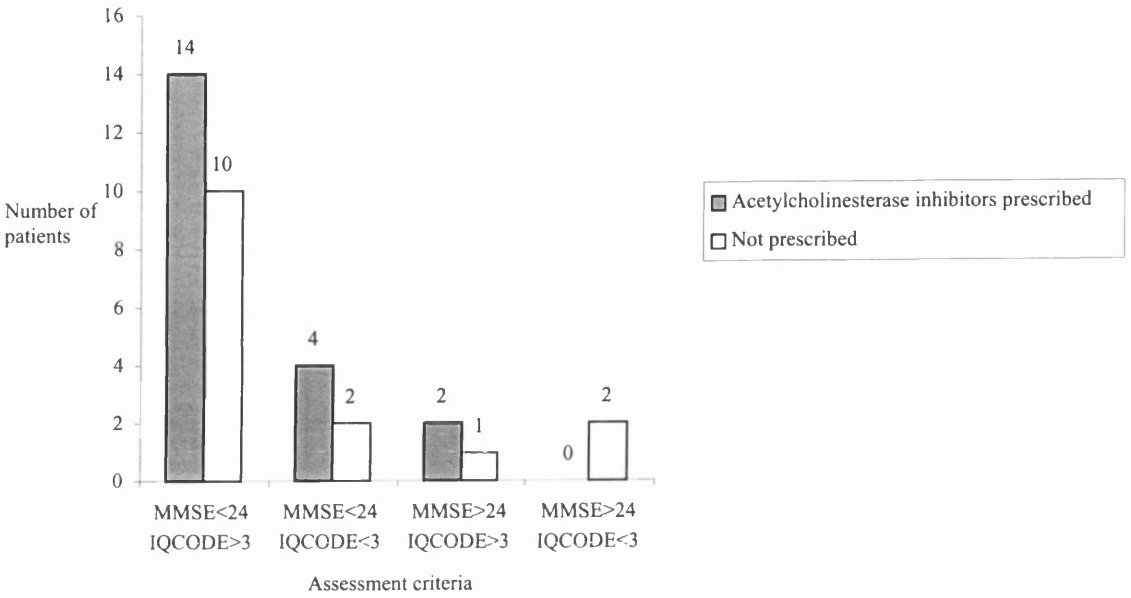


Figure 2.4 Distribution of recorded prescriptions of acetylcholinesterase inhibitors according to scoring on cognitive measures.



CHAPTER TWO

Systematic Review of Literature

Fatigue after Severe Traumatic Brain Injury in Adults: A review

Prepared in accordance with the notes for contributors for *Brain Injury* (see Appendix 2.1).

Summary

Objectives: To assess the prevalence of fatigue after severe traumatic brain injury (TBI), and review the evidence for models attempting to explain the emergence and maintenance of this problem, namely the coping hypothesis and a multifactorial model of stress and coping (Kendall and Terry, 1996).

Search strategy: Electronic search of Medline, Embase, PsycINFO. Hand searches of *Archives of Physical Medicine and Rehabilitation, Brain Injury, Journal of Head Trauma Rehabilitation* and *Journal of Neurology, Neurosurgery and Psychiatry*. Citation search on all references located.

Selection criteria: Studies assessing the prevalence of fatigue were included on the basis of their attempts to follow up representative samples of adults with severe TBI, and make some attempt to assess symptoms of fatigue. Studies assessing evidence for the coping hypothesis model of fatigue, which made explicit reference to this model and involved studying participants with severe TBI were also reviewed. As no studies directly assessing Kendall and Terry's multifactorial model of coping were found using systematic search strageis, a final literature review was carried out which included all other studies attempting to explain the emergence of post-concussion symptoms such as fatigue using a model transactional model of stress and coping.

Data collection and analysis: 9 studies fulfilled criteria for review of prevalence. Studies were all exploratory in nature, with no studies designed to give clear evidence about fatigue. 3 studies fulfilled inclusion criteria for the review of evidence for the coping hypothesis. 14 studies met inclusion criteria for review of the alternative model.

Main results: There is evidence that fatigue is a commonly reported problem after severe TBI, which may persist for up to 15 years after injury and which is resistant to specialist rehabilitation. Estimates of prevalence at 1 year ranged from 61-82%. The coping hypothesis was unable to fully explain the maintenance of this problem.

Reviewer's conclusions: There is a consistent body of evidence that fatigue is a common problem after severe TBI, though given the poor quality and exploratory nature of studies reviewed, studies designed to specifically assess fatigue using validated measures are needed to make more precise estimates of prevalence. The coping hypothesis cannot fully account for the maintenance of this problem, though a review of literature based on an alternative stress and coping model (Kendall and Terry, 1996) suggests that further research should be targeted at directly assessing this model.

Background

Severe traumatic brain injury has been defined as a traumatic insult to the brain, which results in loss of consciousness and a period of post-traumatic amnesia (PTA) lasting for longer than 24 hours (Russell, 1971; Teasdale and Jennett , 1974). Using this definition the annual incidence of severe traumatic brain injuries (TBI) has been estimated at 14-16 per 100 000 population in the UK (McMillan and Greenwood, 1993). A recent study carried out in Glasgow has suggested that the incidence of head injuries resulting in continuing disability at one year post-injury may be more than 100 per 100 000 population per year (Thornhill, Teasdale, Murray, McEwen, Roy and Penny, 2000).

Disabilities may be experienced in a number of areas of neuropsychological, physical and psychosocial functioning after TBI. One symptom believed to be important in moderating disability in each of these domains is fatigue. Chronic symptoms of fatigue are reported by up to 50% of individuals who have experienced such injuries (Thomsen, 1984). Fatigue may cause excess disability by impairing the individual's ability to engage in numerous everyday tasks requiring sustained physical and/or mental effort, such as engagement in intensive rehabilitation programmes or return to paid employment (Luria, 1963; Crepeau and Scherzer, 1993).

Given the potential impact fatigue may have on a wide range of individual outcome variables, and on service effectiveness and use, the lack of research into causes for the emergence and maintenance of fatigue is surprising. Early attempts to explain fatigue as a direct symptom of physical causes were rejected by van Zomeren and van den Burg (1985) who cited evidence that the presence and severity of symptoms such as fatigue after TBI could not be directly predicted by brain injury severity. A review of the neurological literature on outcomes after TBI (Kendall and Terry, 1996) also found inconsistent evidence for the association between brain injury severity or type and psychosocial outcomes. These authors concluded that the available evidence to date suggests that neurological factors cannot alone account for the wide variation in individual outcomes after TBI.

This has led to an increase in research interest on the contribution of psychological factors to a number of outcomes after severe TBI. One model attempting specifically to address the problem of symptoms of fatigue after TBI was the coping hypothesis outlined by van Zomeren, Brouwer and Deelman (1984). Under their coping hypothesis it is argued that individuals commonly experience reductions in their information-processing capacity after head injury, and that this can lead to disability in a number of everyday tasks. However, as individuals may show good recovery in other areas of functioning, such disabilities may not be apparent to others, and so the individual may be under pressure from relatives and employers to resume normal functioning. The individual is argued to then try to cope with this pressure by expending increased effort on tasks, to compensate for impaired processing capacity. Such compensatory effort can lead to secondary symptoms of chronic stress, and will be maintained by the individual continuing to try to cope with ongoing difficulties created by persisting cognitive deficits. Fatigue may represent one such symptom.

Some support for the presence of impaired information processing in individuals who have experienced a mild TBI has been provided (Gronwall and Wrightson, 1974; Levin, Mattis, Ruff, Eisenberg, Marshall, Tabaddor, High and Frankowski, 1987; Montgomery, Fenton, McClelland, MacFlynn and Rutherford, 1991). Lishman (1988) and Jacobson (1995) provide reviews of this literature. Van Zomeren and van den Burg (1985) have also provided some evidence from epidemiological studies for a two factor model of psychosocial complaints after severe TBI, with differences found between injury related cognitive impairments and secondary adjustment related symptoms. Some experimental attempts have also been made to test the coping hypothesis directly, by exploring the relationship between ability, performance and stress symptoms in individuals who have experienced TBI.

Riese, Hoedemaker, Brouwer, Mulder, Cremer and Veldman, (1999) have applied this model directly to the problem of mental fatigue after severe TBI, by using an experimental situation to determine the effects of task demand on fatigue in healthy

and TBI groups. However, this work has suggested that the coping hypothesis may require some modification if it is to describe problems such as fatigue, with results suggesting that fatigue may still be experienced even when task demands are experimentally manipulated to be within an individual's capabilities. These authors have therefore speculated about the potential importance of other cognitive processes such as beliefs and appraisal in also contributing to continuing fatigue.

When discussing the limitations of the coping hypothesis in explaining the symptoms of chronic stress in their sample, van Zomeren et al (1984) also suggested that future research in the area would profit from considering developments in stress research where cognitive processes are accounted for as mediators of stress and coping. One theoretical model from the psycho-physiological literature that may be useful in this endeavour is the transactional model of adjustment and stress proposed by Lazarus and Folkman (1984) [see Figure 3.1].

INSERT FIGURE 3.1 HERE

These authors argued that cognitive processes are crucial in the adjustment process, as events will only be stressful when they are perceived as such by the individual. For an event to be perceived as stressful requires the individual to make an initial appraisal of the event as threatening or harmful, and for them then also to make a secondary appraisal of the event as something they do not have the resources to control or cope with. Once an event has been perceived as stressful, the individual's adjustment is governed by their choice of coping response. Events identified as uncontrollable may be associated with the use of more emotion-focused, avoidant coping strategies. In contrast, when events are perceived as stressful, but potentially controllable, active problem-solving coping strategies are more likely to be used.

Within this model, individual variables such as beliefs about the nature of events and personal resources will clearly be important in mediating stress-related outcomes by influencing the appraisal stages. The process is also expected to be recursive, with outcomes resulting in anxiety or mood symptoms expected to lead to a greater likelihood that the individual will perceive future events as stressful and outwith their coping capacity. Therefore once established, this process may mean that symptoms of chronic stress may be experienced on encountering numerous everyday challenges that the individual may previously have been able to cope with satisfactorily.

INSERT FIGURE 3.2 HERE

Kendall and Terry (1996) have suggested that this model could be elaborated to apply to the problem of explaining individual differences in adjustment and outcome after TBI, and the maintenance of specific post-concussional symptoms such as fatigue. Previous researchers have demonstrated the utility of the model in the determination of outcome following other acquired injuries, such as spinal cord injury (Buckelow, Baumstark, Frank and Hewlett, 1990) and myocardial infarction (Terry, 1992). The focus of the model on the impact of chronic daily stressors on adjustment and outcome also seems particularly relevant to an understanding of the impact of TBI, as the noted impairments in information-processing capability common after TBI would be expected to make a number of routine tasks challenging for the individual. Added to this are well documented increases in detrimental life events after severe TBI including high rates of separation and divorce (Thomsen, 1984; Tate, Lulham and Brie, 1989), decreased numbers of social supports out with the family (Thomsen, 1984), decreased participation in leisure activities (Oddy and

Humphrey, 1980), high levels of family distress (Lezak, 1978; 1988; Kinsella, Packer and Olver, 1991) and an increase in sexual problems (Kreutzer and Zasler, 1989) [for review, see Oddy, 1993].

Kendall and Terry have therefore used this model as a basis for creating a theoretical model for the prediction of psychosocial difficulties after TBI. Given the noted potential importance of information-processing and neurological factors in predicting outcome and influencing appraisals, these are also included in the model, as well as pre-morbid psychosocial variables such as self-esteem and psychiatric history. The final model is outlined in Figure 3.2. As fatigue has been suggested to be a commonly reported complaint after TBI, and may not be fully accounted for by injury severity factors or the coping hypothesis, this model could provide a useful structure for future research on factors associated with chronic fatigue after TBI. It potentially provides a means of allowing for the inclusion of cognitive processes neglected in previous research, and also offers a clear theoretical structure from which to begin this work.

However, given the at present lack of any systematic reviews of the literature to determine the significance of the problems fatigue and the relevance of the research to date in furthering understanding of the problem, this should be a priority before planning any future research. This is therefore the task of the current paper.

Aim

To systematically review the literature to determine

1. the prevalence of fatigue after severe TBI in adulthood
2. the evidence for the ability of the coping hypothesis to explain fatigue after severe TBI
3. the evidence for the ability of the modified multifactorial coping model to explain fatigue after severe TBI.

PART 1

Objectives

To assess the prevalence of symptoms of fatigue after a severe traumatic brain injury which are consequent on the injury.

Criteria for considering studies for this review

Types of studies

Prospective or retrospective longitudinal outcome studies.

Types of participants

Persons aged 18 to 65 years who have experienced a severe TBI as defined by a closed head injury which results in loss of consciousness and a period of PTA lasting for 24 hours or more (Russell and Smith, 1962; Russell, 1971), or a Glasgow Coma Scale (GCS) score of 3-8 (Teasdale and Jennett, 1974).

Type of outcome study

Any study of outcomes after severe TBI conducted within the last fifty years which includes a measure of fatigue. This may include studies on psychosocial outcomes after severe TBI, or studies on neuropsychological functioning or outcome of rehabilitation after severe TBI.

Excluded:

1. Any studies which do not include a measure of fatigue.
2. Studies where insufficient information on PTA, duration of loss of consciousness (LOC) or GCS is given to make a judgment of brain injury severity.
3. Studies assessing outcome after non-traumatic brain injury.
4. Studies involving predominantly child, adolescent or older adult populations.
5. Articles based on single case reports or series, or expert opinion.

Types of outcome measures

Instruments

Post Concussion Symptom Checklists, Katz Adjustment Scale, Comprehensive

Psychopathological Rating Scale, Head Injury Symptom Checklist, other self-report measures or relative ratings.

Duration of follow-up

Studies recording outcomes after a minimum of 1 month post-injury were included.

Search strategy for identification of studies

DATABASES

Medline, Embase, PsycINFO.

ELECTRONIC SEARCH STRATEGY

1. All references to severe traumatic brain injury/brain injury/brain damage/closed head injury/head injury and fatigue or outcome (including psychosocial, rehabilitation or neuropsychological).
2. Medline (1966 – July 2001), Embase (1980 – July 2001), PsycINFO (1967 – July 2001).

HAND SEARCH

Four journals were selected for hand searches, based on the results of literature searches and a review of contributors' notes for article selection:

Archives of Physical Medicine and Rehabilitation (last 10 years)

Brain Injury (last 10 years)

Journal of Head Trauma Rehabilitation (last 10 years)

Journal of Neurology, Neurosurgery and Psychiatry (last 10 years).

Reference lists for all papers identified in the above searches.

Methods of the review

All potential studies were read by the reviewer to determine if they fulfilled inclusion criteria.

Quality Assessment

Criteria for the assessment of epidemiological studies were written by modifying the Scottish Intercollegiate Guideline Network (SIGN, 2001) criteria for systematic reviews of intervention studies.

For details see Appendix 2.2.

Data Handling

Information on relevant studies was collated in the results table. Results from studies with similar methodologies were then grouped for pooled statistical analysis.

Description of studies

See: Table of studies (figure 1).

Patient characteristics

Studies included participants ranging in age from 12-78 years, with an often broad range of ages included within individual studies. The proportion of male participants ranged from 64-86%. The mean number of years of education of participants was cited in 3 studies (Dikmen, Machamer and Temkin, 1993; Olver, Ponsford and Curran, 1995; 1996; Koskinken, 1995; 1998) and ranged from 9.13-11.7 years of education. Information on social class of participants was given in 3 studies (Thomsen, 1984; 1987; Oddy, Humphrey and Uttley, 1978; 1980; 1985; McKinlay, Brooks, Bond, Martinage and Marshall, 1981; 1983; 1986). The majority of participants in these studies were in social classes 3-5, with the exception of Oddy et al.'s studies where the majority of participants were in the upper social classes. Causes of TBI were cited in all studies and included predominantly road traffic accidents, followed by assault and falls, with other causes including accidents at work, sports accidents, cycling injuries, riding accidents and falls. The duration of PTA was given in all studies, and ranged from 2 days to greater than 6 months.

Cultural settings

United Kingdom (4 studies), Sweden (1 study), Australia (1 study), Denmark (1 study), USA (1 study), Finland (1 study).

Sample size

The number of TBI patients followed up ranged from 15 to 254.

Description of study design

Studies were all naturalistic and longitudinal, and ranged from a prospective representative cohort study of incidence, to retrospective studies which made no attempt to control for the influences of pre-morbid or demographic influences. All studies followed patients up after an initial hospital admission, and three studies

specifically followed patients who had engaged in specialist rehabilitation programmes.

Duration of follow-up

3 months to 15 years.

Methodological quality

Quality assessment

The reviewer assessed the quality of each study using the criteria given in Appendix 2.2 for guidance.

Results

Grouping all uncontrolled studies of participants not receiving specialist rehabilitation, a total of 375 participants have been followed up for periods varying between 6 months and 15 years. Combining results across studies, the point prevalence of fatigue symptoms in the first year following injury is estimated as 82% at 3 months, 61% at 6 months, and 63% at 12 months. Researchers have tended to combine reports of fatigue lasting for longer than this period, on the assumption that most recovery will occur in the first year following TBI. Therefore considering all uncontrolled studies reporting on fatigue after this period, the estimated prevalence of fatigue ranges from 28-50% at 2 years to 36-70% at 2 to 15 years.

Considering only studies of non-rehabilitation populations which attempt to control for the possible effects of high baseline reporting of fatigue symptoms in other populations, a total of 85 TBI recruits and 123 controls have been followed up for periods of 1 month to 7 years. The point prevalence of fatigue in the TBI population was significantly higher in all cases, and estimated to be 62% at 1 month, 33-44% at 6 months, 38% at 1 year, 25% at 2 years and 43% at 7 years.

Three papers focused on individuals who had received specialist rehabilitation after TBI, following up a total of 269 individuals at periods of 2, 5 and 10 years after

initial injury. Estimates of the point prevalence of fatigue in this group ranged from 68% at 2 years, to 42-73% at 5 years and 67-64% at 10 years.

It was possible in 3 studies to compare directly patient and relative reports. Two studies found discrepancies in reporting of symptoms in relatives as compared with individuals, with relatives reporting a prevalence of fatigue symptoms as 33% at 6 months compared with patient reports of 44%, and between 2 and 7 years relatives rating fatigue as problematic in 70-73% of patients, with patients reports rating fatigue as problematic in only 42-43% of cases. However in a study assessing outcome at 10 years, there was little difference in patient and relative reports.

One study also attempted to follow-up a representative population of all individuals sustaining a severe TBI within one community (Glasgow) over a 1 year period. At follow-up, of 73 people, 47 reported problems with tiredness on a problem checklist, leading to an estimated annual incidence of fatigue of 64% in all individuals sustaining a severe TBI within the Glasgow health district.

Discussion

Using the evidence reviewed, there is evidence that fatigue is a commonly experienced problem after severe TBI, and that the point prevalence of such symptoms may range from 82% at 3 months, to 36-73% at 5 years and 50% at up to 15 years. The results of this review also suggest that fatigue may be a highly persistent and chronic symptom after TBI, with long term follow-up studies suggesting that many patients continue to experience problematic symptoms of fatigue at up to 15 years post injury. These results may however represent an over-estimate of the problem as all studies include patients who would fall into the "extremely severe" as well as "severe" category, based on information given on PTA duration.

There is also some evidence that fatigue symptoms may be unresponsive to specialist rehabilitation interventions, with no difference in prevalence of fatigue noted in patients who received normal aftercare versus specialist rehabilitation.

However, this could also represent a sampling bias with more severely injured persons being more likely to receive inpatient rehabilitation, and so it might be expected that their fatigue problems could have been greater had rehabilitation not taken place.

Further caution must also be taken in interpreting the above results, given the methodological problems with the studies involved. Firstly, studies tended to combine participants with a varying range of ages. Whilst there was evidence that the majority of studies had sampled a representative populations of predominantly 19-25 years old males (Morton and Wehman, 1995), the combination of this age group with older individuals may have led to higher estimates of fatigue due to the effects of ageing on fatigue levels. It should also be noted that many of the studies reviewed made use of specially designed measures. This means that comparisons of prevalence across studies may be confused by the differing definitions of fatigue used in individual studies, and differences in the reliability and validity of measures used. The studies reviewed were also all exploratory in nature, making use of interviews or checklists designed to examine a number of potential problems after TBI to describe general changes in psychosocial functioning. No studies were designed to specifically assess the incidence or prevalence of fatigue, and none used a standardised measure of fatigue, therefore making the reliability of estimates based on these studies questionable.

The way in which some researchers have managed discrepancies between patient and relative reports of fatigue by reporting only on relative data where differences exist, may also have led to an over-estimate of symptoms of fatigue. Some researchers have argued that relatives may be better able to report on symptoms given that severity of injury in individual sufferers may lead to problems with insight into cognitive and psychosocial complaints in particular (Sbordone, Seyranian and Ruff, 1998). However, given that relatives may be under considerable amounts of strain following head injury there is also a risk that their reporting of symptoms in the patient may be biased by their own feelings of stress

(McKinlay et al., 1981). Therefore, fatigue estimates from the present review based on relative ratings alone may again represent an overestimate of the problem.

Finally, the lack of any or adequate control groups in the studies reviewed may also have led to overestimates of fatigue, by failing to control for potential high baseline reporting of fatigue in healthy individuals. This problem cannot be fully addressed by simply asking individuals to rate the presence of new onset symptoms of fatigue since injury, as given the severity of injuries involved memory and insight problems would be expected to be highly prevalent in this population. As only the studies of Oddy et al. made use of a clinical control group, it is also possible that any increased prevalence of fatigue symptoms in the groups studies could have been the result of none specific clinical factors such as the effects of hospitalisation or post-traumatic syndromes rather than specific effects of brain injury leading to increased fatigue.

In summary, using the grades of acknowledgement outlined in Appendix 2.2, a grade of C can be assigned to the evidence to date. This means that a body of retrospective studies, some of which have a low risk of bias or confounding, have demonstrated consistent estimates for the prevalence of the fatigue after severe TBI. This suggests that fatigue is a serious problem for this population, though further evidence from prospective studies with clearer inclusion and exclusion criteria, and describing more representative populations using well validated research measures is needed to allow more accurate estimates of the true prevalence of the problem to be made.

PART 2

Objectives

To review the existing evidence for the coping hypothesis, and to assess the strengths and limitations of this model as an explanation for the problem of fatigue after severe TBI.

Criteria for considering studies for this review

Types of studies

Comparisons of TBI groups and controls on measures of stress related symptoms and information-processing abilities, and correlational studies using factor analytic techniques to assess the association between cognitive and psycho-physiological symptoms, of which fatigue may be one, in TBI groups.

Types of participants

Persons aged 18 to 65 years who have experienced a severe TBI as defined by a closed head injury which results in loss of consciousness and a period PTA lasting for 24 hours or more (Russell and Smith, 1962), or a GCS score of 3-8 (Teasdale and Jennett, 1974).

Type of outcome study

Any study designed to assess the adequacy of the coping hypothesis as an explanation of continuing psychosocial symptomatology after severe TBI. This may include studies looking at the association between features of injury severity and psychological distress after TBI, or studies comparing TBI groups and controls on indicators of performance related stress.

Excluded:

1. Studies focusing on individuals with mild to moderate levels of TBI, as indicated by PTA of less than 1 day, as they may be expected to experience different adjustment related problems to groups with more severe traumatic brain injuries.
2. Studies involving children, adolescents or older adults.
3. Articles based on single case reports or series, or expert opinion.

Types of outcome measures

Instruments

Cognitive measures and daily functioning measures: Categories Test, Divided Attention Driving Task, Dot counting, Glasgow Assessment Schedule.

Psycho-physiological stress measures: Heart rate variability (HRV), mean heart beat interval (HBI), Rating Scale for Mental Effort.

Other measures of psychological distress: Trauma Complaints List, Brief Symptom Inventory, Katz Adjustment Scale – Relatives version, Indices of Coping, Experienced Distress Questionnaires.

Search strategy for identification of studies

DATABASES

Medline (1966 – July 2001), Embase (1980 – July 2001), PsycINFO (1967 – July 2001).

ELECTRONIC SEARCH STRATEGY

1. All references to traumatic brain injury/brain injury/brain damage/closed head injury/head injury were searched.
2. Results of this search were combined with results from a search for the term 'coping hypothesis'.

HAND SEARCH

Four journals were selected for hand searches, based on the results of literature searches and review of contributor's notes for article selection:

Archives of Physical Medicine and Rehabilitation (last 10 years).

Brain Injury (last 10 years).

Journal of Head Trauma Rehabilitation (last 10 years).

Journal of Neurology, Neurosurgery and Psychiatry (last 10 years).

Reference lists for all papers identified in the above searches.

Methods of the review

All potential studies were read by the reviewer to determine if they fulfilled inclusion criteria.

Quality Assessment

Criteria for the assessment of studies of association were written by modifying the Scottish Intercollegiate Guideline Network (SIGN, 2001) criteria for systematic reviews of intervention studies.

For details see Appendix 2.3.

Data Handling

Information on relevant studies was collated in the studies table.

Description of studies

See: Table of studies (figure 2).

Patient characteristics

The mean ages of TBI participants were given as 27.6 years, and 23.3 years (sd=6.4) in Hinkeldey and Corrigan (1990) and Riese et al. (1999) respectively. No information on age was provided in van Zomeren et al. (1984). Van Zomeren et al. (1984) and Riese et al. (1999) looked only at male participants, and males comprised 80% of Hinkeldey and Corrigan's (1990) study population. Causes of TBI were cited in Hinkeldey and Corrigan (1990), and included motor vehicle accidents, falls and assaults. The duration of PTA was given in all studies, with this ranging from 10-380 days. The time since injury ranged from > 2 months to 5 years.

Cultural settings

Netherlands (1 study), United Kingdom (1 study), USA (1 study).

Sample size

TBI groups ranged in size from 8 to 55.

Description of study design

Two types of study design were used. One study used confirmatory factor analytic methods to investigate the ability of the two-factor coping hypothesis model to explain the association between cognitive and psychosocial outcomes for a group of individuals who had experienced a TBI. Two studies used experimental designs to compare the stress responses of TBI and control groups exposed to laboratory testing situations.

Methodological quality

Quality assessment

The reviewer assessed the quality of each study using the criteria given in Appendix 2.3 for guidance.

Results

Van Zomeren et al. (1984) carried out an initial comparative study to test the predictions outlined by the coping hypothesis. They used a laboratory situation to test hypotheses that reaction time would be slower in individuals with TBI compared to controls, and that slowed information-processing ability in task performance would be associated with increased task-related stress in the TBI group compared to controls. Their results supported the first hypothesis, with the TBI group having significantly slower motor and cognitive reaction times in a simple reaction time task. However, whilst the TBI group showed significantly faster and less variable heart rate than controls across rest and testing situations, there were no significant between group differences in the effects of task load on heart rate. These results were taken to suggest only partial support for the coping hypothesis, with symptoms of chronic stress rather than task-related stress apparently found.

Hinkeldey and Corrigan (1990) attempted to replicate van Zomeren and van den Burg's initial factor analytic study, using confirmatory factor analytic methods to examine the ability of the two-factor coping hypothesis to describe the relationship between cognitive impairments and post-concussional symptoms after extremely severe TBI. Their data did not fit the two factor model, though using exploratory factor analysis techniques the authors suggested that the symptoms reported by individuals best fitted a 3 factor model, consisting of separate clusters of severity related, somatic and general complaints. The authors concluded that these results could support a modified version of the coping hypothesis, with the somatic and general complaints symptoms representing the effects of chronic stress. However, as somatic symptoms were found to be distinct from more general emotional complaints, an alternative explanation for these problems could be that somatic changes such as fatigue represent the effects of structural brain damage not detected by traditional measures of severity.

Riese et al (1999) later looked specifically at the utility of the coping hypothesis in explaining the emergence and maintenance of chronic mental fatigue after severe TBI. They compared heart rate, mental effort and distress of TBI and accident

control groups completing a driving simulator task. When task demands were experimentally manipulated to accommodate individual differences in attentional and information-processing capacity, there were no group differences in heart rate or self-reported mental effort, though subjective distress remained much higher in the TBI group.

These results contradict the original coping hypothesis, which would suggest that when task demands are within an individual's capabilities, no excess distress should be present. However, the authors suggest that the results support a modified version of the hypothesis, consistent with van Zomeren et al.'s (1984) findings. This suggests individuals who have suffered TBI will experience increased distress and therefore fatigue in any potentially demanding situations, as they have learnt to expect all task demands to be outwith their capabilities. Therefore cognitive processes relating to beliefs about the injury, and its impact on personal capabilities and resources, may be important in mediating stress responses and in predicting distress when the individual is presented with any task demand. In this case fatigue represents a symptom of chronic stress which will be present when confronting a number of daily stressors, which may account for its noted high prevalence for many years after the initial injury.

Discussion

Taken together the above studies suggest some support for a modified version of the coping hypothesis. This modified version of the hypothesis states that individuals with severe TBI will experience chronic stress and therefore fatigue in response to any task demands, and these symptoms of stress will continue to be apparent even when task demands are modified to compensate for deficits in information processing capability.

However, these results must be interpreted with some caution, due again to the methodological limitations of the studies used to reach this conclusion. For instance the lack of reliable measures for injury severity and cognitive impairment, make it difficult to assess the possible contributions of injury related organic changes to

general and somatic complaints in the Hinkeldey and Corrigan (1990) correlational study. The sample size in this study was also small, and the sample was not homogenous, with wide variations in level of PTA and time since injury within the group. In the two experimental studies, numbers in TBI groups were also small, and consisted entirely of male participants.

The small numbers also meant that pre-morbid factors such as psychiatric history and intellectual abilities could not be controlled for, and therefore pre-morbid dispositions towards stress or the use of certain coping styles could also have confounded the findings of differences in chronic stress levels between groups. This may be particularly relevant given the population under study, as Fenton, McClelland, Montgomery, MacFlynn and Rutherford (1993) have found some evidence that individuals who experienced a TBI and who reported post-concussional symptoms had more experiences of pre-morbid social adversity than TBI controls with no persisting symptoms of post concussional syndrome. The lack of clinical control groups in the experimental studies also represents a methodological limitation, with this again making it difficult to conclude that any differences in fatigability are due to specific effects of TBI rather than any traumatic injury.

In summary a grade B can be assigned to support for the coping hypothesis after severe TBI. This means that a small but consistent body of evidence exists for a modified version of the coping hypothesis, which states that individuals who have experienced a severe TBI may experience chronic symptoms of stress as a result of attempts to cope with cognitive deficits resulting from the acquired brain injury, and this may explain the high prevalence of fatigue symptoms. This grading reflects the lack of high quality experimental studies comparing task-related stress in representative TBI and control samples and methodological problems in studies carried out to date such as failure to consider pre-morbid factors.

PART 3

Objectives

To review the existing evidence for the applicability of a modified model based on Lazarus and Folkmans' transactional model of stress and coping to explain the maintenance of fatigue after severe TBI.

Criteria for considering studies for this review

Types of studies

Comparisons of TBI groups and controls on measures of variable included in the transactional model of coping: beliefs about locus of control, coping styles and activity levels.

Types of participants

Persons aged 18 to 65 years who have experienced a severe TBI as defined by a closed head injury which results in loss of consciousness and a period PTA lasting for 24 hours or more (Russell and Smith, 1962), or a GCS score of 3-8 (Teasdale and Jennett, 1974).

Type of outcome study

Any study attempting to describe the above variables in severe TBI populations.

Excluded:

1. Studies focusing on individuals with mild to moderate levels of TBI, as indicated by PTA of less than 1 day, as they may be expected to experience different adjustment related problems to groups with more severe traumatic brain injuries.
2. Studies involving children, adolescents or older adults.
3. Articles based on single case reports or series, or expert opinion.

Types of outcome measures

Instruments

Measures of life events and stressors, including clinical interview and individually designed questionnaires.

Measures of locus of control beliefs: Multidimensional Health Locus of Control Scale.

Measures of coping: COPE, Ways of Coping.

Physiological measures of exercise tolerance levels: tests of muscle endurance and oxidative capacity.

Search strategy for identification of studies

DATABASES

Medline (1966 – July 2001), Embase (1980 – July 2001), PsycINFO (1967 – July 2001).

ELECTRONIC SEARCH STRATEGY

1. All references to traumatic brain injury/brain injury/brain damage/closed head injury/head injury were searched.
2. All references to 'transactional model of stress/coping', 'locus of control', 'coping', 'activity', 'exercise tolerance/physical fitness/aerobic capacity/deconditioning' were searched. Author searches under Kendall, Terry, Lazarus and Folkman were also carried out.
3. The results of the above searches were then combined.

HAND SEARCH

Four journals were selected for hand searches, based on the results of literature searches and review of contributor's notes for article selection:

Archives of Physical Medicine and Rehabilitation (last 10 years).

Brain Injury (last 10 years).

Journal of Head Trauma Rehabilitation (last 10 years).

Journal of Neurology, Neurosurgery and Psychiatry (last 10 years).

Reference lists for all papers identified in the above searches.

Methods of the review

Systematic searches for papers specifically assessing Kendall and Terry's modified model of coping in TBI found no published studies. Therefore a decision was made to review any studies assessing individual elements of these studies, as this might

suggest any findings which should be considered before planning research based on the model.

Results

Cognitive beliefs and locus of control

Two studies were found which attempted to explore the relationship between locus of control beliefs and psychosocial outcomes after severe TBI. Lubusko, Moore, Stambrook and Gill, (1994) found a significant association between locus of control beliefs about the future and employment status at 4-5 years post-injury. Compared to patients with comparable length of coma and Glasgow Coma Score(GCS) on admission to hospital who successfully returned to work, patients who did not return to their pre-injury level of employment were found to have lower scores on internal locus of control measures, higher scores for belief in the powers of others, and higher Beck Hopelessness Scale scores.

However, the group who failed to return to work also had a significantly greater average duration of PTA than the control group, and therefore it is unclear whether the association between cognitive effects and employment status is causal or the result of a confounding effect of injury severity. The study also fails to comment on other psychosocial symptoms demonstrated by this group, and so again it is unclear whether the effects of cognitive beliefs are direct influences in employment status, or act indirectly by causing symptoms of stress such as fatigue which then disable individuals in a number of areas of everyday functioning, as proposed by Kendall and Terry (1996).

However, an earlier study carried out by Moore, Stambrook and Wilson (1991) suggested some evidence for Kendall and Terry's model. These authors investigated the relationship between post-injury quality of life outcome and locus of control beliefs following TBI. They also found a significant association between locus of control beliefs and poor quality of life outcomes in a group of moderately and severely head injured individuals, and using multiple regression techniques showed that these effects persisted even after pre-injury education levels and post-injury

GCS scores were controlled for. In summary therefore, there is some preliminary evidence that individuals may show a tendency to perceive more events as outwith their control after a severe TBI, and that this tendency may lead to poor quality of life outcomes. However, the factors mediating these beliefs and outcome have not been investigated in a single study, and therefore the role of symptoms of chronic fatigue in this process remains obscure.

Coping style

Two studies explored the relationship between preferred coping strategies and outcome after traumatic brain injury, with two looking specifically at the hypothesis that avoidant coping strategies would be more common in a TBI group and would be associated with poor psychosocial outcomes.

In their study of the coping hypothesis, Hinkeldey and Corrigan (1990) also looked at the coping strategies used by the TBI group to cope with their difficulties. They found that the TBI group reported significantly greater use of avoidance as a method of coping as compared with normative data from their coping measure. The TBI group also showed less use of logical analysis and information seeking to cope with problems. Later, Malia, Powell and Torode, (1995) demonstrated an association between the use of more emotion-focused and avoidant coping strategies, and poorer psychosocial outcomes in sample of traumatically brain injured individuals. However, these authors failed to control for potential confounding factors such as the location of the brain lesion in explaining both passive coping and poor quality of life outcomes.

Finset and Andersson (2000) therefore looked further at the association between coping strategies, lesion location and mood symptoms in a group of brain-injured individuals, including some who had experienced TBI. The results of this study indicated that coping styles were not related to lesion location, but that avoidant, behavioural dis-engaged coping in the patients group was associated with symptoms of depression. There was also evidence that the TBI group used significantly more 'behavioural disengagement' coping strategies than controls. This study therefore

demonstrates some support for the hypothesis that individuals who have sustained a TBI may make more regular use of avoidant behavioural coping strategies than controls, and that this is associated with symptoms of low mood and chronic stress such as fatigue.

Activity and exercise tolerance

No studies have explored the hypothesis that behavioural disengagement and avoidance should lead to generally lowered activity after TBI. However, results from two studies of exercise tolerance after TBI may provide some support for the suggestion that this group engage in less activity, and as a consequence experience deconditioning and therefore increased fatigue in daily functioning, which may in turn contribute to continuing appraisals of personal resources as depleted.

In a study examining physical endurance and mood in brain-injured patients, Walker, Cardenas, Guthrie, McLean and Brooke, (1991) found a significant correlation between depression, anxiety and fatigue scores in the brain-injured group, and a tendency for the BI group to show decreased isokinetic strength. The authors suggested that this decrease in strength may represent the effects of deconditioning, though the contribution of co-ordination impairments, spasticity or motor unit recruitment difficulties to these problems could not be ruled out using the study deign.

Jankowski and Sullivan (1990) also assessed muscular endurance and oxidative capacity in a TBI group before and after aerobic and neuromuscular training, and found subnormal oxidative capacities and above average oxygen costs of locomotion in the TBI group at baseline assessment. After 16 weeks of circuit training, the group showed increased oxidative capacity and abdominal muscular endurance, though the oxygen cost of walking was not reduced. These authors concluded that exercise training might reduce fatigability in patients, though factors moderating uptake of exercise programmes were not studied.

Conclusions

The results of this review suggest that fatigue is a common and highly persistent problem after severe TBI, which may be resistant to treatment using conventional rehabilitation approaches. This problem cannot be fully explained by the coping hypothesis, which would predict that fatigue should only be present when demands are placed upon on individual which they cannot cope with because of cognitive difficulties consequent on the injury. However, a modified model of psychosocial adjustment and coping after TBI which allows for cognitive belief processes in predicting the psychosocial consequences of TBI may offer a more successful framework for understanding fatigue. This review suggests that Kendall and Terry's multifactorial model of adjustment and coping (1996) has the potential to integrate research into a number factors which may apparently contribute to poor psychosocial functioning and fatigue, including changes in locus of control beliefs and adoption of dysfunctional coping styles. The application of this model to specific problems such as fatigue offers one means of testing the predictive utility of the model in relation to clinically significant problems, and of identifying potential means of intervening in fatigue in clinical settings by targeting factors described within the model.

As is apparent from the reviews above, previous research in the area of TBI has often failed to make use of theoretical principles in the design of studies. This has led to studies often ignoring potentially important confounding factors such as injury severity when looking at associations between variables or comparisons between groups. Future research therefore needs a stronger basis in theoretical principles if such mistakes are to be avoided. The well-researched stress literature provides one means of achieving this aim, and ensuring that future studies on fatigue can also contribute to our understanding of factors relevant in the treatment or management of this problem. An initial study using the model outlined by Kendall and Terry (1996), is therefore recommended, with a focus on assessing the association between separate elements identified in the review such as locus of control, coping and activity as possible contributors to fatigue, as each of these factors may potentially be amenable to intervention.

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Figure 1. Results table for review of prevalence of fatigue after severe traumatic brain injury in adults.

Author	Year	Study type	Quality rating	Population – severity * and age	Outcome measure	Time since injury	Prevalence	Comments
Oddy et al	1978 1980 1985	Prospective naturalistic follow-up	1-	Severe to very severe TBI (n=54) Limb injury clinical controls (n=35) Ages16-39	Semi-structured relative interview Symptom Checklist Katz Adjustment Scale Wakefield Depression Inventory	6 months 2 years 7 years	33% (self-report) 44% (relative report) 43% (relative report)	TBI group consecutive admissions series. Also limb fracture control group matched for age and socio-economic status. 80% of sample under 25 years of age, and also predominantly upper social classes so would expect better outcome in this group? Relatives interviewed to allow control for retrospectively reported pre-morbid factors. No relationship found between subjective symptoms, sex, social class or pursuit of compensation. Fatigue in 'most frequent triad of symptoms'. Controls more likely to be symptom free and reported fewer total symptoms. At 7 year follow-up 33/48 of original group were available for follow-up, and 28/48 relatives.
McKinlay et al Brooks et al	1981 1983 1986	Retrospective naturalistic follow-up	2+	Severe to extremely severe TBI (n=42) Ages 16-60 years	Structured relative interview	3months 6months 12 months 5 years	82% 69% 69% 62%	Very severely injured sample –78% in the extremely severe TBI range. Patients recruited from a specialist service, though demographic and injury information suggests they provide a typical TBI population. Second study also controlled for effects of compensation on patient and relative reporting of symptoms.

Thomsen	1984	Retrospective naturalistic follow-up	2-	Extremely severe TBI (n=40) Ages 15-44	Patient and relative questionnaires (when discrepancies in reporting, relative ratings only used)	2.5 years 10-15 years	28% 50%	Sample constituted an extremely severely injured population, with 27/40 having PTA>3 months. Also included participants from 15 years of age. Causes of injury disproportionately RTAs (37/40). Some received unspecified neuropsychological intervention in interim period. Statistically significant increase in reporting of tiredness over follow-ups, but as no control could be explained by ageing? No systematic exclusion of participants with premorbid psychiatric problems.
Brooks et al.	1987	Retrospective naturalistic follow-up	2-	Severe to extremely severe TBI (n=134) Ages 15-70	Structured relative and patient questionnaire based interviews	2-7 years (combined group)	70% (relative report) (43% patient report)	Very severely injured sample, majority PTA>2 weeks. Relatives ranged from first-degree relatives and spouses to remote relatives such as aunts and cousins, though all had daily personal contact with person. None of group had received formal rehabilitation, though some in contact with various out-patient therapy services so treatment as usual group. Combining varying times since injury may present a problem, given that previous studies suggest symptom reporting may decline with time, though no significant effects of time since injury noted here.
Schalen et al	1989 1994	Retrospective naturalistic follow-up	2-	Severe to extremely severe TBI (n=106) Ages 11-70	Comprehensive Psycho-pathological Rating Scale	5-8 years	36% (self-rating) 48% (relative rating)	CPRS has not been validated in TBI populations. Patients recruited at two different time points, and therefore may have been differences in care services they had access to. Also 64% patients had PTA > 2 weeks.

Dikmen et al.	1993	Prospective naturalistic follow-up	1-	Severe to extremely severe TBI (n-=31) Matched friend controls (n=88) Ages 18-30	Sickness Impact Profile (SIP) Head Injury Symptom Checklist (HISC) Function Status Index Structured Patient Interview (assessing wider functional outcomes)	1 month 1 year 2 years	62% 38% 25%	TBI patients significantly more likely to report new onset fatigue than controls, with it rated as the most severe symptom at 1 month, though with reporting of it as a problem decreasing over time. All measures were based on self-report, which given severity of injury may have been affected by cognitive deficits in insight. Also HISC and SIP not given to more severely neurologically impaired patients, so findings may underestimate extent of problem in severe head injury group. Fatigue items are reported as new since injury by comparing patient's reports of pre- vs. post-injury severity, though no checks for reliability of patient reporting of pre-injury functioning.
Olver et al	1995 1996	Retrospective longitudinal follow-up after rehabilitation	2-	Severe to extremely severe TBI (n=175) Mean age given, 27.4 years (sd=11.9)	Structured self-report questionnaire (n=254)	2 years 5 years	68% 73%	Participants victims of work or vehicle accidents only, and at 5 years attrition rate of >50%. Not all adults, lowest age 11 years. All subjects received specialist rehabilitation at one centre. No information available on pre-morbid psychiatric diagnoses. No validity or reliability information available for questionnaire measure.

Koskinen	1995 1998	Retrospective naturalistic follow-up	2+	Extremely severe TBI (n=15) Ages 12-39	Patient and relative questionnaires Clinical observer ratings Neurobehavioural Rating Scale Barthel Index Functional Assessment Scale Patient Competency Rating Scale	5 years 10 years	42% (self-report) 74% (relative report) 67% (self-report) 64% (relative report)	Participants consecutive series of admission to rehabilitation facility, exclusion criteria for previous BI or psychiatric disorder. Included 3 participants under age of 18 at time of injury. Detailed evaluation lasting approx. 4 hours. Fatigue ratings based on retrospective self-reports of changes since injury. Patient awareness of general functioning problems was assessed and it was found almost half had a degree of unawareness compared to relatives. Fatigue correlated highly with relative strain.
Hellawell et al.	1999	Prospective naturalistic follow-up	1-	Severe to extremely severe (n=53) TBI (moderate group also reported on but results will not be discussed for the purpose of this review) Ages 15-78	Cognitive battery Head Injury Symptom Checklist (HISC) Relative's Questionnaire Glasgow Outcome Scale Hospital Anxiety and Depression Scale	6 months 12 months 24 months	55% 60% 50% (self-ratings)	Criteria for inclusion allowed for all consecutive admission to a neurosurgical service to be included, therefore participants with alcohol, drug, psychiatric and mental health problems were all included. No direct check of reliability of fatigue reporting by patients, as no equivalent item in relative's questionnaire cited in results, though good overall correspondence between relative and patient reports of psychosocial symptoms noted when symptoms grouped. Also reporting of items in HISC showed no difference according to severity of injury, which authors cite as evidence that insight may not be limiting reporting in severe group, though moderate group could be expected to have fewer symptoms.

Thornhill et al.	2000	Prospective cohort study	1+	Severe TBI (n=73) Ages 14-98 years (mild and moderate groups also studied but results will not be discussed for the purpose of this review)	Glasgow Outcome Scale(GOS) Problem Orientated Questionnaire	1 year	64%	Assesses' tiredness' rather than fatigue. Use of GCS scores at admission to classify severity of injury. Advantage that as a prospective cohort study included all cases available for follow-up within a city and so may be less vulnerable to bias in reporting due to population sampling population bias. However, as no control group and a cross sectional design, cannot conclude fatigue symptoms due to the brain injury given that there may also be high baseline reporting of fatigue symptoms in the general population.

- Using Russell's (1971) definition of severity, PTA of between 1 and 7 days indicates a severe injury, PTA of greater than 7 days indicates a very severe injury, and PTA of greater than 4 weeks indicates an extremely severe injury.

Figure 2. Results table for review of research support for the coping hypothesis in adults after TBI.

Author	Year	Study type	Quality rating	Populations *	Outcome measures	Results	Comments
Van Zomeren et al.	1984	Controlled comparison of stress responses at rest and when undertaking a simple reaction time task in a healthy and CHI group	1-	Closed head injury group (n=11) Healthy age matched controls (n=11) (All male) Ages not given	Heart Rate Variability Mean Heart Beat Interval	CHI group had faster and less variable heart rate than controls under resting and test conditions. CHI group was significantly slower in the RT task than controls, though there were no significant group and task interaction effects on heart rate.	CHI group tested within two months of the end of PTA and so may still have been undergoing an acute adjustment reaction. Study also included some with milder brain injuries. Not a clinical control group, and matched on age only, and so pre-morbid factors such as psychiatric history and cognitive ability may also have contributed to any between group differences. There may also have been ceiling effects in heart rate of CHI group at baseline. Overall, no direct support for the coping hypothesis though results do support the view that the CHI group showed features of chronic stress. However, changes in heart rate may also represent the effect of problems with respiratory function resulting from CHI.

Hinkeldey and Corrigan	1990	Correlational study using confirmatory factor analysis techniques to look at support for the two factor coping hypothesis model of post-TBI symptoms	2-	Very to extremely severe TBI group (n=55) Mean age given, 27.6 years	Trauma complaints List Brief Symptom Inventory Katz Adjustment Scale – Relatives Glasgow Assessment Schedule Indices of Coping Category Test	Attempts to replicate the two-factor coping hypothesis structure were unsuccessful. Instead exploratory factor analysis revealed 3 factors; severity, general complaints and somatization. The second two groups of complaints may reflect the direct results of un measured injury factors, or the results of chronic stress as suggested by the coping hypothesis.	Small sample size. No formal objective assessment was made of information processing speed in the TBI group. Also no valid assessment of PTA. Great variability in time since injury within the group. Lack of controls and wide variability within participants in stage of recovery and severity of injury makes it difficult to assess which possible explanation for this structure of symptoms is most plausible. Also reliance on self-report measures to assess cognitive symptoms such as slowing means stress responses may have biased reporting of other cognitive complaints assumed to reflect severity.
Riese et al	1999	Comparison of fatigue in TBI and healthy control groups at two levels of workload in a driving simulator task	1+	Very to extremely severe TBI group (n=8) Mean ages given, 23.3 years (sd=6.4) Matched accident control group (n=8) Mean age given, 28.9 years, (sd=5.9)	Accuracy and RT score on driving task Rating Scale for Mental Effort Mean heart arte and heart rate variability Experienced Distress Questionnaires	CHI group slower RT than controls in training. When task demands adjusted to accommodate individual differences in accuracy and RT CHI group showed greater distress on subjective measures. CHI group also showed a tendency to increased systolic blood pressure from pre-post -task, whilst controls' systolic blood pressure decreased from pre- to post task.	Two groups matched on sex, age and educational level – though given very small numbers (8 in each group) this matching process may mean sample is unrepresentative of general population. By manipulating task load to accommodate individual abilities based on information from the training phase, design should be successful in excluding differences in performance ability in directly influencing mental effort and distress involved in completing the task.

* Using Russell's (1971) definition of severity, PTA of between 1 and 7 days indicates a severe injury, PTA of greater than 7 days indicates a very severe injury, and PTA of greater than 4 weeks indicates an extremely severe injury.

Figure 3.1. A diagrammatic representation of the major components of the Lazarus and Folkman (1984) theory of stress and adjustment. Taken from Kendall and Terry (1996).

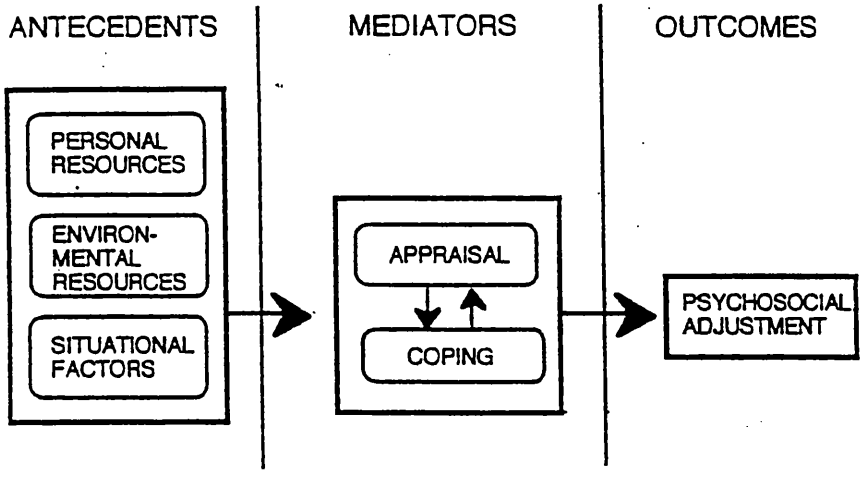
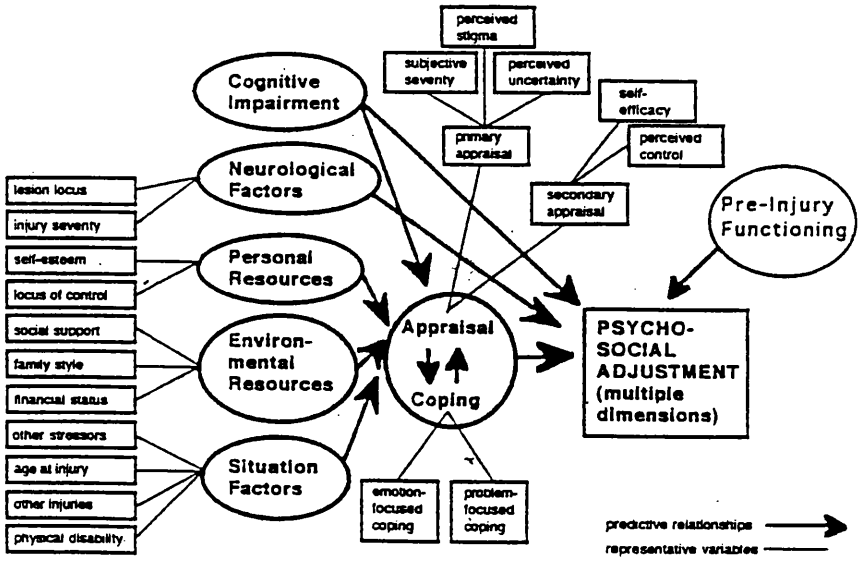


Figure 3.2. The specific model proposed for the prediction of psychosocial adjustment following CHI showing the anticipated relationships and representative variables (Kendall and Terry, (1996).



CHAPTER THREE

Proposal for Major Research Project

Investigation of a Multifactorial Model for the Maintenance of Fatigue After Severe Traumatic Brain Injury: Research Proposal

Submitted to Greater Glasgow Primary Care NHS Trust and Glasgow Royal Infirmary Research Ethics Committees (for letters of approval see Appendix 3.1).

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TITLE

Investigation of a multifactorial model for the maintenance of fatigue after severe traumatic brain injury

SUMMARY

Fatigue is a commonly reported symptom in the immediate aftermath of a traumatic brain injury. In one to two thirds of people who have sustained a moderate to severe brain injury such symptoms can persist for a number of years, and long after recovery in other areas is complete. Persisting fatigue can contribute to significant disability and distress, and may have a detrimental effect on an individual's ability to engage fully in any prescribed rehabilitation programme. However, to date fatigue as a chronic condition has not been widely studied in this population, and so it remains a widely acknowledged but often untreated complaint.

One theory of fatigue that has been the subject of some research interest is the coping hypothesis outlined by van Zomeren and colleagues. Unfortunately few attempts have been made to empirically validate this model, with the limited evidence available at present suggesting that a modified version of this hypothesis incorporating behavioural as well as cognitive elements is required. The aim of the present study is therefore to conduct a preliminary investigation of fatigue in individuals who have sustained a severe traumatic brain injury, using a multifactorial framework adapted from Kendall and Terry (1996) incorporating neuropsychological, cognitive, behavioural and physiological variables. The similarity of this group to medical outpatient and healthy controls will also be subject to investigation.

INTRODUCTION AND BACKGROUND

The prevalence of symptoms of fatigue at one year following a moderate to severe traumatic brain injury (TBI) has been estimated to range between 33 and 69 % (Oddy, Humphrey and Uttley, 1978; McKinlay, Brooks, Bond, Martinage and Marshall, 1983). As a chronic problem fatigue may contribute to significant disability and distress (Oddy, 1984) in the absence of the persistence of more specific impairments in executive functioning, information processing and physical ability (van Zomeren and Brouwer, 1994; Crepeau and Scherzer, 1993). It may therefore also be a strong independent predictor of an individual's capacity to benefit from rehabilitation and successfully return to work (Luria, 1963). However, in spite of the frequency with which this symptom is reported and the associated level of disability, few attempts have been made to explore the nature and correlates of fatigue in this population and no consensus exists on the most effective management strategy.

Early efforts to describe the emergence and maintenance of fatigue symptoms were hampered by attempts to divide causes into those of organic and so called "neurotic" origin according to the supposed presence or absence of persisting organic damage. However, van Zomeren and van de Burg (1985) in a study investigating the relationship between severity of traumatic brain injury and the prevalence of residual complaints of fatigue and other aspects of psychological distress, found no association between a measure of trauma severity (post-traumatic amnesia; PTA) and frequency of symptom reporting 2 years after injury. This gave some support to van Zomeren, Brouwer and Deelmans' (1984) suggestion that the emergence and maintenance of chronic symptoms such as fatigue after TBI may be best explained using a multifactorial model, encompassing cognitive and organic factors.

These researchers argued that individuals who have experienced a traumatic brain injury may experience a number of cognitive difficulties associated with acquired information processing and memory deficits. Such difficulties will in many cases mean that individuals are less able to deal efficiently with daily life demands and therefore will have to compensate for this by expending more effort. When this

compensatory effort becomes chronic it may result in secondary symptoms of chronic stress, including fatigue. It is therefore hypothesised that chronic symptoms such as fatigue may emerge as a result of an attempt by the individual to cope with their decreased cognitive resources. Under this hypothesis the severity of the brain injury is not the only influential factor in predicting fatigue, with cognitive and behavioural factors associated with how an individual appraises their ability to complete a task, and how they then attempt to cope with it also expected to be important in the maintenance of fatigue.

Some preliminary support for this model has been provided by Riese, Hoedemaker, Brouwer, Mulder, Cremer and Veldman (1999). They found significant differences in the reports of mental fatigue and subjective distress between a TBI and control group completing a driving simulation task. This difference existed even after performance demands were experimentally altered to accommodate individual differences in performance capacity. This finding was taken to support a modified version of the coping hypothesis which states that fatigue may persist in individuals with TBI as a chronic condition which is apparent in all tasks, even when no compensatory effort is required. This would imply that individual variables such as appraisal and coping style may be as important as task related variables in predicting fatigue.

One framework for describing the role of individual appraisal and coping styles in predicting psychosocial outcomes after TBI has been outlined by Kendall and Terry (1996). They modified Lazarus and Folkmans' (1984) model of stress and coping to develop a model of how neurological, cognitive and behavioural factors may interact to predict adjustment and psychosocial outcome after closed head injury. This model could be simplified to describe variables influencing the development and maintenance of fatigue after TBI, as outlined in figure 1. Such a model would provide a framework for the investigation of cognitive, behavioural and physiological variables in fatigue. However, to date this framework has not been the focus of any research on fatigue, and no experimental support for the application of this model to specific psychosocial outcomes exists.

AIMS AND HYPOTHESES

Aim

The aim of the present study is therefore to apply this multifactorial model to the problem of the maintenance of fatigue after severe traumatic brain injury, and to empirically assess the association between identified cognitive, behavioural and physiological variables and fatigue in a TBI population. These variables will also be assessed in trauma and healthy control groups, to allow between groups comparisons of fatigue and factors associated with fatigue.

Hypotheses

Using this model, it is predicted that the maintenance of fatigue after a severe TBI relies on individuals appraising themselves as having decreased skills and resources as a consequence of their brain injury, whilst also facing demands to cope with a number of stressful life events. The appraisal of personal resources as being depleted leads to daily events being perceived as outwith the individual's control, so attempts to cope with these demands are more likely to be emotion-focused than action-oriented. Such coping will often involve the use of avoidant strategies, which may lead to decreases in physical activity, resulting in physiological deconditioning and increased fatigue. This fatigue and decreased tolerance of exercise will then contribute to further appraisals of the individuals' personal resources as depleted, which may contribute to further avoidance and fatigue.

In order to empirically assess this model the following hypotheses are to be quantitatively tested:

Within the traumatic brain injury (TBI) group:

- Fatigue will correlate positively with self-report measures of external locus of control.
- Fatigue will correlate positively with self-reports of emotion-focused and avoidant coping.
- Fatigue will correlate negatively with objective measures of activity.

- Fatigue will correlate negatively with physiological measures of exercise tolerance.

Between the TBI group and controls:

- The TBI group will report more fatigue at the initial interview and on mean hourly ratings than other groups.
- The TBI group will be more likely to report a more external locus of control and the use of more emotion-focused coping strategies.
- The TBI group will engage in less activity and will have a lower tolerance of exercise than other groups.

PLAN OF INVESTIGATION

Participants

Participants will be aged between 16 and 64. They will be selected on the basis of having a severe traumatic brain injury, as defined by their reporting a period of PTA lasting for greater than 24 hours. TBI patients will be recruited from the Glasgow Headway service and the Central Scotland Brain Injury Rehabilitation Centre (CSBIRC), with inclusion subject to their having experienced a head injury within the last year. Individuals will be excluded at this point if initial screening reveals difficulties in language or memory skills that may impair their ability to rate fatigue over the study period. Those on psychotropic medications known to increase risk of fatigue will also be excluded, as will those still involved in active in-patient rehabilitation programmes that may involve the prescription of physical activity.

Controls will be recruited from 2 other groups. An outpatient trauma control group will be recruited from individuals attending as outpatients at the Soft Tissue Clinic, Glasgow Royal Infirmary, following their discharge from an accident and emergency inpatient ward. Inclusion in this group will also be subject to their having experienced their accident and injury within the last year. A healthy control group will be recruited from students at a local technical college and from health board employees and their friends and relatives.

Sample size

The use of conventional methods to estimate the numbers required in each group to achieve sufficient statistical power to detect significant effects was not possible, given the noted lack of any previous studies investigating activity in TBI groups and the use of actigraphs which provide a large number of related data points for each individual. The estimate of group size is therefore based on considerations of previous studies using actigraphs as a measure of activity in individuals with CFS (Verity, unpublished doctorate thesis) and sleep problems (Morin and Azrin, 1988; Espie, Lindsay, Brooks, Hood and Turvey, 1989; Guilleminault, Clerk, Black, Labanowski, Pelayo and Claman, 1995). Such studies detected statistically significant between group differences using groups ranging in size from 9 to15. Therefore it is aimed in the present study to recruit between 12 and 15 participants to each group.

Measures

The following measures will be taken;

1. Demographic and cognitive variables will be assessed at the initial interview. Cognitive ability will be described using the Speed and Capacity of Language Processing Test (SCOLP; Baddeley, Emslie and Smith, 1992) to estimate premorbid ability, the Adult Memory and Information Processing Battery (AMIPB; Coughlan and Hollows, 1985) to assess memory and information processing speed, the Trail Making Test (Reitan, 1958) to assess visuomotor functioning, a clock drawing task to assess constructional praxis and the Hayling and Brixton Tests (Burgess and Shallice, 1997) to assess executive functioning.
2. PTA will be assessed retrospectively in the TBI group, using the Post-Traumatic Amnesia Scale (McMillan, Jongen and Greenwood, 1996). This will be used as an estimate of brain injury severity. The Brain Injury Community Rehabilitation Outcome Scales (BICRO-39; Beckers, Powell and Greenwood, 1997) will also be administered to individuals in this group, and where possible to a carer or relative, to obtain an estimate of post-injury functioning in daily living activities.

3. Mood and anxiety symptoms will be measured at the first interview using the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983). All groups will also be asked to complete the Postconcussion Syndrome Checklist (PCSC; Gouvier, Cubic, Jones, Brantley and Cutlip, 1992) to assess the presence, frequency, intensity and duration of post-concussion symptoms.
4. The Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash and Steinberg, 1989) will be used at the first interview to assess the presence of clinically significant fatigue, and as an initial measure of fatigue severity.
5. Exercise tolerance will be assessed at the first interview by measuring the time taken for pulse recovery after completion of a simple 2-minute step test.
6. Use of emotion-focused, avoidant coping will be assessed at the first interview using the COPE (Weinman, Wright and Johnston, 1989).
7. Locus of control will be assessed at the first interview using the Health Multidimensional Locus of Control Scale (Wallston, Wallston and DeVellis, 1978).
8. A 48 hour objective measure of activity will be taken using an ambulatory monitoring device (wrist actigraph) to assess the frequency and intensity of activity. This device will also be used to alert people to make a simple 0-10 rating of fatigue at hourly intervals, following training from the researcher on what fatigue is and on how to rate it using this device.

Design and procedure

The study will make use of elements of within and between subjects design. Information on demographic and cognitive variables will be available to describe each group. For the purposes of this study, quantitative measures will be used to assess and describe fatigue, locus of control, coping style, activity and exercise tolerance in each group. The relationships between these variables within the TBI group will be examined, and the differences between groups on these variables will also be tested.

Settings and Equipment

The proposed initial assessment protocol is designed such that it may be administered at any day centre, hospital or college site. It is therefore proposed that the researcher will travel to see participants at these sites for the initial assessment on a Monday and will return after 2 days to collect actigraphs.

The equipment used will consist of questionnaires, neuropsychological tests, actigraph, portable step and pulse monitor.

Data analysis

Data for each participant will be kept in a secure storage area, before entry on a computerised database using coding to ensure confidentiality is maintained. Descriptive statistics will be used to present quantitative data on cognitive abilities, fatigue, locus of control, coping style, activity level and exercise tolerance for each group. The ITSACORR computer package (Crosbie, 1993) will be used to carry out interrupted time series analysis of actigraph data. The association between each individual variable and fatigue in the TBI group will be tested using Spearman's rank correlation coefficient. MANCOVA will be used to test between group differences on the key elements of the model, with age included as a covariate. ANOVAs and post-hoc Scheffe F-tests will then be used to locate any between group differences. Between group differences on any non-normally distributed data will be analysed using Kruskal-Wallis and post-hoc non-parametric tests.

PRACTICAL APPLICATIONS

Whilst fatigue has for many years been recognised to contribute to significant disability and distress in the years following severe traumatic brain injury, there remains little consensus on how best to manage this problem in clinical rehabilitation settings. A better understanding of the factors moderating and maintaining fatigue in this population could be used to suggest specific points for intervention using cognitive and behavioural therapies of established efficacy in other populations. This could then be used to provide the impetus for more

experimental research on the benefits of adding such interventions to existing rehabilitation packages.

TIMESCALES

April 2001 – Pilot use of actigraphs in non-clinical population and consult staff at Gartnaval Royal Hospital to assess feasibility of recruiting control groups.

May – July 2001 – Complete ethics applications.

July – September 2001 - Recruitment of TBI and outpatient controls. Data collection will begin during this period, with 1 day per week spent on this task.

September – December 2001 - Recruitment of healthy college controls and continuing data collection for all groups.

January – April 2002 - Data analysis.

ETHICAL APPROVAL

Permission will be sought from Greater Glasgow Primary Care NHS Trust ethics committee to conduct the study and recruit participants from Headway, CSBIRC, health board employees, relatives and local colleges. Ethical approval will also be sought from Glasgow Royal Infirmary's ethics committee for recruitment of outpatient controls.

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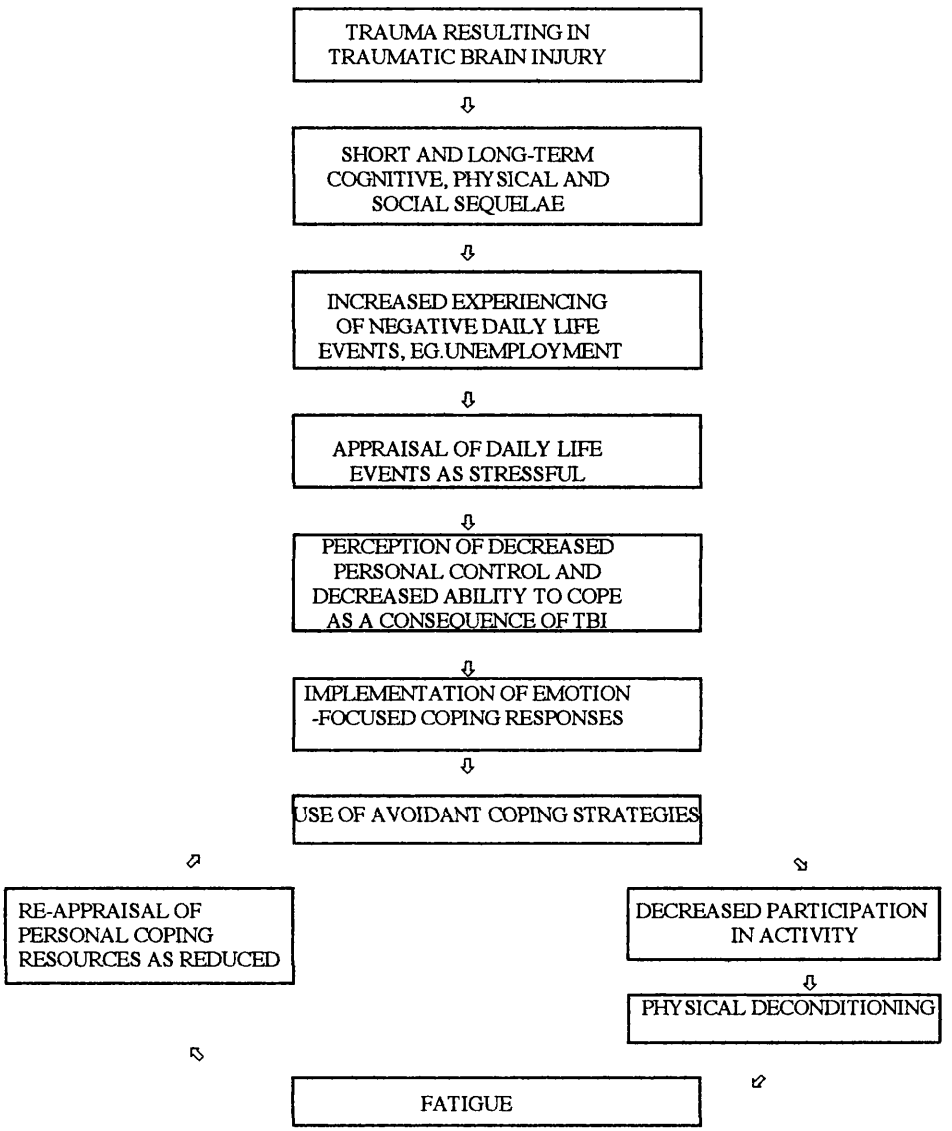
Figure 1. Model for the prediction of fatigue after traumatic brain injury, derived from Kendall and Terry (1996), adapted from Lazarus and Folkman (1984).



CHAPTER FOUR

Major Research Project Paper

Investigation of a Multifactorial Model for the Maintenance of Fatigue After Severe Traumatic Brain Injury

Prepared in accordance with the notes for contributors for the journal *'Brain Injury'* (see Appendix 2.1).

ABSTRACT

The present study made use of a multifactorial model based on Lazarus and Folkmans' (1984) model of coping, to investigate possible factors maintaining fatigue in a population who had suffered severe traumatic brain injury (TBI) more than 12 months previously. This involved investigating the association between fatigue, locus of control beliefs, coping styles and activity levels in 15 participants with severe to extremely severe brain injury. Comparisons with healthy controls were also used to control for the distribution of these variables in the general population, and in a group who had sustained a physical injury requiring hospitalisation but whose injury involved no neurological trauma. As predicted the TBI group reported greater fatigue than controls and had lowered cognitive ability and activity. Fatigue was found to be significantly negatively correlated with activity in the TBI group. Multivariate analysis did not however support the role of locus of control and coping in predicting group differences when fatigue was controlled for, with only anxiety and mood scores differentiating between groups on questionnaire measures.

INTRODUCTION

Fatigue has received much attention of late in the psychological and neurological literature, with the increasing recognition of chronic fatigue syndromes leading to a growing body of research focusing on the definition, assessment and treatment of this problem (Holmes, Kaplan, Gantz, Komaroff, Schonberger and Straus, 1988; Fukuda, Straus, Hickie, Sharp, Dobbins and Komaroff, 1994; Sharpe, Hawton, Simkin, Syraway, Hackmann and Klimes, 1996). Surprisingly, in spite of early descriptions of the high prevalence of fatigue and its highly disabling effects in the rehabilitation of individuals with traumatic brain injury (TBI) (Luria, 1963), research into this problem has been relatively scarce in this population. As a consequence little is known about how to assess fatigue after brain injury or what advice or help should be offered. This has led some authors to comment on the increasing frustration of professionals working with individuals who have sustained severe TBI (Wesseley and Edwards, 1997), who are repeatedly confronted by the effects of this disabling symptom but who are unable to refer to any evidence base to guide their management of the problem.

The scale of the problem of fatigue after TBI has been recognised for a number of years, with estimates of the prevalence of symptoms of fatigue at one year following a moderate to severe TBI ranging from 33 to 69 % (Oddy, Humphrey and Uttley, 1978; 1984; Oddy and Humphrey, 1980; Oddy, Coughlan, Tyerman and Jenkins, 1985; Oddy, 1993; McKinlay, Brooks, Bond, Martinage and Marshall, 1981; 1983; Thomsen, 1984; 1987; Brooks, Campsie, Symington, Beattie and McKinlay, 1986; 1987; Tate, Lulham and Brie, 1989; Schalen, Hansson, Nordstrom and Nordstrom, 1994; Olver, Ponsford and Curran, 1996). However, these studies have been criticised on the grounds that they relied on poor measures of fatigue; some studies relied on unstandardised interviews to assess the problem, and others estimated the scale of the problem on the basis of single item endorsements on rating scales of post-concussional symptoms (LaChapelle and Finlayson, 1998). Further investigations of fatigue may therefore have been hampered by a lack of clarity about the definition and measurement of the problem, with later etiological studies considering fatigue as a symptom of a wider post concussion syndrome.

An exception is the explanation offered by van Zomeren, Brouwer and Deelman (1984), who suggested that the emergence and maintenance of chronic symptoms such as fatigue after TBI, could be understood as an interaction between organic and psychological factors. They argued that cognitive deficits caused by brain injury (e.g. slowing in information processing and memory deficits) mean that individuals are less able to cope with daily life demands. Individuals are confronted daily with the need to compensate for these difficulties when carrying out everyday tasks and they have to expend greater effort to overcome disability caused by cognitive impairments. Over time this compensatory effort can result in secondary symptoms of chronic stress, including fatigue. It is therefore hypothesised that chronic symptoms such as fatigue may emerge as a result of an attempt by the individual to cope with their decreased cognitive resources. Under this coping hypothesis the severity of the brain injury is not the only influential factor in predicting fatigue. Cognitive and behavioural factors associated with appraisal of ability to complete a task and how to cope, are also expected to be important in the maintenance of fatigue.

Riese, Hoedemaker, Brouwer, Mulder, Cremer and Veldman, (1999) provided some preliminary support for this model. They found significant differences in the reports of mental fatigue and subjective distress between TBI individuals and controls completing a driving simulation task. This difference existed even after performance demands were experimentally altered to accommodate individual differences in performance capacity. This finding was taken to support a modified version of the coping hypothesis which states that fatigue may present in individuals with TBI as a chronic condition which is apparent in all tasks, even when no compensatory effort is required. This would imply that more stable individual variables such as appraisal and coping style may be as important as task related variables in predicting fatigue.

One framework for describing the role of individual appraisal and coping styles in predicting psychosocial outcomes after TBI has been outlined by Kendall and Terry (1996). They modified Lazarus and Folkmans' (1984) model of stress and coping to

develop a model of how neurological, cognitive and behavioural factors may interact to predict adjustment and psychosocial outcome after closed head injury. This model could be simplified to describe variables influencing the development and maintenance of fatigue after TBI, as outlined in figure 1. This model again relies on the assumption that individuals who have sustained a severe TBI will suffer more daily life stressors than their peers.

INSERT FIGURE 1 HERE

Lazarus and Folkman (1984) have argued that when individuals are confronted with life events that demand adjustment and coping, they initially appraise whether they can exert any control over the event, and this dictates the strategy they choose for coping. Kendall and Terry (1996) argue that life events caused by brain injury such as unemployment and relationship loss are more likely to be judged by individuals to be outwith their control, as they are perceived as being caused by irreversible effects of the injury. Individuals may therefore choose to save scarce coping resources by using avoidant strategies in preference to active problem-solving strategies. In practice, this avoidant coping may involve actual behavioural disengagement from activities perceived as being unachievable, leading the individual to engage in decreasing amounts of activity which may in turn lead to physical deconditioning. This avoidant behaviour would be expected to lead to fatigue as well as other symptoms of anxiety.

Support for a similar model of adjustment related difficulties in traumatic injury groups with spinal injuries has been provided (Buckelow, Baumstark, Frank and Hewett, 1990), though it has not been applied to a neurological population with cognitive difficulties. However, some preliminary support for the applicability of various elements of this model to brain injury populations is available, with evidence

that individuals who have sustained severe TBI may have a more external locus of control than healthy peers (Moore, Stambrook and Wilson, 1991; Lubusko, Moore, Stambrook, and Gill, 1994), make greater use of avoidant coping strategies (Hinkeldey and Corrigan, 1990; Malia, Powell and Torode, 1995; Finset and Andersson, 2000) and may engage in less activity resulting in physical deconditioning (Walker, Cardenas, Guthrie, McLean and Brooke, 1991). However, no single study has attempted to understand the possible inter-relationship between these factors, and their relevance to fatigue.

The present study therefore aims to assess the ability of this model to explain reporting of fatigue in individuals who have sustained severe traumatic brain injuries. This will involve using standardised measures of fatigue, cognitive impairment, locus of control, coping style and exercise tolerance in addition to an objective measure of activity, to investigate the possible relationships between these variables and fatigue in individuals who have sustained TBI. Comparisons will also be made with healthy controls and a trauma control group who have sustained non-neurological traumatic injuries. This group is included to control for non-specific effects of sustaining any injury requiring hospitalisation and a period of physical recovery on psychological adjustment and stress.

The following hypotheses are therefore to be tested:

1. The TBI group will exhibit greater levels of fatigue than controls.
2. The TBI group will show impaired cognitive abilities, particularly in information processing speed, relative to controls.
3. The TBI group will be less active than controls.
4. In line with the model, fatigue in the TBI group will be associated with lowered activity, i.e. the less active they are the more fatigued they will be. In contrast in controls fatigue will correlate positively with activity, i.e. the more active they are the more fatigued they will be.
5. The TBI group will show a more external locus of control and will make greater use of avoidant disengaged coping strategies, resulting in lowered exercise tolerance relative to controls.

METHOD

Participants

The experimental TBI group consisted of 15 individuals who had sustained a severe TBI, defined by post-traumatic amnesia (PTA) in excess of 24 hours, or a recorded Glasgow Coma Scale score of 3-8 on admission to hospital (Russell and Smith, 1962; Teasdale and Jennett, 1974; Jennett, 1983). Hospital notes were consulted for all individuals to confirm that these criteria were met, and a retrospective measure of PTA was also completed (McMillan, Jongen and Greenwood, 1996). Participants were recruited from attendance at community brain injury support groups, and from discharge records of a local hospital and brain injury rehabilitation centre. For inclusion, participants had to be aged between 18 and 65 years of age and have no history of pre-morbid psychiatric or psychological problems. Participants were excluded if they reported using psychotropic medication known to increase fatigue or if actively participating in any rehabilitation program.

Participants were 12 males and 3 females with TBI resulting from assaults (n=8), road traffic accidents (n=4), sports accidents (n=2) or work accidents (n=1). Average age was 40 (range 20-58; sd=10.98), and average time since injury was 43.9 months (range= 13 to 150 months; sd=41.4). Average duration of retrospectively measured PTA was 27.3 days (range=1.2-91 days; sd=27.9 days), average disability rating on the Brain Injury Community Rehabilitation Outcome Scales was 93.6 (sd=22.0). Average years of education was 11.3 (sd=1.91).

14 healthy control participants were recruited from attendees at a local technical college, and 14 trauma controls from accident and emergency discharge records at a local hospital were recruited. Within these groups, participants were excluded if they had a history of head injury or neurological disorder, or if on medications known to have fatigue as a possible side effect. Healthy controls were also excluded if they had any history of psychological or psychiatric problems.

The trauma control group were 6 males and 8 females, who had sustained bony fractures and soft tissue injuries resulting from sports accidents (n=4), work

accidents (n=4), assaults (n=2), falls (n=3), or road traffic accidents (n=1). They had a mean age of 40.2 (range=20-62; sd=14.95). Groups did not differ significantly in time since injury (U=71.5, p>0.05), though the trauma group tended to be more recently injured than the TBI group (mean time since injury of controls=26.1 months; range=4-72; sd=22.9). Average years education was 12.4 (sd=2.39).

Participants in the healthy control group consisted of 7 males and 7 females, with an average age of 23.8 (range=18-5; sd=9.2) and average years education of 13.4 years (sd=1.79).

There were no significant differences between groups in sex ($\chi 2=4.67$, df=2, p>0.05). There were significant differences in age between groups ($\chi 2=15.67$, df=2, p<0.001), with participants in the healthy control group being younger than the TBI (Z=16.21, p<0.05) and trauma control groups; (Z=16.0, p<0.05). There were also significant between group differences in education level ($\chi 2=9.21$, df=2, p=0.01), with participants in the healthy control group having a greater number of years education than the TBI group (Z=13.07, p<0.05).

Instrumentation

An AW2 model Actiwatch Score manufactured by Cambridge Neurotechnology Limited provided wrist actigraphy. This device was chosen due to small size (27 x 26 x 9mm) and light weight (16g) making it comfortable and unobtrusive to wear, and because it provided the means of alerting participants and allowing them to rate their fatigue each hour. The Actiwatch utilises an accelerometer to monitor the occurrence and degree of motion. A piezoelectric sensor integrates the degree and speed of motion to produce the activity counts that are recorded. Each Actiwatch was programmed with a calibration coefficient to normalise data between watches. The recording epoch length was set to 1.00 minutes, which allowed 48 hours of actigraphy to be recorded in addition to 26 hours of fatigue self-report ratings which were taken between 9am and 9pm. The 26 hours of activity recording covering the period where fatigue ratings were taken were selected for subsequent analysis. Participants wore the Actiwatch on their non-dominant wrist throughout the

recording period to ensure consistency. The watch was only removed when bathing or swimming to prevent damage by water.

Stored data, including the participant's personal code, start and stop time, sampling interval, actigraph accounts and fatigue scores, were downloaded onto an IBM compatible personal computer and analysed. Using the rhythmwatch/sleepwatch programme, a total activity score for each hour per participant could then be calculated. This was transferred directly onto a Windows Excel spreadsheet. The data was subsequently transferred from the Excel spreadsheet onto the statistics package – Statistics Package for the Social Sciences (SPSS) for analysis.

Measures

Before the 48-hour activity recording was started, participants completed a short neuropsychological battery for the purpose of describing group characteristics. This consisted of:

1. Speed and Capacity of Language Processing Test (SCOLP; Baddeley, Emslie and Smith, 1992). Used to assess premorbid ability and current language information processing speed in all groups.
2. Hayling and Brixton Tests (Burgess and Shallice, 1997). Used to assess response inhibition and rule guessing and shifting ability as a measure of executive functioning.
3. Adult Memory and Information Processing Battery (AMIPB; Coughlan and Hollows, 1985). List learning sub-test used to assess episodic verbal recall ability and the information processing test-part A used to assess processing speed for numeric material.
4. Trail Making Test (Reitan, 1958). Part A used to assess visuomotor functioning, Part B to assess flexibility in thinking.
5. Clock drawing task. Used to assess constructional praxis and visual neglect.
6. The Brain Injury Community Rehabilitation Outcome Scales (BICRO-39; Beckers, Powell and Greenwood, 1997). Completed by participants in the TBI group and where possible their carers to provide an estimate of current and premorbid disability.

Participants in all groups also completed questionnaires to assess key study variables:

1. The Fatigue Severity Scale (FSS; Krupp, LaRocca, Muir-Nash and Steinberg, 1989). A 9-item scale used to rate the presence and severity of fatigue and has been validated for use in a TBI population (LaChapelle and Finlayson, 2000).
2. COPE (Weinman, Wright and Johnston, 1989). Used to estimate preferences for one of 15 identified coping strategies, including active coping, behavioural and mental disengagement strategies.
3. Health Multidimensional Locus of Control Scale (HMLCS; Wallston, Wallston and DeVellis, 1978). Used to assess strength of beliefs about the control of powerful others, chance and self on health related outcomes.
4. Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983). Used to assess the presence of other symptoms of stress or anxiety and mood, chosen for its limited interference from physical illnesses.
5. Exercise tolerance was also assessed in all groups by measuring the time taken for pulse rate to recover after a two-minute step test. A pulse oximeter was used for this purpose.

Procedure

Suitable candidates for the TBI group were identified from discharge records at local hospital and rehabilitation facilities, and from attendees at local voluntary groups, and contacted by letter to ask if they would be interested in participating. Out-patients in the trauma control group were also identified from local hospital records and contacted initially by post. Healthy controls were recruited from a local technical college. Participants first completed the neuropsychological screening tests and questionnaire measures. They were then given further information and training on using the Actiwatch. The Actiwatch was programmed to start recording from 9pm that night, with all recording taking place during weekdays only. They were then instructed to wear the watch for 48 hours and to return the watch to the hospital or centre where they had been recruited (for details of adaptations made to protocol for TBI recruits, see Appendix 2).

Statistical Analysis

Statistical analysis was carried out using SPSS for Windows (version 9.0). All tests were performed one-tailed at the 5% level of significance.

The Actiwatch data were aggregated by subject to the level required for each analysis, and adjustments made for periods when the watch was removed for bathing or swimming. Hourly totals were used for assessments of association between activity level and hourly rated fatigue, with a single mean activity level calculated and used for tests of group differences. Correlations were calculated between using Spearman's rank rho correlations. As hourly data was expected to be highly related, interrupted time-series analysis (ITSACORR; Crosbie, 1993) was used to assess between group differences in activity.

Normality of variables was assessed using Kolmogorov-Smirnov analysis. As might be expected scores on tests of cognitive ability and self-ratings of fatigue using the Actiwatch were not normally distributed and so non-parametric statistics were used to analyse this data. Similarly due to problems with missing data as a number of participants were unable or unwilling to complete a step-test (completed by 12 of the TBI group, 6 of the trauma group and 5 of the healthy control group), this data was not normally distributed and so non parametric tests were used for comparisons on this measure (Siegel and Castellan, 1988). The remaining questionnaire data and actiwatch activity data was however normally distributed, with the exception of the HADS-depression subscale, COPE-disengagement sub-scales and HMLCS-chance subscale. A logarithmic transformation of COPE-mental disengagement sub-scale scores and square root transformations of HADS-depression, HMLCS-chance and COPE-behavioural disengagement sub-scale scores were therefore undertaken prior to analysis to achieve normal distribution (Tabachnick and Fidell, 1996). MANCOVA was then used to allow analysis of the original model with fatigue and age as covariates, using Pillai's trace as the test statistic. Post-hoc univariate analyses using ANOVA and Scheffe F tests were used to locate sources of any between group differences.

RESULTS

Fatigue levels between groups

As predicted the TBI group and controls differed significantly on self-reported levels of fatigue as measured using the Fatigue Severity Scale (see Figure 3.1 for mean scores)($F=13.00$, $df=2$, $p<0.001$). Post hoc testing revealed fatigue was significantly greater in TBI individuals as compared to healthy controls ($Z=20.95$, $p<0.001$), and as compared to trauma controls ($Z=17.64$, $p=0.001$), with no significant differences between healthy and trauma control groups ($Z=3.31$, $p>0.05$). Comparisons of mean hourly fatigue ratings revealed a trend for TBI individuals to rate greater fatigue on an hourly basis, though this was not statistically significant ($\chi 2=4.44$, $df=2$, $p>0.05$). The subjective hourly ratings of fatigue did however correlate highly with fatigue as measured using the standardised fatigue measure ($r=.804$, $p<0.001$), supporting the use of the hourly ratings for investigating the relationship between activity and fatigue on an hour by hour basis.

INSERT FIGURE 3.1 HERE

Group differences in cognitive abilities

As expected the TBI group showed impaired performance relative to controls on tests of information processing speed, episodic verbal recall, executive functioning and visuospatial functioning, with scoring illustrated in figure 3.2. In all cases post hoc testing revealed that between group differences were attributable to significantly poorer performance by the TBI group relative to healthy and trauma controls. As expected no significant between group differences in premorbid cognitive ability as assessed using the 'Spot the Word' test were found ($\chi 2=1.78$, $df=2$, $p>0.05$).

INSERT FIGURE 3.2 HERE

Activity levels between groups

To maximise the quality of the data, mean hourly activity levels for each group were calculated for each daytime hour of the study period, with mean results across the two used to give a mean activity score per group for each hour between 9am and 9pm. Figure 3.3 illustrates group differences in activity over an averaged day. As data were judged to be related, time series analysis using the ITSACORR package (Crosbie, 1993) was used to assess any between group differences. As predicted significant overall differences were found between TBI and healthy control groups ($F(2,21)=5.61$, $p<0.05$; slope $t(21)=1.48$, $p=0.15$; intercept, $t(21)=0.61$, $p=0.35$), and TBI and trauma controls ($F(2,21)=7.87$, $p<0.01$; slope, $t(21)=1.77$, $p=0.09$; intercept, $t(21)=1.20$, $p=0.25$). Significant differences were also found between trauma and healthy controls on activity ($F(2,21)=5.48$, $p<.05$; slope, $t(21)=0.37$, $p=0.71$; intercept, $t(21)=0.29$, $p=0.78$).

No significant group differences were detected in the physical step test ($\chi 2=4.61$, $df=2$, $p>0.05$).

Association between fatigue and activity

To maximise the quality of the data, hourly aggregates of activity were compared with hourly rated fatigue in each group, using Spearman's rank correlations. As predicted, intercorrelations between hourly activity and fatigue were negative (i.e. the less active the individual the more fatigued they were) and highly significant in the TBI group ($r=-0.383$, $p<0.001$). Tests of association between activity and fatigue in controls revealed smaller, though still statistically significant, correlations. In the trauma control group a significant positive correlation was found between hourly

activity ratings and hourly fatigue scores (r=-0.144, p=0.008). However in the healthy control group a significant negative correlation was found between activity and hourly fatigue rating (r=-0.155, p=0.005).

INSERT FIGURE 3.3 HERE

Testing the model: relationship between locus of control beliefs, coping strategy, activity levels and fatigue

As illustrated in figure 3.4, inspection of mean scores on the above variables reveals a tendency for the TBI group to have a higher belief in the control of powerful others such as heath professionals and family over their recovery, and to report greater use of coping strategies emphasising behavioural disengagement, resulting in lower levels of activity. To analyse the differences between groups on the variables targeted by the model, a MANCOVA was carried out, with group taken as the factor in the analysis and locus of control beliefs, coping style and activity level taken as dependent variables. Mood and anxiety were also included as dependent variables given their potential to contribute to fatigue independently of the hypothesised model. As fatigue and activity were significantly correlated, fatigue was included in the present analysis as a covariate to detect whether any group difference in dependent variables persisted once the potential influence of fatigue on causing change in the dependent variables had been removed. Given the significant age differences between groups and the potential effects of age on fatigue and activity level, age was also included as covariate in this analysis.

Results of the MANCOVA revealed significant between group differences (F=2.25, df=18, p=0.011). Post-hoc ANOVAs based on the corrected model found no significant between group differences in locus of control, preferred coping strategies or mean activity level (F<2.7, NS). However, significant differences in anxiety

(F=7.33, df=40, p<0.001) and depression (F=11.18, df=40, p<0.001) were found after the effects of age and fatigue were removed. Scheffe F tests revealed that differences were due to reporting of greater anxiety in the TBI group compared to trauma controls (F=3.60, p=0.033). There was a tendency for the TBI group to also report higher levels of depression than the trauma group, though in post hoc testing this difference did not reach statistically significant levels (F=0.6807, p=0.073).

DISCUSSION

Fatigue after TBI

Fatigue levels were significantly higher in individuals with a TBI than those with non-neurological injuries or healthy controls, and this is consistent with the literature (Oddy et al., 1978; 1980; 1985; McKinlay et al., 1981; 1983; Thomsen, 1984; 1987; Brooks et al., 1986; 1987; Tate et al., 1989; Schalen et al., 1994; Olver et al., 1996). Further evidence was also provided that the Fatigue Severity Scale was capable of detecting differences between a TBI group and 2 other groups (LaChapelle and Finlayson, 1998).

Cognitive change after TBI

Again consistent with the study hypotheses and previous research, individuals in the TBI group showed poorer performance on a range of measures of cognitive ability than controls. This would support the suggestion that individuals who have sustained a brain injury may be more likely to experience a number of daily tasks or demands as being outwith their capabilities with long-term deficits in information-processing, memory and executive functions expected to contribute to a history of this group being confronted with more daily stressors requiring compensatory effort than other groups.

Activity levels between groups

It was hypothesised that experience of cognitive difficulties leading to regular insurmountable daily problems would lead to the TBI group having a more external locus of control, resulting in use of disengaged coping styles and reduced daily levels of activity. This hypothesis was again supported, with individuals in the TBI

group engaging in significantly less activity on an hour by hour basis than healthy and trauma controls. The additional significant differences between trauma and healthy controls on inspection of hourly activity data may also support the view that some inactivity may be accounted for the necessity for rest and physical recovery after any serious injury. Significant differences between TBI and trauma groups may therefore represent the additive effects of cognitive difficulty, as predicted by Kendall and Terry's model, in biasing appraisals of controllability of problems and subsequent coping behaviours.

Decreased activity in the TBI group, if representative of a typical daily routine, would be expected to coincide with deconditioning relative to controls. This hypothesis was not supported, with no significant between group differences in exercise tolerance. This result could be taken to suggest that the reduced activity observed in the TBI group was due to a time sampling problem, with the TBI group engaging in less activity during the study period than they would typically. However, a more likely explanation may be that the test used was not sufficiently sensitive to detect differences in exercise tolerance, particularly when no information on premorbid fitness was available. Future studies may therefore benefit from the use of alternative methods already validated for use in TBI groups to assess aerobic fitness, such as measurement of peak oxygen consumption (VO2peak) during exercise (Coyle and Santiago, 1995).

Association between fatigue and activity

In line with the study hypothesis that the TBI group would show lower levels of activity than controls and that this would be associated with a greater fatigue, a strong negative association was found between objective hourly activity and subjective hourly fatigue in the TBI group, i.e. low activity over a one-hour period was observed to lead to high ratings of fatigue at the end of the hour. However, in contrast to the original study predictions a similar pattern was found for healthy controls. This association was however much weaker, though still statistically significant. In line with the study hypotheses activity and fatigue were positively correlated in the trauma group, with greater activity leading to greater fatigue. This

could be considered a more normal relationship between activity and fatigue, with the opposite association within the healthy control group possibly representing the confounding effects of sampling bias. For instance the healthy control group were on average younger than the accident and TBI groups, and so for them reasonable levels of activity would not be excepted to lead to significant levels of fatigue as they would be expected to a reasonably fit and active population. In contrast the accident group were an older population, and so may be more likely to fatigued by similar levels of exercise, leading to a positive correlation between activity and fatigue in this group.

Predictors of fatigue: exploring the model

Kendall and Terry's (1996) model would suggest that the greater levels of fatigue and lower levels of activity observed in the TBI group could be predicted by cognitive and behavioural variables associated with locus of control and coping style. A trend was observed for the TBI group to report stronger beliefs that powerful others such as health professionals controlled their recovery. This provides some additional support for the role of beliefs in predicting outcome after TBI, in line with the findings of Lubusko et al. (1994) who found higher beliefs in the influence of powerful others in individuals with TBI who failed to return to employment.

No significant group differences in the use of active coping strategies were found, though in line with predictions there was a tendency for the TBI group to make greater use of coping strategies based on behavioural disengagement than trauma controls. This again is in line with previous findings of greater use of avoidant coping strategies in individuals with TBI, particularly in those showing persisting symptoms of emotional distress (Malia et al.,1995; Finset and Andersson, 2000). This group difference may stress the importance of the type of injury in predicting coping, with individuals who have sustained non-neurological injuries which can be recovered from, and which do not tend to impair internal cognitive resources, being less likely to cope by avoiding problems. This finding therefore provides some tentative support for the role of individuals' appraisals of ability in predicting locus

of control beliefs and subsequent strategies for coping. However, as neither locus of control beliefs or coping strategies were found to differ statistically significantly these elements of the model require further support before they can be made use of in clinical settings.

As this study made use of correlation statistics to explore the relationship between fatigue and activity, it is also possible that differences in study variables emphasising cognitions and behaviours could be attributable to, rather than caused by, fatigue. Multivariate analysis with fatigue used as a covariate provided some evidence that this was the case, with no significant group differences in any study variable found when fatigue and age was controlled for. Instead, only anxiety and depression levels could account for group differences. This finding warrants further exploration in future studies, given the potential for management of these types of problem using existing psychological and pharmacological interventions. Given that no longitudinal data were available, it is not known whether such problems could have caused fatigue and lowered activity in the TBI group, or whether perhaps lowered activity and fatigue in the early days after injury may have caused adjustment related stress and mood problems which at the time of this study were maintaining fatigue problems. Similar observations have been made in the case of chronic fatigue syndrome (CFS) where high co-morbidity with mood disorders has been observed with such problems in some cases appearing to play a role in maintenance (Ray, 1991; Kendall, 1991; Lewis, Cooper and Bennett, 1994). Therefore future studies may be advised to make use of the growing literature on management of fatigue in CFS to guide hypothesis testing in individual management of fatigue after brain injury.

Comment on the study

This investigation has attempted to investigate the applicability of a theoretically derived model to the problem of fatigue, whilst also overcoming some limitations of previous attempts to investigate fatigue. The use of actigraphy data for the first time in a TBI population has allowed a detailed analysis of the relationship between hourly activity and fatigue to be made. The use of this method of assessment is

therefore recommended for future studies. Care was also taken to use only questionnaire measures already validated for TBI populations. The exception was the step-test which may have been insufficiently sensitive. Attempts were also made to control adequately for the effects of having received non-neurological injuries to control for the effects of any injury requiring hospitalisation and a period of physical recovery on causing fatigue. However, as mentioned above, some difficulties in recruitment of age matched healthy controls may have led to come erroneous conclusions being drawn about the association between fatigue and activity in healthy groups, which further research projects should attempt to rectify by using where possible age and education matched groups.

CONCLUSIONS AND IMPLICATIONS

Fatigue was found in this study to be a significant problem for a group who had suffered a severe TBI, and this was significantly associated with lowered activity. This was in conjunction with a tendency for the TBI group to report a more external locus of control and more disengaged coping. However, in covariate analysis, when the potential effect of fatigue in causing changes in these variables and activity were removed, only scoring on anxiety and depression measures could differentiate between groups.

This suggests that lowered activity and fatigue may, after 1 year from injury, be maintained by mood and anxiety problems. This would suggest that management should focus on the use of pharmacological or psychological techniques known to be beneficial in reducing these symptoms (for review of treatment methods see Rosenthal, Christensen and Ross, 1998), rather than trying to directly target changes in control beliefs or coping styles using cognitive behavioural techniques. Given the significant associations between lowered activity and fatigue in the TBI group it may also be beneficial to explore further the use of exercise training to reduce fatigability in TBI groups, as there is some preliminary evidence that this may be an efficacious treatment for fatigability (Jankowski and Sullivan, 1990) and depression (Gordon, Sliwinski, Echo, McLoughlin, Sheerer and Meili, 1998). Studies replicating these results as well as treatment studies based on the above recommendations are now

required to begin to allow clinicians to tackle the 'silent saboteur' of fatigue in rehabilitation (Luria, 1963).

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Figure 1. Model for the prediction of fatigue after traumatic brain injury, derived from Kendall and Terry (1996), adapted from Lazarus and Folkman (1984).

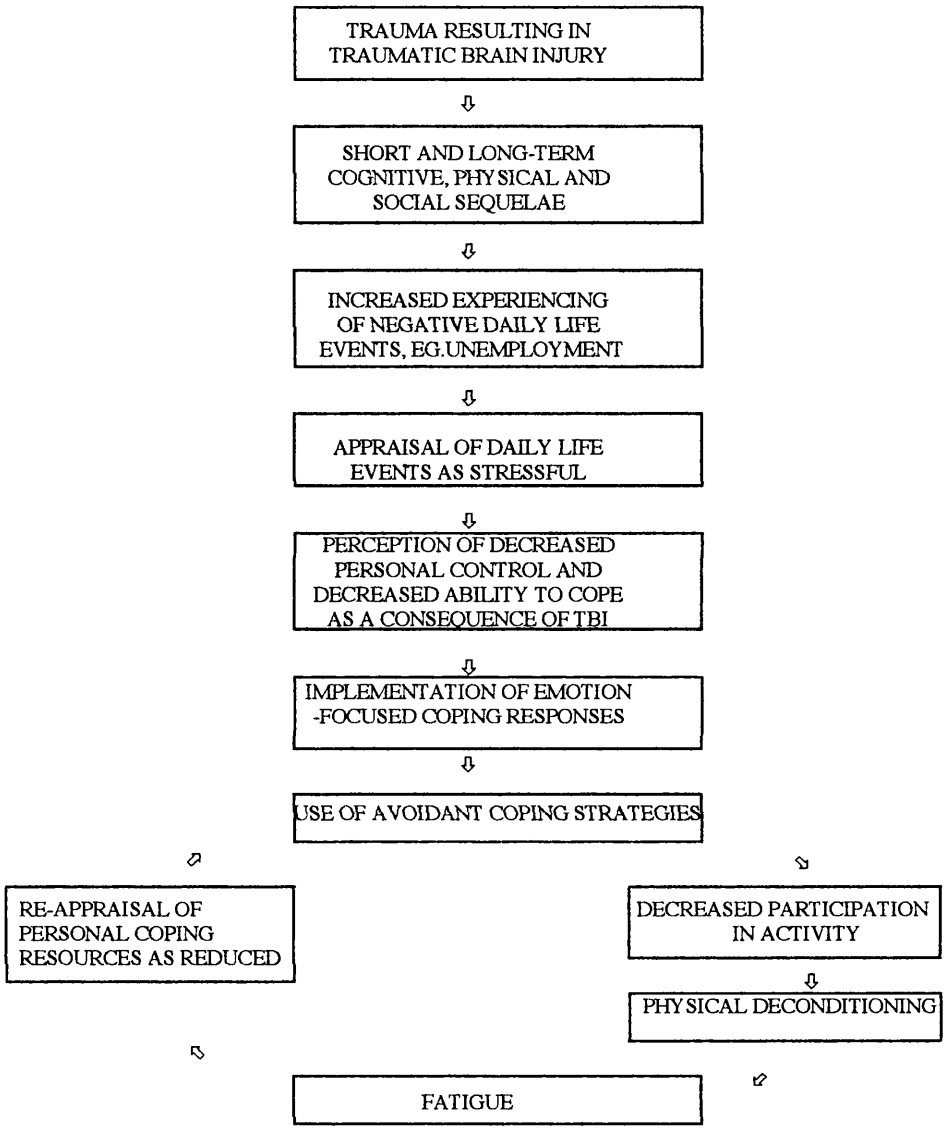


Figure 3.1. Mean Fatigue Severity Scale Scores for TBI, trauma and healthy control groups.

Measure	TBI group (sd) (n=15)	Trauma controls (sd) (n=14)	Healthy Controls (sd) (n=14)
Fatigue Severity Scale	45.33 (13.54)*	27.69 (8.24)	24.38 (12.58)
Actiwatch mean hourly fatigue ratings	4.16 (2.27)	2.51 (1.16)	2.87 (1.57)

*<.01

Figure 3.2. Mean group scores on tests of cognitive ability.

Measure	TBI group (n=15)	Trauma control group (n=14)	Healthy Control Group (n=14)	Between Group Differences ($\chi 2$) [df=2]
Spot the word	45.07 (7.95)	49.33 (4.40)	47.14 (4.50)	1.78
Speed of comprehension	39.60 (18.33)	70.14 (19.07)	67.36 (15.35)	16.53***
AMIPB-Information Processing	55.93 (23.33)	85.21 (23.88)	83.59 (14.78)	11.57**
AMIPB-List Learning Task	33.20 (13.20)	50.43 (12.43)	56.77 (5.59)	19.15***
Hayling Sentence Completion Task	12.80 (4.74)	17.50 (3.52)	17.00 (4.32)	10.71*
Brixton Rule Shift Task (errors)	22.53 (6.69)	13.21 (4.48)	14.08 (8.83)	16.53***
Trail-Making Test-Part A	56.47 (22.91)	29.50 (9.22)	28.29 (6.24)	15.71***
Trail-Making Task-Part B	138.80 (77.80)	64.93 (31.03)	59.79 (15.80)	18.36***
Clock-drawing Task	9.20 (1.08)	9.86 (0.36)	9.64 (0.93)	3.85

*<.01

**<.005

***<.001

Figure 3.3. Average hourly activity levels for each group per daytime hour.

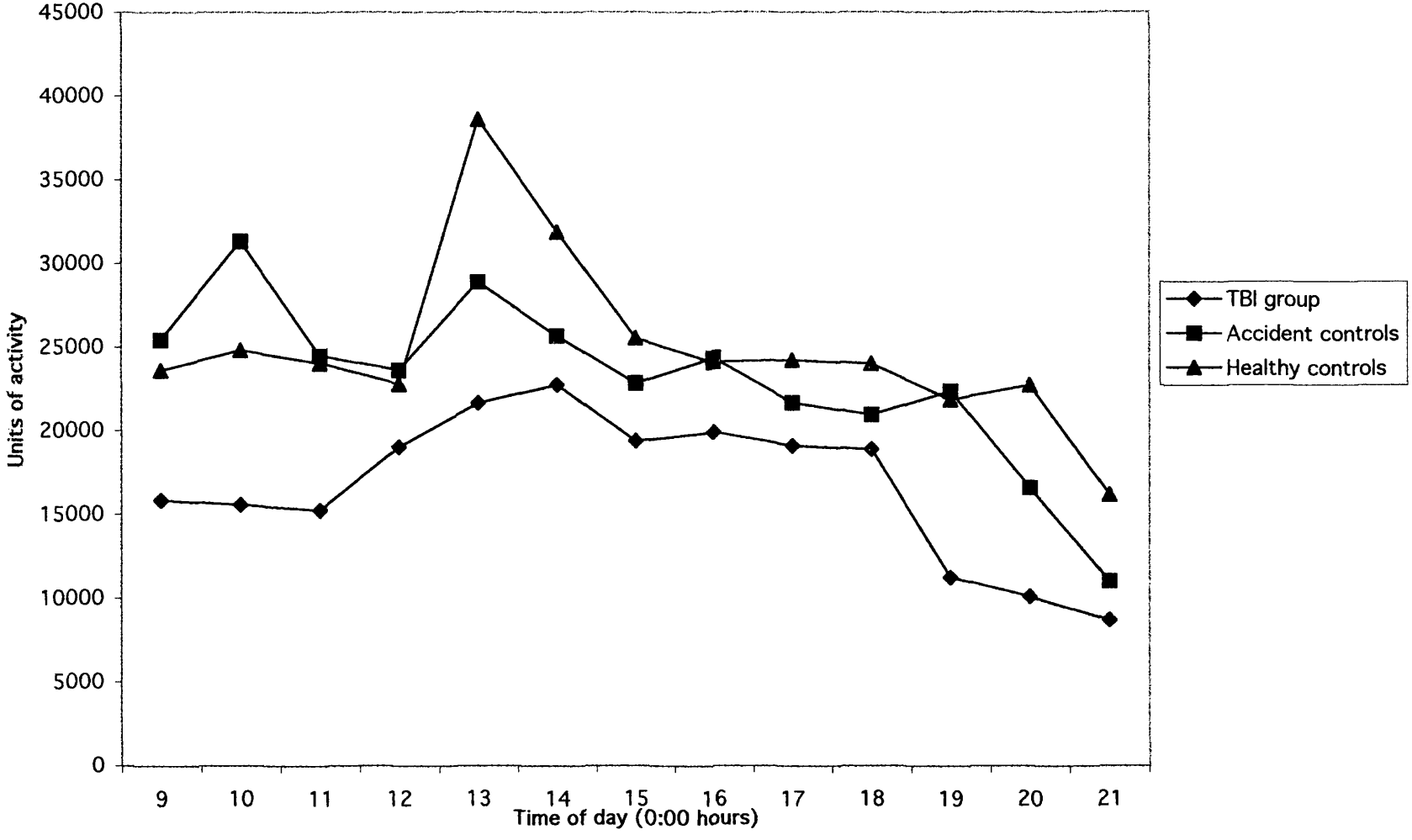


Figure 3.4. Mean scores (sd) on locus of control, coping and mood measures for TBI, trauma, and healthy control groups.

Measure	TBI group (sd) (n=15)	Trauma control group (sd) (n=14)	Healthy control group (sd) (n=14)
HADS-Anxiety	8.79 (4.25)	5.00 (2.04)	5.46 (3.76)
HADS-Depression	4.21 (3.02)	1.85 (1.57)	3.31 (2.29)
HMLCS-Internal	24.29 (6.74)	26.38 (4.54)	22.85 (5.51)
HMLCS-Powerful Others	20.50 (6.68)	17.38 (7.69)	14.00 (3.56)
HMLCS-Chance	18.50 (5.30)	21.08 (3.80)	18.08 (5.99)
COPE-Active coping	9.64 (3.86)	10.15 (3.60)	10.08 (2.50)
COPE-Mental disengagement	9.79 (2.78)	7.54 (2.44)	8.15 (2.19)
COPE-Behavioural Disengagement	8.21 (3.85)	5.08 (1.38)	6.38 (2.43)
Mean activity level	17326 (8972)	23568 (11640)	23830 (8961)
Physical fitness test	71.08 (32.55)	81.75 (14.31)	143.33 (82.42)

CHAPTER FIVE

Clinical Case Research Study

Challenging Behaviour in Minimal Responsiveness: A single case experimental investigation of the efficacy of behavioural treatment for anxiety in reducing aggression and increasing participation in rehabilitation of a minimally responsive female

Prepared in accordance with the notes for contributors for the journal *'Brain Injury'* (see Appendix 2.1).

Abstract

A within-series reversal design with a follow-up session to assess maintenance (A1B1A2B2C1) was used to evaluate the beneficial effects of a distraction task to reduce anxiety and challenging behaviour of a 40-year-old woman who had suffered an extremely severe non-traumatic brain injury. The target behaviour was identified as repetitive verbal complaints or swearing which appeared to serve the function of facilitating the termination of events which the participant found stressful. Interventions therefore focused on manipulating PB's environment using music and modelling of relaxed postures to reduce anxiety to allow her to participate in sessions. Interrupted time series analysis was conducted, revealing significant effects of treatment in decreasing the frequency of repetitive utterances. Following one week of using the same intervention to begin all similar therapeutic sessions, a significant reduction in utterances in a follow-up session was also found, showing that use of this technique also allowed PB sufficient exposure to therapeutic tasks to habituate to the anxiety they provoked. It is concluded that interventions based on classical and operant conditioning principles can therefore be effectively used to manage challenging behaviours in adults with minimal levels of responsiveness. The results are discussed with reference to the clinical implications of findings, for ensuring that individuals with more severe brain injuries and behaviour problems are not excluded from rehabilitation programmes and subsequent reintegration into community settings.

APPENDICES

APPENDIX 1.1

BPS Guidelines for Small Scale Research

1.1 Title

1.2 An introduction to the problem, with reference to relevant literature (a comprehensive review is not required/ and clear statement of specific questions being addressed.

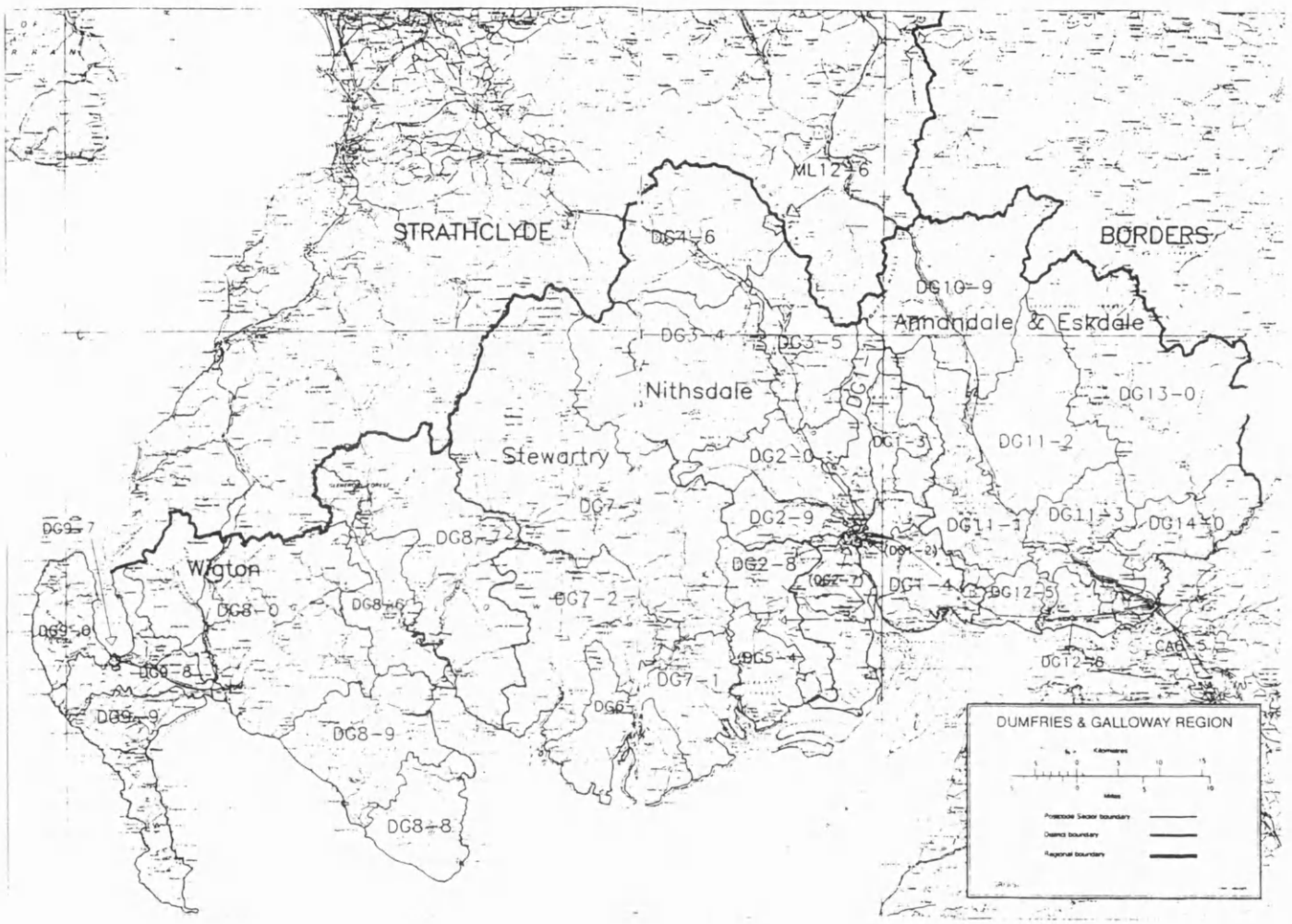
1.3 An account of the sample and methods used in the study and of the practical work undertaken.

1.4 A clear presentation of the results of the study. The emphasis in the Small Scale Research Project is to be placed on the clear presentation of findings rather than on the demonstration of statistical expertise.

1.5 A discussion of the research findings in the context of the specific problem addressed, together with recommendations for service provision and future research.

APPENDIX 1.2

Map of the Dumfries and Galloway region, illustrating the 4 referral areas targeted by memory clinics



APPENDIX 1.3

Aims of the memory service

1 To provide accessible locality based clinics for the assessment and early diagnosis of dementia.
2 To detect preventable early dementia and other conditions masquerading as dementia and either provide treatment, or direct patients towards more appropriate health provision.
3 To ensure the clinics provide evidence based rational investigations and develop a clear management strategy for patients with early dementia.
4 To provide continuity from assessment to ongoing community care for dementia patients and for their carers through close liaison with Community Mental Health Teams.
5 To promote awareness and acceptability of dementia within the local population.
6 To provide the opportunity for early support for patients with dementia and their carers from the time of diagnosis.
7 To prospectively audit the development of the service so that good practice can be assessed and appropriate changes for improvement accordingly made.

APPENDIX 2.1

Guidelines for contributors for the journal *Brain Injury*

General Guidelines
This journal covers all aspects of brain injury from basic science, neurological techniques and outcomes to vocational aspects, with studies of rehabilitation and outcome of both patients and their families. It addresses both adult and paediatric issues and it embraces issues such as family and peer relationships, effects of alcohol and drugs, communication problems and management techniques and creating new programmes. **Brain Injury** uses case studies to illustrate different approaches to a subject, and provides a forum for the appraisal of theories which may influence future research. **Brain Injury** is the official research journal of the *International Brain Injury Association*.

Submitting a paper to Brain Injury
Please read these Guidelines with care and attention: failure to follow them may result in your paper being delayed.

Brain Injury considers all manuscripts on condition they are the property (copyright) of the submitting author(s) and that copyright will be transferred to the journal **Brain Injury** and Taylor & Francis Ltd, if the paper is accepted.

Brain Injury considers all manuscripts on the strict condition that they have been submitted only to **Brain Injury** , that they have not been published already, nor are they under consideration for publication, nor in press elsewhere. Authors who fail to adhere to this condition will be charged all costs which **Brain Injury** incurs, and their papers will not be published.

Abstracts
Structured abstracts are required for all papers, and should be submitted as detailed below, following the title and author's name and address, preceding the main text.

For papers reporting original research, state the **primary objective** and any hypothesis tested; describe the **research design** and your reasons for adopting that methodology; state the **methods and procedures** employed, including where appropriate tools, hardware, software, the selection and number of study areas/subjects, and the central **experimental interventions**; state the **main outcomes and results**, including relevant data; and state the **conclusions** that might be drawn from these data and results, including their implications for further research or application/practice.

For review essays, state the **primary objective** of the review; the reasoning behind your literature selection; and the way you critically analyse the literature; state the **main outcomes and results** of your review; and state the **conclusions** that might be drawn, including their implications for further research or application/practice.

The abstract should not exceed 150 words.

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Code of experimental ethics and practice
Contributors are required to follow the procedures in force in their countries which govern the ethics of work done with human or animal subjects. The Code of Ethics of the World Medical Association (Declaration of Helsinki) represents a minimal requirement.

Notes on style
All authors are asked to take account of the diverse audience of **Brain Injury** . Clearly explain or avoid the use of terms that might be meaningful only to a local or national audience. However, note also that **Brain Injury** does not aspire to be international in the ways that McDonald's restaurants or Hilton Hotels are 'international'; we much prefer papers that, where appropriate, reflect the particularities of each higher education system.

Notes on tables and figures
The same data should not be reproduced in both tables and figures. The usual statistical conventions should be

used: a value written 10.0 ± 0.25 indicates the estimate for a statistic (e.g. a mean) followed by its standard error. A mean with an estimate of the standard deviation will be written 10.0 SD 2.65. Contributors reporting ages of subjects should specify carefully the age groupings: a group of children of ages e.g. 4.0 to 4.99 years may be designated 4 +; a group aged 3.50 to 4.49 years 4 ± and a group all precisely 4.0 years, 4.0.

1. Tables and figures should be referred to in text as follows: figure 1, table 1, i.e. lower case. 'As seen in table [or figure] 1 ...' (not Tab., fig. or Fig).
2. The place at which a table or figure is to be inserted in the printed text should be indicated clearly on a manuscript:

Insert table 2 about here

3. Each table and/or figure must have a title that explains its purpose without reference to the text.
4. All figures and tables must be on separate sheets and not embedded in the text.

Thus tables and figures must be referred to in the text and numbered in order of appearance. Each table should have a descriptive title and each column an appropriate heading. For all figures, original copies of figures should be supplied. All figures should allow for reduction to column width (7.5cm) or page width (16 cm). Photographs may be sent as glossy prints or negatives. The legends to any illustrations must be typed separately following the text and should be grouped together.

Citations in text
References should be cited using the numerical system (e.g. [3], [5-9]). They should be listed separately at the end of the paper in the order in which they appear in the text. 'Ibid.' (and the like) are not used when repeating citations.

Acknowledgements
Any acknowledgements authors wish to make should be included in a separate headed section at the end of the manuscript.

References
References must be cited in the text consecutively by number, and listed at the end of the paper (provide all authors' names for three or less; when there are more than three use *et al.*)

APPENDIX 2.2

Levels of evidence and grades of acknowledgement for epidemiological studies

LEVELS OF EVIDENCE

LEVEL	TYPE OF EVIDENCE
1++	High quality systematic review of prospective studies, or high quality prospective studies with a very low risk of bias (i.e. large, representative sample)
1+	Well conducted systematic review of prospective studies, or prospective studies with a low risk of bias
1-	Systematic reviews of prospective studies, or prospective studies with a high risk of bias
2++	High quality review of retrospective studies High quality retrospective studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal (i.e. broad representative sample, clear attempts to account for pre-morbid variables using
2+	regression techniques) Well conducted retrospective studies with a low risk of confounding, bias or
2-	chance and a moderate probability that the relationship is causal Retrospective studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal (i.e. no attempts to control for the influence of pre-morbid factors)
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF ACKNOWLEDGEMENT

A	At least one systematic review of prospective studies, or prospective study rated as 1++, and directly applicable to the target population; *or* A systematic review of prospective studies or body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results
C	A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results
D	Evidence level 3 or 4

APPENDIX 2.3

Levels of evidence and grades of recommendation for studies of association

LEVELS OF EVIDENCE

LEVEL	TYPE OF EVIDENCE
1++	High quality comparison studies using an experimental design, and with a very low risk of bias, ie include randomisation procedures
1+	Well conducted experimental studies with a low risk of bias
1-	Experimental studies with a high risk of bias
2++	High quality correlational studies based on an a priori model, with a very low risk of confounding, bias or chance and a high probability that the relationship proposed by the model is causal, e.g. use multiple regression analyses
2+	Well conducted correlational studies based on an a priori model with a low risk of confounding, bias or chance and a moderate probability that the proposed relationship is causal
2-	Correlational studies based on an a priori model with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF SUPPORT

A	At least one experimental comparison study rated as 1++, and directly applicable to the target population; *or* A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results
C	A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results
D	Evidence level 3 or 4

APPENDIX 3.1

Guidelines for submission of a research proposal

This must be written in the form of an application to a Local Research Ethics Committee.

APPENDIX 3.2

Copies of letters confirming ethical approval for the major research project

Greater Glasgow Primary Care NHS Trust

Trust Headquarters
Gartnavel Royal Hospital
1055 Great Western Road
GLASGOW G12 0XH
Telephone 0141 211 3600
www.show.scot.nhs.uk/ggpct/

NHS
Greater Glasgow

Ms Sarah Fryer
Department of Psychological Medicine
Academic Centre
Gartnavel Royal Hospital
1055 Gt Western Road
Glasgow
G12 0XH

Date 15 October 2001
Your Ref
Our Ref AMcM/0137

Direct Line 0141 211 3824
Fax 0141 211 3814
Email anne.mcmahon@gartnavel.glacomen.scot.nhs.uk

Dear Ms Fryer

Project No: 01/37 ***Title: Investigation of a multifactorial model of fatigue after severe traumatic brain injury***

Many thanks for sending the amendments regarding the above named submission to the Greater Glasgow Primary Care – Community & Mental Health Research Ethics Committee – they were discussed at our meeting on Thursday, 11 October 2001. I am pleased to be able to tell you that the Committee has no objections from an ethical point of view, to this project proceeding. Ethical approval for the study is formally granted subject to the following conditions.

- The study must start within two years of the date of this letter. After that time approval will be deemed to have lapsed and the project will require to be resubmitted.
- You should notify the Committee if there are any changes, or untoward developments, connected with the study – the Committee would then require to further reconsider your application for approval. Changes to the protocol must not be initiated until written Committee approval is given, except when necessary to eliminate immediate hazards to subjects.
- The Committee expect to receive a brief regular update every 6 months, and then a brief final report on your project when the study reaches its conclusion. (Failure to keep the Committee abreast of the status of the project can eventually lead to ethical approval being withdrawn).

Before your project commences you will also require to obtain management approval via the Research & Development Directorate, Gartnavel Royal Hospital.

The Greater Glasgow Primary Care – Community & Mental Health Research Ethics Committee is fully compliant with the International Committee on Harmonisation/Good Clinical Practice (ICH) Guidelines for the Conduct of Trials Involving the Participation of Human Subjects as they relate to the responsibilities, composition, function, operations and records of an Independent Ethics Committee/Independent Review

Project No: 01/37 ***Title: Investigation of a multifactorial model of fatigue after severe traumatic brain injury***

Board. To this end it undertakes to adhere as far as is consistent with its Constitution, to the relevant clauses of the ICH Harmonised Tripartite Guideline for Good Clinical Practice, adopted by the Commission of the European Union on 17 January 1997.

May I wish you every success with study
Project No: 01/37 *Title: Investigation of a multifactorial model of fatigue after severe traumatic brain injury*

Yours sincerely

A W McMahon
Administrator – Research Ethics Committee

GLASGOW ROYAL INFIRMARY
AUSPICE CÆLO
Part of
The North Glasgow University Hospitals NHS Trust

RESEARCH ETHICS COMMITTEE
4th floor, 10 Alexandra Parade
Glasgow Royal Infirmary
GLASGOW G31 2ER

Chairman: Mr Colin Buck
Administrator: Mrs Sharon Macgregor

Royal Infirmary
16 Alexandra Parade
Glasgow G31 2ER

Switchboard: 0141 211 4000
Direct Dial: 0141 211 4020
Fax Number: 0141 553 2558
Email: sharon.macgregor@northglasgow.scot.nhs.uk
Website: www.ngt.org.uk/research

Ms S Fryer
Trainee Clinical Psychologist
Department of Psychological Medicine
Gartnavel Royal Hospital
1055 Great Western Road
GLASGOW
G12 0XH

8th August 2001

Dear Ms Fryer,

Submission: Investigation of a multifactorial model of fatigue after severe traumatic brain injury.
Project number: 01AC004 (Please quote)

I am pleased to advise you that the Research Ethics Committee has now approved this project, the Patient Information Sheet & Consent Form and the GP Information Sheet. This is granted subject to the following conditions:

- The study must **start** within two years of the date of this letter. After that time approval will be deemed to have lapsed and the project will require to be resubmitted.
- A short "Progress Report" questionnaire will now be forwarded to you every **6 months** until project completion. This information will contribute to our Annual Report to the Scottish Executive and therefore these forms **must** be completed. Failure to do so may result in future projects being held up for processing.
- The Committee must be informed **immediately** of any proposed changes to the original application, patient information sheets, consent forms, or any serious adverse events. These should be sent to the **Administrator** at the address above, stating the project number of the study.
- The approval contained in this letter is valid for all sites that form part of the North Glasgow Trust. **If however, this research is to be carried out at any other sites, then a covering letter signed by the person responsible for the research on that site must be sent to their local LREC listing names, titles and addresses of all collaborating researchers. A copy of this letter should be enclosed.**

Yours sincerely

Mrs Sharon Macgregor
LREC Administrator

HQS
accredited by the
Health Quality Service

APPENDIX 3.3

Copy of patient information sheet and consent forms

INFORMATION SHEET FOR PATIENTS/VOLUNTEERS IN A CLINICAL RESEARCH STUDY

PROJECT TITLE: INVESTIGATION OF A MULTIFACTORIAL MODEL OF FATIGUE AFTER SEVERE TRAUMATIC BRAIN INJURY: AN INVESTIGATION OF INDIVIDUAL WAYS OF COPING AND LEVELS OF ACTIVITY AFTER A HEAD INJURY

Patient/Volunteer Summary

You are being invited to take part in a research study on fatigue. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your consultant/psychologist/GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for taking the time to read this.

Purpose of the study

We know that it is common for people to feel very tired and lacking in energy immediately after they have suffered a head injury, but for some people these feelings of fatigue can carry on for many years and after other sorts of recovery are complete. This fatigue can be very disabling and can prevent people from doing their usual day to day activities and can even stop them returning to work. Unfortunately we know very little about what people can do to overcome this fatigue, and therefore people often receive very little help with this problem.

This study aims to find out why some people continue to suffer from persistent symptoms of fatigue after a head injury by looking at how people deal with this problem on a day-to-day basis. In particular it aims to look at how people mentally and physically approach everyday activities and at how a head injury affects people's ways of coping and behaviour. By taking part in this study you will be helping the medical and psychological profession understand more about the sort of fatigue people have after head injury. This might in turn help them develop better ways of treating it and preventing it.

Why have you been chosen

To find out how people's lives can be affected by a brain injury it would be useful to get some information from people who have had a brain injury on how fatigued they feel from day to day, and on what they do on an average day. By looking at different ways people have to cope with everyday problems, we might be able to tell what sorts of things some people can do to feel less fatigued.

To understand what makes people feel fatigued after a head injury in particular, it would also be useful to check that the fatigue is not caused by something unrelated to the injury. For example we know that sometimes when people are feeling depressed or worried they might report feeling fatigued. This study will therefore involve looking at people with these sorts of problems to see if their fatigue and behaviour is the same as the head injured group. This is important because we know certain sorts of medicine and psychological therapies help people with these sorts of problems feel less fatigued. This means that if people with head injuries have the same sorts of problems then getting the same sorts of treatment might help them.

We also know that sometimes having an accident of any sort can make you feel worried and tired while you recover. We will therefore also be asking people who have recovered from an accident to take part, to see if feeling fatigued is normal part of recovery from any sort of accident.

We will also look at how people who have none of these sorts of problems behave, to see if they have special ways of thinking or behaving that stop them from feeling fatigued.

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

What will happen to you if you take part

1. You will be asked to meet with Sarah Fryer, the researcher, at the clinic/college/centre you are attending. At the first meeting she will go over the details of the study again and answer any questions you might have about it. She will also ask you to fill in a consent form and four short questionnaires about how you are feeling at the time. She will then ask you to complete a small number of drawing, memory and reading tasks. You will also be asked to do a two-minute physical step test. This should all take no more than 1 hour to do.

2. You will then be shown an "actiwatch". This is a little device, about the same size as a wristwatch. You wear it on your wrist and it records how much activity you do. You will be asked to wear it on your wrist for 48 hours.

3. During the 48 hours that you are wearing the actiwatch, it will also make a small beep every hour to ask you to rate your fatigue levels at that time. This will be by simply giving your fatigue a mark out of 10, and so should not take more than a few seconds to do. Sarah will give you some training on how to do this in your first session. This beep will not go off during the night and should not be so loud as to interfere with your work.

4. At the end of the 48-hour period you will be required to come back to the clinic/college/centre to return the actiwatch.

5. If at the end of the study you have any further questions, Sarah can be contacted by telephone at the number below. Once the study is complete Sarah will also be giving a talk at Headway, to give sufferers and their relatives/friends some information on fatigue and how to manage it after a brain injury. If you feel this would be useful for you we can send you an invitation for this. If you would like any personal feedback on your performance during the study this can also be requested from Sarah at the telephone number or address below.

If you would like to take part in the study you will need to fill in a consent form. You will be offered one by Sarah Fryer. Please read the form carefully, it should be signed by both yourself and the researcher.

If you are unsure whether you wish to take part in the study please feel free to discuss with Sarah any questions or concerns you have about taking part. You are under no obligation to take part in the study after talking to her.

Thank you for your help.

Sarah Fryer
Trainee Clinical Psychologist
Dept. of Psychological Medicine
University of Glasgow
Gartnaval Royal Hospital
1055 Great Western Road
Glasgow G12 0XH
Tel: 0141 211 0607

PATIENT OR VOLUNTEER CONSENT TO PARTICIPATE IN RESEARCH STUDY

Project Title: Investigation of a Multifactorial Model of Fatigue after Traumatic Brain Injury.

- I have been given a complete explanation of the research in which I am being invited to take part, including details of the procedures I would undergo as part of the study.
- I have had the opportunity to ask questions.
- I have received the Information Sheet on the study which has been approved by Greater Glasgow Primary Care NHS Trust and Glasgow Royal Infirmary NHS Trust Research Ethics Committees, which I have read and should keep.
- I understand there is no obligation to take part in the study and I need not give any reason if I do not wish to take part in the study.
- I may withdraw from the study at any time without the need to give a reason and without any effect on my normal care.

Consent

I .....(name in block capitals)

of

.....

.....(address in block capitals)

agree to take part in this research project, the nature, purpose and possible consequences of which have been described to me
by .....(name in block capitals).

If necessary, I may/may not (delete as applicable) be contacted at home by the researcher.

My telephone number is .....

Subject signature

..... dated .....

Researcher signature

..... dated .....

If you consent to take part in this study, it may be useful for the researcher to view your medical records to find out more information about when you had your head injury and how severe it was. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

If necessary, my medical records may/may not (delete as applicable) be consulted by the researcher.

Subject signature

..... dated .....

Researcher signature

..... dated .....

APPENDIX 4.1

Copies of the Post-Concussion Syndrome Checklist and the Fatigue Severity Scale

PCSC

ID _____ Date_____

Please rate the frequency, intensity and duration of each of the following symptoms based on how they have affected you today according to the following scale:

FREQUENCY	INTENSITY	DURATION
1 = Not at all	1 = Not at all	1 = Not at all
2 = Seldom	2 = Vaguely present	2 = A few seconds
3 = Often	3 = Clearly present	3 = A few minutes
4 = Very often	4 = Interfering	4 = A few hours
5 = All the time	5 = Crippling	5 = Constant

	FREQUENCY	INTENSITY	DURATION
Headache	_____	_____	_____
Dizziness	_____	_____	_____
Irritability	_____	_____	_____
Memory Problems	_____	_____	_____
Difficulty Concentrating	_____	_____	_____
Fatigue	_____	_____	_____
Visual Disturbances	_____	_____	_____
Aggravated by Noise	_____	_____	_____
Judgment Problems	_____	_____	_____
Anxiety	_____	_____	_____

Thank you for your time and effort in the completion of this form.

FSS

ID _____ Date_____

Please rate your degree of agreement with each of the following statements on a scale of 1 to 7, where 1 indicates strongly disagree and 7 indicates strongly agree.

	Strongly disagree						Strongly agree
	1	2	3	4	5	6	7
1. My motivation is lower when I am fatigued	___	___	___	___	___	___	___
2. Exercise brings on my fatigue	___	___	___	___	___	___	___
3. I am easily fatigued	___	___	___	___	___	___	___
4. Fatigue interferes with my physical functioning	___	___	___	___	___	___	___
5. Fatigue causes frequent problems for me	___	___	___	___	___	___	___
6. My fatigue prevents sustained physical functioning	___	___	___	___	___	___	___
7. Fatigue interferes with carrying out certain duties and responsibilities	___	___	___	___	___	___	___
8. Fatigue is among my three most disabling symptoms	___	___	___	___	___	___	___
9. Fatigue interferes with my work, family or social life	___	___	___	___	___	___	___

Thank you for your time and effort in the completion of this form.

APPENDIX 4.2

Notes on practical considerations in use of actigraphy with TBI populations

Strategies used to facilitate participation for individuals in the TBI group.

Given that the traumatic brain injured group had all sustained severe to extremely severe brain injuries, many had significant memory difficulties. In an attempt to limit the effects of these difficulties in study participation, the following strategies were used with this population to make participation as easy as possible;

1. The researcher visited the majority of TBI participants either within their own homes or at a local resource centre they were attending. This circumvented problems in arranging transport.
2. All participants were given individuals training on how to sue the watch, and a printed sheet describing this training complete with contact numbers for the main researchers should problems arise.
3. The main researcher travelled to collect watches from participants' own homes on completion of the study.