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Cognitive and physical fatigue are associated with distinct problems in daily functioning, role fulfilment, and quality of life in multiple sclerosis.

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Highlights

- Cognitive and physical fatigue limit daily functioning and role fulfilment in MS.
- Dimensions of fatigue are associated with distinct aspects of quality of life.
- Cognitive fatigue is related to poorer psychosocial functioning and wellbeing.
- Physical fatigue is related to poorer mobility and participation and greater pain.
- In clinical practice each dimension of fatigue should be thoroughly assessed.

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Running head: COGNITIVE AND PHYSICAL FATIGUE IN MS

Cognitive and physical fatigue are associated with distinct problems in daily functioning, role fulfilment, and quality of life in multiple sclerosis.

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Short title: Cognitive, and Physical Fatigue Associated with Distinct Problems in MS

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Declaration of conflicting interests

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Research ethics

Approval was granted by the Behavioural and Social Sciences Ethical Review Committee at the University of Queensland (project ID 2007001094).

Abstract

Objective. To examine whether cognitive and physical fatigue are differentially associated with problems in self-care, mobility, relationships, participation, psychological well-being, and quality of life in people with multiple sclerosis. *Methods.* A cross-sectional study involving seventy-four community-dwelling people with MS was undertaken. Between-groups analysis was used to compare ratings on the Perceived Impact of Problem Profile (PIPP) in a range of functional domains and the SF-36 quality of life measure, across median-split groups based on level of both physical and cognitive fatigue using the Modified Fatigue Impact Scale. *Results.* The impact of poor psychological well-being ($p = .005$), and associated distress ($p = .008$) on PIPP was greater in the ‘high-level’ cognitive fatigue group than the ‘low-level’ cognitive fatigue group. By contrast, the ‘high-level’ and ‘low-level’ physical fatigue groups differed significantly in their self-reported impact of problems in the areas of mobility ($p = .002$), relationships ($p = .014$), participation ($p = .001$), and psychological well-being ($p = .004$). Overall mental quality of life was significantly lower ($p < .001$) in those high in cognitive fatigue comparative to the low-level group, and overall physical quality of life was significantly lower ($p = .002$) in people with multiple sclerosis high in physical fatigue as opposed to low. *Conclusion.* Cognitive and physical fatigue were associated with distinct problems in daily functioning, which impact differentially on role fulfilment and quality of life in multiple sclerosis. Therefore, these two types of fatigue should be considered distinct domains of the fatigue experience in MS.

Introduction

Fatigue is a common and disabling symptom that can interfere with daily functioning in multiple sclerosis (MS) and greatly reduce quality of life (Krupp, Alvarez, LaRocca, & Scheinberg, 1988; Turpin et al., 2017). Typically defined as an overwhelming sense of tiredness, feeling of exhaustion or lack of energy; fatigue is reported to affect 60-96% of people with MS (PwMS; Giovannoni, 2006; Strober & Arnett, 2005; van Kessel & Moss-Morris, 2006) with up to 40% identifying it as their most disabling symptom (Kos, Kerckhofs, Nagels, D'Hooghe & Ilsbrouckx, 2008). Fatigue is a poorly understood symptom, which may be categorised as primary fatigue (due to disease factors including demyelination, central nervous system involvement, and immunological causes) or secondary fatigue (due to other factors such as sleep disturbance, mood disturbance, pharmacological treatments, pain or stress; van Kessel & Moss-Morris, 2006). Several past studies have endeavoured to elucidate the aetiology of fatigue in MS; however, no single cause has been established. Current evidence clearly points towards a multi-dimensional underpinning (DeLuca, Genova, Hillary & Wylie, 2008; Kaminska, Kimoff, Schwartzman & Trojan, 2011; Marrie, Miller, Chelune & Cohen, 2003; Tartaglia, et al., 2004).

Beyond the high prevalence of fatigue in MS, the individual experience of fatigue in PwMS can be due to a unique combination of factors (Turpin et al., 2017). For some PwMS, fatigue may be the first manifestation of the disease (Fisk et al., 1994; Kos et al., 2008); it may be more severe during periods of disease exacerbation; aggravated by heat and physical effort; and worsen at certain times of day or during warmer months (Freal, Kraft & Coryell, 1984; Krupp et al., 1988; Kos et al., 2008). MS-related fatigue, often referred to as

“lassitude”, may be both pathophysiological and psychological in nature. There is emerging evidence that the subjective experience of fatigue in MS is characterised by distinct physical and cognitive components. Hence, it is now conceptualised as being “a subjective lack of physical and/ or mental energy that interferes with daily activities” (Kaminska et al., 2011).

Previous research has shown that PwMS often report a decrease in physical energy as well as a lack of mental stamina (Bryant, Chiaravalotti & DeLuca, 2004; Elkins, Krupp & Scherl, 2000; Ford, Trigwell & Johnson, 1998). This early work has been influential in distinguishing between cognitive and physical components of fatigue and developing new approaches to measuring these distinct components via questionnaire (Chalder, Berelowitz, Pawlikowska, Watts, Wessely & Wright, 1993; Ford et al., 1998). For instance, Ford and colleagues were the first to report that depression and anxiety strongly correlated with mental but not with physical fatigue. More recent studies, such as the work of Trojan et al. (2007) evaluated predictors for general, physical and mental (or cognitive) fatigue separately and found a different pattern of variables to be associated with each dimension, adding support to a multidimensional conceptualization of fatigue in MS. These authors advocate a multidimensional approach to assessing fatigue utilising a biopsychosocial model, which takes into account disease-related, behavioural and psychosocial variables. In their study, correlates of general and physical fatigue included all three of these variables, while correlates for cognitive fatigue were psychosocial factors only (Trojan et al., 2007). Accordingly, the Modified Fatigue Impact Scale (MFIS) has been developed, which allows for the calculation of scores for physical, cognitive, and psychosocial subscales, as well as an overall score. This multi-dimensional measure is recommended by the Multiple Sclerosis Council because it was devised for use specifically in MS, and has good discriminative properties (Flachenecker et al., 2002).

Iriarte, Subira and de Castro (2000) have similarly proposed that fatigue is a heterogeneous symptom in MS involving three clinical entities, namely asthenia (fatigue at rest), fatigability (fatigue with exercise) and worsening of symptoms with effort, each with particular underlying mechanisms. Utilising the Fatigue Descriptive Scale (FDS), these authors showed that fatigue was prevalent in 76% of PwMS in their study, with 22% describing their experience of fatigue as asthenia, 72% as fatigability, and 6% as a worsening of symptoms with effort (i.e. paresthesias, blurred vision, and unsteadiness). Severity of pyramidal involvement was significantly more prominent in PwMS with fatigue. In addition, immunoactivation parameters were associated with asthenia, whilst pyramidal tract involvement was associated with fatigability (Iriarte et al., 2000). Thus, distinct aspects of underlying pathology may be differentially related to distinct aspects of fatigue in MS.

Fatigue is known to have an effect on aspects of daily functioning and quality of life. It has been shown to affect work and social relations as well as mental and physical daily activities, and contribute to unemployment in PwMS (Edgley, Sullivan & Dehoux, 1991). Janardhan and Bakshi (2002) showed that fatigue was associated with impaired quality of life (QoL; as measured by Multiple Sclerosis Quality of Life (MSQOL) measure) with respect to health perception and limitations due to physical dysfunction after controlling for disability level (on Expanded Disability Status Scale) and depression (on Hamilton Depression Inventory). Importantly, however, this study only assessed overall fatigue, not cognitive and physical fatigue separately. Pittion-Vouyovitch and colleagues (2006) found strong correlations amongst cognitive, physical, social role, and psychological dimensions of fatigue and the SF-36, a measure of health-related QoL. However, no previous study has examined the distinct role of cognitive and physical fatigue in daily functioning and QoL in PwMS

through group comparison (Pittion-Vouyovitch et al., 2006). This study aims to build on previous work and fill the identified gap.

In summary, fatigue, is best conceptualised as a multi-dimensional phenomenon, with underlying psychological and pathophysiological facets. Furthermore, PwMS identify unique cognitive and physical components underpinning their experience of this symptom. Until recently, fatigue has been regarded as a unidimensional construct. It is important, therefore, to determine whether these physical and cognitive aspects of MS-related fatigue are related to different functional outcomes. Clarification of the association of both physical and cognitive fatigue with functioning will enable clinicians to plan more appropriate and directed treatment approaches for PwMS.

To facilitate this clarification, the present study used items from the International Classification of Functioning, Disability and Health (ICF; WHO, 2001), a widely utilised classification system for health and health-related domains in research, public health and clinical care. Fatigue is known to have a substantial impact on daily life as it can prevent sustained physical and mental exertion, which limits work and social role performance. Such functional limitations in turn are likely to impact negatively on quality of life (Fisk et al., 1994; Schwartz, Coulthard-Morris & Zeng, 1996). However, few studies have endeavoured to pinpoint the effect of physical and cognitive fatigue separately on various functional outcomes.

This study aimed 1) to determine the degree to which fatigue relates to disability in PwMS, by examining its relationship to individuals' perceived impact of problems with daily functioning and role fulfilment, as well as health status and quality of life; and 2) establish whether cognitive and physical fatigue are associated with differential problems in daily

functioning, particularly in the areas of self-care, mobility, relationships, participation, and psychological well-being.

Method

Participants

Participants recruited to the study were community-dwelling individuals with a definite diagnosis of multiple sclerosis living within South-East Queensland. Advertisements were sent to 649 clients of the Multiple Sclerosis Society of Queensland living in Brisbane, Australia in a two-phase mail out conducted by volunteers at the Society to maintain confidentiality. The inclusion criteria were: a) clinical diagnosis of multiple sclerosis; b) aged between 18 and 80 years; c) ability to communicate in English; d) ability to write; e) ambulant or independently mobile; f) living within the community; and g) ability to give informed consent. Participants were excluded from the study if they had: a) severe communication deficits; b) significant visual impairment; c) significant upper limb impairment; d) significant premorbid psychiatric or neurological disorder; e) an exacerbation in the past four weeks; f) been prescribed psychoactive medications in past two months; or g) were accommodated in a residential care facility.

One hundred and eight individuals (16.72%) expressed interest in participating in the study, which is considered a good response rate to mail-out (Hoyle, Harris & Judd, 2002). Of those 108 individuals, six had previously nominated, four missed their scheduled appointments, two reconsidered due to family commitments, four had consistent scheduling conflicts, eight were unavailable via phone, two had a change in contact information, two cancelled due to health issues, one was admitted to respite care, two were currently living

outside Brisbane, one was away on an overseas trip, and two were excluded due to residing in high-care facilities. The final sample comprised 74 PwMS (see Figure 1).

Insert Figure 1 here

Participants contacted the independent researcher following receipt of the study advertisement to express interest in participating and were screened against criteria prior to inclusion in the study. A home visit was arranged with the researcher who was a registered Occupational Therapist and an interview conducted within each participant's home, at a time of day which they identified as a period of low fatigue based on their lived experience. Participants were asked to provide documentation demonstrating a definite diagnosis of MS, such as a report from their neurologist or Magnetic Resonance Imaging (MRI) evidencing the condition. A detailed account of symptom history and experience was reported by each participant along with completion of self-report measures. During the interview, data were collected on a range of demographic, disease and psychosocial variables.

Measures

Participants' fatigue was measured using the Modified Fatigue Impact Scale (FIS; Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994) consisting of 21 items, which assess domains including physical fatigue, cognitive fatigue and social fatigue. It includes items developed to assess the perceived impact of fatigue on a range of daily activities that are scored from 0 (*no problem*) to 4 (*extreme problem*). For example, "Because of my fatigue

during the past four weeks: I have had to pace myself in my physical activities”; or “I have been unable to think clearly”; or “I have been less motivated to participate in social activities”. The MFIS has good internal reliability (Cronbach’s alpha of .91 and .95 for the Physical and Cognitive subscales, respectively; Ritvo, Fischer, Miller, Andrews, Paty, & LaRocca, 1997). For the purposes of this study, the Cognitive and Physical Subscales only were utilised to clearly delineate these distinct aspects of fatigue. To comprehensively assess the frequency and type of fatigue experienced by participants, a second fatigue scale was utilised. The Fatigue Severity Scale (FSS; Krupp et al., 1989) has a physical focus and consists of nine items on a seven-point scale relating to how participants felt the statement applied to them over the preceding week (e.g., “Fatigue interferes with my work, family or social life” and “Fatigue is among my three most debilitating symptoms”). The measure is scored by calculating the average rating across items and was used for descriptive purposes in the current study.

The Perceived Impact of Problem Profile (PIPP; Pallant, Misajon, Bennett, & Maderson, 2006), which is based on the Biopsychosocial Model of Health and the International Classification of Functioning, Disability and Health (ICF; World Health Organisation, 2001) was used to assess the impact of MS on self-care, mobility, participation, relationships and psychological well-being, as well as associated distress from the individual’s perspective. Participants were directed to respond to questions concerning their current health problem i.e. multiple sclerosis, and how it has affected their ability to perform daily activities. For each item respondents were asked to rate on a 6-point scale (a) 'how much impact has your current health problem had on [item of function or activity]'; and (b) 'How much distress has been caused by the impact of your health problem on [same item of function or activity]'. For example, for item 1, respondents were asked: “How much impact

has your health problem had on your overall satisfaction with life?”, and “How much distress has been caused by the impact of your health problem on your overall satisfaction with life?” The PIPP is an integrated tool with items tapping into the physical, social and psychological impact of, and associated distress caused by a health condition from the individual’s perspective. It has been found to have adequate psychometric properties and construct validity (Pallant et al., 2006).

To determine the degree to which fatigue relates to participants’ role fulfilment and health-related quality of life, ratings on the SF-36 were compared across ‘low’ and ‘high’ fatigue groups. The Short Form-36 (SF-36; Stewart, Hays & Ware, 1988) Health Status Questionnaire is a generic measure of perceived health status and quality of life. It has been used in a great variety of clinical and research settings and has demonstrated a capacity to effectively discriminate between subjects with different chronic conditions, and between subjects with different severity levels of the same disease (Stewart et al., 1988). The SF-36 has a single item covering change in health status over the last year, referred to as ‘Health Transition’, as well as eight multi-item scales. The subscales include: Physical Functioning Scale, Role-Physical Scale, Bodily Pain Scale, General Health Scale, Vitality Scale, Social Functioning Scale, Role-Emotional Scale, and Mental Health Scale. Higher scores on each of the subscales are indicative of better health. Raw scores were transformed to a 0-100 scale according to Ritvo and colleagues’ guide (1997). The measure may also be scored to derive a Physical Component Summary Scale (PCS) and a Mental Component Summary Scale (MCS), which were designated using factor analytic methods (Ritvo et al., 1997).

Data Analysis

To determine the relationship between fatigue and impact of problems/ associated distress, role fulfilment and quality of life amongst the sample of participants with MS, group means were compared using independent-groups *t*-tests. Participants' were divided into a 'high-level' fatigue group, and a 'low-level' fatigue group for both cognitive (median-split; > 20 and ≤ 20 , respectively) and physical fatigue (median-split; > 23 and ≤ 23 , respectively) based on MFIS subscale scores.

Results

Descriptive Statistics

The final sample comprised 74 participants aged between 23 and 80 years ($M = 52.72$, $SD = 12.06$) of which 59 (79.7%) were female and 15 (20.3%) were male. Current evidence suggests that MS is significantly (i.e., 3 times) more common in women than men; therefore, the study sample is representative of PwMS in Australia (Multiple Sclerosis Research Australia, 2011). The majority (49, 66.2%) were diagnosed with relapsing-remitting MS, with 12 (16.2%) having primary progressive, and the other 13 (17.6%) secondary progressive disease courses, which is also consistent with disease composition of the MS population at large (Australian Institute of Health and Welfare, 2004). Fifty-three (71.6%) individuals identified as having Australian heritage, and the other 21 as being of British 13 (17.6%), European 7 (9.5%) or Canadian 1 (1.4%) descent.

Participants rated the mean overall impact of their perceived problems at 67.62 ($SD = 29.46$, range 12-132), and their mean overall level of distress associated with these problems at 62.83 ($SD = 29.69$, range 13-135), each out of a possible 138 on the PIPP. Participants

rated the perceived impact of their problems in the areas of self-care ($M = 8.60$, $SD = 6.26$), mobility ($M = 16.32$, $SD = 8.95$), relationships ($M = 9.45$, $SD = 5.03$), participation ($M = 23.55$, $SD = 10.28$), and psychological well-being ($M = 11.37$, $SD = 3.64$), which correspond with codes outlined in the International Classification of Functioning, Disability, and Health (ICF; see Table 1). Regarding fatigue, 48 participants' (77.4%) past-week fatigue on the FSS scored within a 'severe' clinical category, with the other 14 (22.6%) being classified as 'mild' or 'moderate'.

Main Analysis

To determine the relationship between fatigue and impact of problems/ associated distress amongst the sample of participants with MS, group means were compared. Results of between groups analysis for high and low cognitive and physical fatigue are outlined in Table 1. Findings suggest that the impact of poor psychological well-being ($d = 0.823$), and associated distress ($d = 0.730$) was significantly greater in the high-level cognitive fatigue group than the low-level cognitive fatigue group, and of a large magnitude.

Findings also showed that the high-level physical fatigue group reported significantly greater overall impact of problems and overall distress than those low in physical fatigue. Specifically, those high in physical fatigue reported a significantly greater impact of problems in the areas of mobility, relationships, participation, and psychological well-being, but not self-care with large effect sizes for these differences.

Insert Table 1 here

Results of between groups analysis using the same approach for role fulfilment and quality of life are outlined in Table 2. Findings suggest that overall Mental QoL (based on mental components summary score) was significantly lower in the high-level cognitive fatigue group than the low-level cognitive fatigue group ($p < .001$), which is indicative of poorer Mental QoL. In addition, the high-level cognitive fatigue group had significantly poorer Role-Physical ($p = .005$), Vitality ($p = .002$), Social Functioning ($p = .010$), Role-Emotional ($p < .001$), and Mental Health scores ($p = .005$) than the low-level cognitive fatigue group.

Insert Table 2 here

Findings suggest that overall Physical QoL (based on physical components summary score) was significantly lower in the high-level physical fatigue group than the low-level physical fatigue group ($p = .002$), which is indicative of poorer Physical QoL. In addition, the high-level physical fatigue group had significantly poorer Physical Functioning ($p = .017$), Vitality ($p < .001$), General Health ($p < .001$), and Social Functioning ($p = .028$), and greater Bodily Pain ($p < .001$) than the low-level physical fatigue group. There was no significant difference in Health Status between groups based on change in health status or transition over the past year. The overall pattern of results is summarised in Figure 2.

Insert Figure 2 here

Discussion

Findings of the current study provide the first detailed account of the varied impact of cognitive and physical fatigue on daily functioning, role fulfilment, and the associated

influence on clients' disability, and perceived quality of life. Findings suggested that PwMS were experiencing significant levels of both physical and cognitive fatigue, with four out of five rating their fatigue as severe, which is consistent with past work demonstrating many PwMS experiencing fatigue identify it as their most disabling symptom (Kos et al., 2008).. Participants rated the mean overall impact of their perceived functional problems at 49%, and their overall level of distress associated with these problems at 46%, which would suggest prominent issues in daily functioning and fulfilment of occupational roles.

The impact of poor psychological well-being and associated distress was significantly greater in those high in cognitive fatigue compared with low. This finding is consistent with the highly significant association between cognitive fatigue and depression in PwMS reported in previous studies (for example, Ford et al., 1998), and speaks to the importance of providing intervention for individuals experiencing cognitive fatigue. Furthermore, findings suggest that overall Mental QoL was significantly lower when high-level cognitive fatigue existed, with those high in cognitive fatigue reporting significantly poorer role fulfilment, social/ emotional functioning, and mental health. Pittion-Vouyovitch and colleagues (2006) found similar results in that fatigue scores increased when QoL was impaired on all dimensions of the SF-36. However, these authors noted that various components of fatigue on the EMIF-SEP (a French adaptation of the Fatigue Impact Scale), including physical, cognitive, social role and psychological dimensions, each highly correlated with all dimensions of the SF-36 (Pittion-Vouyovitch et al., 2006) i.e. they did not differentially correlate.

The high-level physical fatigue group reported significantly greater overall impact of problems and overall distress than those low in physical fatigue. Specifically, the high- and low-level physical fatigue groups differed significantly in their self-reported impact of

problems in the areas of mobility, relationships, participation, and psychological well-being, confirming the need to tackle physical fatigue in order to improve daily functioning in PwMS. These findings support previous work by Iriarte et al., (2000) who found that fatigue produced functional limitations in 50% of their sample (and 66% of those reporting fatigue). Specifically, of those PwMS with fatigue who reported limitations, work was limited in 61%, social activities in 37% and self-care was affected in one patient.

Findings of the current study also suggest that overall Physical QoL was significantly lower in the high-level physical fatigue group along with differences in physical functioning, bodily pain, and general health compared with those low in physical fatigue. Previous studies have also found that fatigue is predictive of poorer quality of life in MS and people high in physical fatigue report lower QoL scores than PwMS low in physical fatigue (Janardhan & Bakshi, 2002; Pittion-Vouyovitch et al., 2006). Fatigue has been independently associated with impaired QoL after adjusting for physical disability and depression (Janardhan & Bakshi, 2002).

Taken together, these findings provide clear evidence that high-level cognitive and physical fatigue significantly limit daily functioning and role fulfilment, which may be reflective of greater disability.

As predicted, cognitive and physical fatigue were differentially related to specific areas of daily functioning. The distinct associations of cognitive and physical fatigue with various aspects of daily functioning, role fulfilment and quality of life may prove helpful in allowing clinicians to predict potential problems in these issues for PwMS. The differential impact of cognitive and physical fatigue on functioning and quality of life in MS may inform clinical judgements regarding how best to approach clients' care (see Figure 2).

Limitations

It should be noted that data from the present study was collected using a convenience community-based sample. Therefore, results may not be representative of the wider population of PwMS and findings may differ to other studies utilising clinic-based populations. In addition, the study was cross-sectional in design. Hence, it is not possible to infer a causal relationship between fatigue and poor daily functioning.

Conclusion

In conclusion, findings suggest that cognitive and physical fatigue are linked to distinct problems in daily functioning and role fulfilment, which impact differentially on the experience of disability in MS. Therefore, they should be considered distinct domains of the fatigue experience in MS and assessed and managed as such in the healthcare environment.

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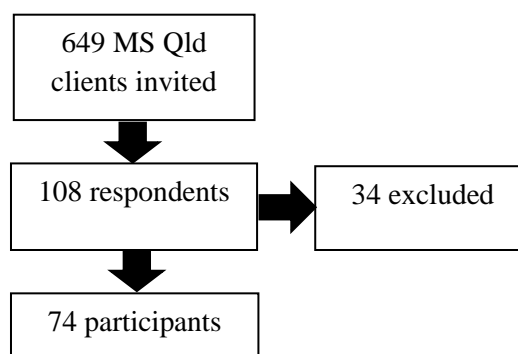


Figure 1. Flow chart outlining recruitment to the study.

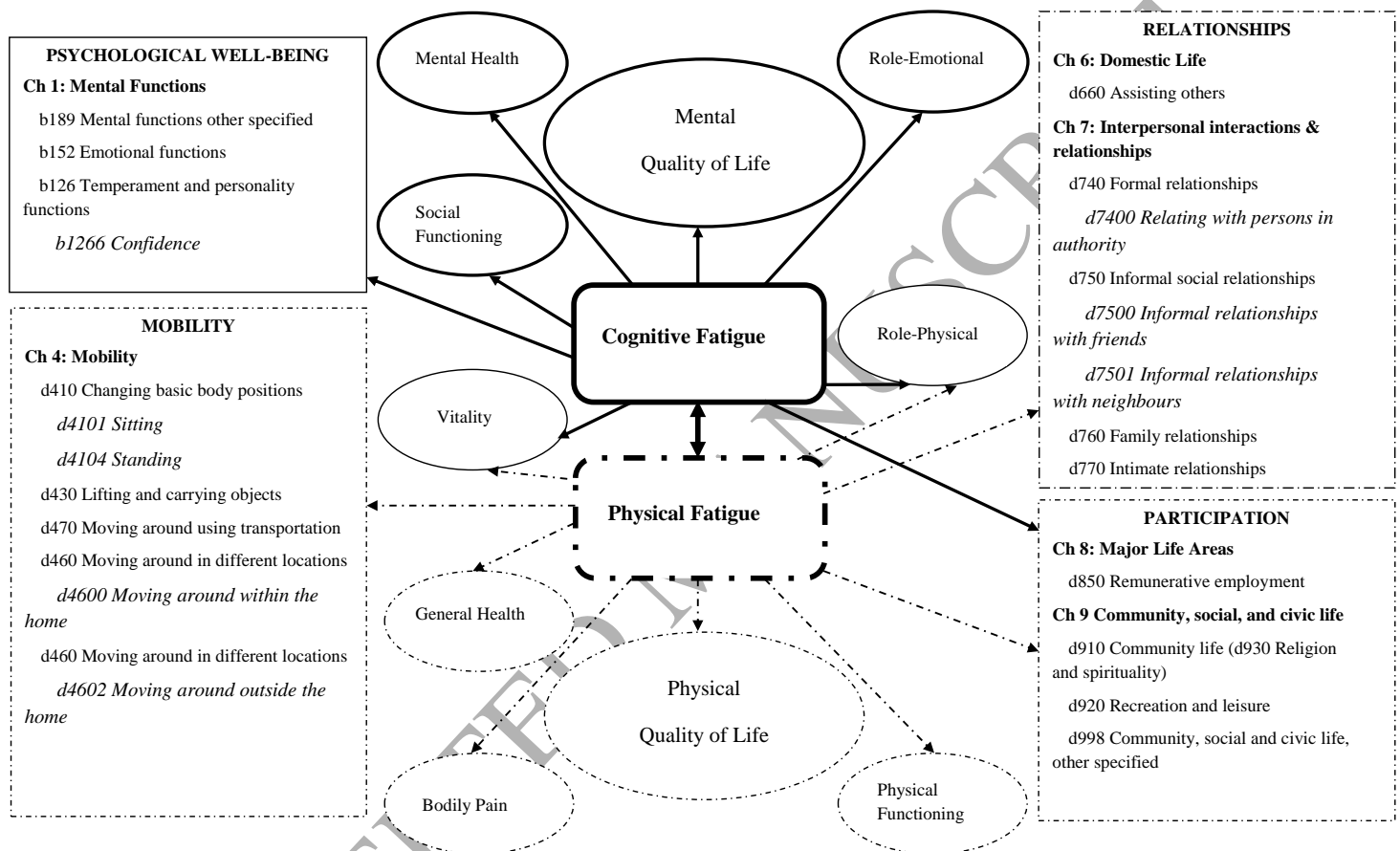


Figure 2. Diagrammatic representation of differential impact of cognitive and physical fatigue on functioning and quality of life in MS to guide clinicians. *N.B. Perceived Impact of Problem Profile subscales are linked with relevant chapters of the International Classification of Functioning, Disability and Health.*

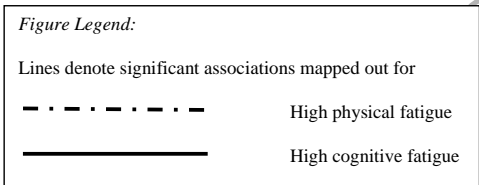


Table 1. Comparison of Perceived Impact of Problems Profile amongst 'High-' and 'Low-level' Cognitive and Physical Fatigue Groups

PIPP	Low-Level Cognitive Fatigue (N = 36)		High-Level Cognitive Fatigue (N = 26)		'Low-Level' Vs 'High-Level' Cognitive Fatigue			Low-Level Physical Fatigue (N = 36)		High-Level Physical Fatigue (N = 26)		'Low-Level' Vs 'High-Level' Physical Fatigue		
	Mean	(SD)	Mean	(SD)	t	p	d	Mean	(SD)	Mean	(SD)	t	p	d
Overall														
Impact	64.13	(29.11)	73.19	(29.83)	1.098	.227	.307	56.94	(27.50)	82.91	(25.60)	3.486	.001***	.978
Distress	59.13	(29.49)	68.48	(29.80)	1.124	.266	.315	51.94	(27.22)	78.18	(26.50)	3.497	.001***	.977
Self-Care														
Impact	8.55	(6.45)	8.26	(5.93)	-.168	.867	.047	7.65	(6.65)	10.00	(5.48)	1.404	.166	.386
Distress	8.30	(6.43)	7.83	(5.93)	-.282	.779	.076	7.24	(6.33)	9.70	(5.81)	1.487	.143	.405
Mobility														
Impact	15.97	(9.12)	16.46	(8.91)	.210	.835	.054	13.44	(8.63)	20.31	(7.94)	3.195	.002**	.828
Distress	14.49	(8.85)	15.08	(8.64)	.261	.795	.067	12.28	(8.25)	18.54	(8.16)	2.962	.004**	.763
Relationships														
Impact	8.38	(4.39)	10.64	(5.54)	1.745	.086	.455	8.11	(4.79)	11.32	(4.83)	2.546	.014*	.667
Distress	8.32	(4.46)	10.44	(5.37)	1.651	.104	.431	8.17	(4.87)	11.00	(4.79)	2.233	.029*	.586
Participation														
Impact	21.90	(9.70)	25.82	(11.10)	1.373	.176	.377	19.72	(9.58)	28.87	(8.90)	3.597	.001***	.990
Distress	19.81	(9.62)	24.18	(10.63)	1.572	.122	.432	17.19	(8.87)	27.39	(8.81)	4.218	.001***	1.154
Psychological well-being														
Impact	10.22	(3.29)	13.04	(3.56)	2.934	.005**	0.823	10.24	(3.35)	13.04	(3.47)	3.061	.003**	.821
Distress	9.39	(3.64)	12.35	(4.43)	2.733	.008**	0.734	9.15	(3.84)	12.57	(3.98)	3.251	.002**	.875

*p<.05; ** p<.01; ***p<.001. Abbreviations. PIPP = Perceived Impact of Problems Profile; SD = Standard Deviation. N.B. Effect size d=.20 [small effect], d=.50 [medium effect], and d=.80 [large effect].

Table 2. Comparison of Role Fulfilment and Quality of Life amongst 'High-' and 'Low-level' Cognitive and Physical Fatigue Groups.

SF-36 (QoL)	Low-Level Cognitive Fatigue (N = 36)	High-Level Cognitive Fatigue (N = 26)	'Low-Level' Vs 'High-Level' Cognitive Fatigue			Low-Level Physical Fatigue (N = 36)	High-Level Physical Fatigue (N = 26)	'Low-Level' Vs 'High-Level' Physical Fatigue		
	Mean (SD)	Mean (SD)	t	p	d	Mean (SD)	Mean (SD)	t	p	d
Mental	54.89 (9.75)	40.04 (12.46)	4.82	.001***	1.337	51.42 (13.02)	44.59 (12.73)	1.90	.063	.530
Summary										
Physical	34.94 (12.19)	36.01 (12.70)	-.31	.761	.086	39.51 (11.79)	29.38 (10.39)	3.24	.002**	.913
Summary										
Health	3.38 (0.89)	3.27 (0.83)	.50	.617	.128	3.33 (0.72)	3.38 (1.06)	-.214	.832	.056
Transition										
Physical	44.12 (34.74)	42.50 (30.70)	.19	.852	.050	50.14 (36.10)	31.15 (24.71)	2.46	.017*	.614
Functioning										
Role-Physical	46.32 (39.47)	22.12 (23.80)	2.94	.005**	.765	43.06 (36.16)	25.96 (32.77)	1.91	.061	.496
Bodily Pain	59.42 (27.22)	56.23 (27.55)	.45	.657	.116	69.33 (22.75)	42.27 (24.04)	4.51	.001***	1.157
General Health	57.90 (25.73)	54.83 (20.85)	.47	.642	.132	66.58 (18.59)	43.17 (22.53)	4.22	.001***	1.139
Vitality	48.38 (21.59)	29.62 (22.49)	3.28	.002**	.851	51.11 (21.55)	25.38 (16.73)	5.08	.001***	1.344
Social	73.90 (25.81)	54.33 (31.41)	2.65	.010**	.684	72.92 (28.89)	56.25 (28.24)	2.26	.028*	.584
Functioning										
Role-	76.47 (34.36)	37.18 (38.10)	4.19	<.001***	1.084	66.67 (37.37)	47.44 (43.38)	1.87	.067	.476
Emotional										
Mental Health	78.79 (17.28)	64.15 (20.78)	2.95	.005**	.769	76.11 (20.20)	67.50 (19.21)	1.65	.105	.437

*p<.05; ** p<.01; ***p<.001. Abbreviations. SF-36 = Short Form-36; QoL = Quality of Life; SD = Standard Deviation. N.B. Effect size d=.20 [small effect], d=.50 [medium effect], and d=.80 [large effect].