The relationship between subjective and objective cognitive functioning in Multiple Sclerosis; the role of self-efficacy

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Word count

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Empirical paper	2978

Thesis overview

Multiple Sclerosis (MS) is an autoimmune disease involving demyelination and neurodegeneration of the central nervous system (Compston & Coles, 2002). In the UK it is the most common form of non-traumatic neurological disability in young adults (Compston & Coles, 2008). Common symptoms of MS include sensory disturbance in limbs, visual loss, fatigue, mood disturbance and motor disturbance (Bobholz & Gremely, 2011). MS is often categorised depending on symptoms. The most common type is relapsing remitting, experienced by approximately 80% of people at onset (NICE, 2014). It is characterised by relapses, where new or existing symptoms become more severe, and remissions, a partial or total recovery of symptoms. Other types of MS include secondary progressive (gradual progression of symptoms and only partial recovery during remissions) and primary progressive (no periods of remission and gradual progression of symptoms). There is currently no cure for MS, current treatments include medications aimed at modifying disease activity and symptom management.

Approximately 50% of people with MS experience cognitive symptoms (NICE, 2014). Cognitive difficulties in people with MS have been shown to effect social functioning and quality of life (Rao et al., 1991). Clinicians often rely on MS patients' subjective reports of their difficulties in cognitive functioning. However, studies have shown that the relationship between MS patients' self-reported cognitive difficulties and their objective cognitive functioning, as measured by neuropsychological tests, is inconsistent. Several studies have demonstrated a discrepancy between self-reported cognitive functioning and objective performance on neuropsychological tests (Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman, 2005; Julian, Merluzzi, & Mohr, 2007; Lovera et al., 2006; Middleton, Denney, Parmenter, & Lynch, 2006). Both fatigue (Kinsinger, Lattie, & Mohr, 2010) and depression (Kinsinger et al., 2010; Maor, Olmer, & Mozes, 2001) have been shown to influence MS patients' self-reported cognitive functioning, more than their objective functioning. MS patients with higher levels of

depression and fatigue report more subjective cognitive difficulties. Chapter 1 of this thesis systematically reviews the literature examining the relationship between subjective and objective cognitive functioning, and examines whether depression and fatigue influence MS patients ability to accurately perceive their cognitive functioning.

The systematic review demonstrated inconsistent findings when examining the relationship between subjective and objective cognitive functioning. Both fatigue and depression were found to be associated with subjective cognitive functioning, explaining some of the variance. However, other variables are likely to influence this relationship and these influential variables are investigated in Chapter 2.

Self-efficacy has previously been shown to play an important role in the MS population. It can be described as a level of self-confidence about an individual's ability to manage specific situations or conditions, relating to perceptions of competency, rather than actual performance (Ng et al., 2013). A recent study by Schmitt, Goverover, DeLuca, and Chiaravalloti (2014) demonstrated that self-efficacy influences MS patients subjective cognitive functioning, after controlling for both depression and functional impairment. Chapter 2 builds upon the findings of the review paper and additionally examines the role of self-efficacy as a predictor of subjective cognitive functioning and quality of life.

The empirical paper has demonstrated that self-efficacy is a significant predictor of subjective cognitive functioning and quality of life even after controlling for age, MS duration, depression, anxiety, fatigue and objective cognitive functioning. People with MS reporting higher levels of self-efficacy reported fewer cognitive difficulties and greater quality of life. As self-efficacy was shown to be a significant predictor of subjective cognitive functioning and quality of life, even after controlling for other influential variables, it seems prudent for future research to target self-efficacy for intervention. Interventions aimed at improving self-efficacy in people with MS could potentially improve their accuracy at appraising their cognitive functioning and improve their quality of life.

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Chapter 1: The association of depression and fatigue with the accuracy of subjective reports of cognitive functioning in Multiple Sclerosis: A systematic review[1]

[1] To be submitted to: Health Psychology Review, author guidelines can be found in Appendix C

Abstract

Health clinicians often rely on MS patients' self-reports of their cognitive functioning to inform treatment planning. However, a number of studies have found discrepancies between MS patients' reports of subjective cognitive functioning and their objective cognitive functioning, as measured by neuropsychological tests. This discrepancy is of particular interest to researchers and clinicians when people with MS report cognitive difficulties that are not present on objective cognitive testing. It has been reported that fatigue and depression may be associated with this discrepancy. This systematic review aims to examine the extent to which fatigue and depression are associated with MS patients' self-reported cognitive functioning. Four electronic databases were systematically searched, identifying 37 articles, of which seven met the inclusion criteria for the review. Of the studies reviewed, a weak relationship was observed between subjective and objective cognitive functioning. Fatigue, and to a lesser extent depression, were found to be positively associated with MS patients' subjective reports difficulties with their cognitive functioning. The findings are discussed in relation to clinical implications for assessment and treatment, and also in terms of recommendations for future research.

Keywords

Depression, fatigue, Multiple Sclerosis, objective cognitive functioning, subjective cognitive functioning

Introduction

Multiple Sclerosis (MS) is an autoimmune disease involving demyelination and neurodegeneration of the central nervous system (Compston & Coles, 2002). The most common symptoms of MS include sensory disturbance in limbs, visual loss, fatigue, mood disturbance and motor disturbance (Bobholz & Gremely, 2011). Decline in cognitive function is also common affecting approximately 50% of MS patients (Grazioli, Yeh, Benedict, Parrish, & Weinstock-Guttman, 2008). The cognitive functions most commonly affected are information processing speed, complex attention, learning and memory, perceptual skills, word finding and executive functioning (Bobholz & Gremely, 2011). Research has shown that cognitive dysfunction in MS patients has a significant impact on daily living, lifestyle, social functioning, overall quality of life (Rao et al., 1991), medication adherence (Bruce, Hancock, & Lynch, 2010) and employment status (Moore et al., 2013).

Health clinicians often rely on MS patients' self-reports of their cognitive functioning in order to inform their treatment planning and evaluation. A small proportion of studies have found participants are accurate at reporting their cognitive functioning, when compared to their objective cognitive functioning, as measured by neuropsychological tests. These studies have found MS participants who perform poorly on neuropsychological tests report greater cognitive difficulties (Chiaravalloti & DeLuca, 2003; van der Hiele, Spliethoff-Kamminga, Ruimschotel, Middelkoop, & Visser, 2012). However, the majority of the studies in this area have noted only weak associations, or no associations, between MS patients' self-reported cognitive functioning and objective assessments of their cognitive functioning (Benedict et al., 2004; Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman, 2005; Christodoulou et al., 2005; Deloire et al., 2006; Demers et al., 2011; Gold, Schulz, Mönch, Schulz, & Heesen, 2003; Julian, Merluzzi, & Mohr, 2007; Kinsinger, Lattie, & Mohr, 2010; Lovera et al., 2006; Maor, Olmer, & Mozes, 2001; Middleton, Denney, Parmenter, & Lynch, 2006). These studies have demonstrated either no systematic relationship, or demonstrated that sometimes MS patients might over-report cognitive

difficulties when none are apparent on objective neuropsychological tests, or conversely, under-report cognitive difficulties that are apparent on objective tests. Researchers and clinicians are particularly interested when people with MS report cognitive difficulties when none are objectively present, as this can be incorrectly attributed to MS related neurological change, possibly leading to unnecessary treatment. Clinicians need to be able to formulate whether self-reported cognitive difficulties are due to MS related change or other factors, to inform the most appropriate intervention. The focus of the research has been to explore the factors that might be associated with these discrepant presentations. Factors that appear to have some association with discrepancies in cognitive functioning include levels of fatigue (Bol, Duits, Hupperts, Verlinden, & Verhey, 2010; Deloire et al., 2006; Kinsinger et al., 2010; Marrie, Chelune, Miller, & Cohen, 2005; Middleton et al., 2006; Roberg, Bruce, Lovelace, & Lynch, 2012) and depression (Benedict et al., 2004; Bruce & Arnett, 2004; Christodoulou et al., 2005; Deloire et al., 2006; Demers et al., 2011; Julian et al., 2007; Kinsinger et al., 2010; Lovera et al., 2006; Maor et al., 2001; Middleton et al., 2006; van der Hiele et al., 2012). However, the findings have been variable.

Depression and subjective reports of cognitive functioning

Depression is experienced by approximately 50% of people with MS (Siegert & Abernethy, 2005). Several studies report that MS patient's perceptions of their cognitive functioning are influenced more by depression than objective functioning. For example, Maor et al. (2001) objectively assessed a number of cognitive domains and found depression influenced subjective reports of cognitive functioning more than objective assessments of cognitive functioning. These findings have been corroborated by a number of studies (Benedict et al., 2004; Bruce & Arnett, 2004; Christodoulou et al., 2005; Deloire et al., 2006; Demers et al., 2011; Julian et al., 2007; Kinsinger et al., 2010; Lovera et al., 2006; Maor et al., 2001; Middleton et al., 2006; van der Hiele et al., 2012). The majority of these studies demonstrate that the more depressed the person is, the more they overestimate cognitive functioning difficulties.

Conversely, Smith and Arnett (2010) did not find depression to be related to subjective cognitive impairment. They found that MS participants who overestimated their executive functioning difficulties were no more depressed than those who were more accurate at reporting their cognitive functioning. In addition, Gold et al. (2003) found a discrepancy between MS patients' self-reported cognitive functioning and their objective functioning. However, this discrepancy didn't appear to be related to levels of depression.

A review of the literature has concluded that there is no consistent relationship between depression and objective cognitive functioning in MS patients (Brassington & Marsh, 1998).

Fatigue and subjective reports of cognitive functioning

Fatigue, which is reported to affect up to 92% of people with MS (Brañas, Jordan, Fry-Smith, Burls, & Hyde, 2000), is also observed to be associated with perceptions of cognitive functioning. Bol et al. (2010) found that fatigue, along with anxiety and depression, significantly contributed to discrepancies in subjective cognitive functioning. In addition, several authors have corroborated these findings, demonstrating fatigue to influence MS patient's accuracy at reporting their cognitive functioning. As self-reported fatigue increases, so do MS patients' subjective cognitive complaints (Deloire et al., 2006; Kinsinger et al., 2010; Marrie et al., 2005; Middleton et al., 2006; Roberg et al., 2012). Middleton et al. (2006) found fatigue, along with disability, anxiety and depression were unique predictors of subjective cognitive functioning, even when the variance accounted for by objective cognitive performance was removed.

The majority of studies report that there is no association between fatigue and objective cognitive functioning (Bol et al., 2010; Fraser & Stark, 2003; Paul, Beatty, Schneider, Blanca, & Hames, 1998). Although MS patients often perceive fatigue to affect their cognitive ability, their neuropsychological test performance does not appear to be associated with their levels of fatigue (Parmenter, Denney, & Lynch, 2003).

It is the case that discrepancies sometimes occur between subjective and objective cognitive functioning. Both depression and fatigue appear to be associated with subjective reports of cognitive functioning. However, neither seems to be consistently associated with objective reports of cognitive functioning in MS patients. Clarifying and understanding these relationships will be important to the formulation and treatment planning for MS patients. For example, if a person with MS reports cognitive difficulties, it might be assumed that the most helpful intervention would be medical treatment for a relapse or compensatory cognitive strategies. However, if they are reporting memory difficulties that are not observed on objective neuropsychological tests, cognitive strategies alone are unlikely to be useful. In this case, the most appropriate intervention might be a therapeutic psychological intervention. In order to usefully formulate MS patients' appraisals of their cognitive functioning it is necessary to determine whether depression and fatigue influence their subjective cognitive functioning. To date, there has not been a systematic review of these studies specifically looking at the relationship of fatigue and depression with subjective reports of cognitive functioning. Therefore, the aim of this review is to systematically analyse the current literature, investigating the accuracy of individuals with MS at reporting their cognitive functioning when compared to their objective cognitive functioning on neuropsychological tests. In addition, depression and fatigue will be examined to determine whether these factors influence participants' subjective reporting of their cognitive functioning. Given the high prevalence of depression and fatigue in MS, and that research suggests both can influence MS patient's ability to accurately perceive their cognitive functioning, the focus of this review will be to examine the individual and combinatorial effects.

Method

Inclusion criteria

Studies were included that met the following criteria: (a) patients had a diagnosis of MS (b) included a measure of subjective cognitive impairment (c) included a measure of objective cognitive impairment (d) included both a measure of depression and fatigue (e) available in English language. All studies that did not meet these criteria were excluded.

Search strategy

The initial strategy involved the search of four major electronic databases (MEDLINE, Scopus, Psych Info and Web of Knowledge). To limit the search to the desired studies, key words anywhere in the title for the terms 'MS', 'cogniti* impairment', 'fatigue' and 'depression' were used and returned a total of 1109 studies. After removing duplicates, 696 studies titles and abstracts were screened for content relevance by applying the inclusion and exclusion criteria. Where the title and abstract did not clearly indicate the degree of relevance to the topic, the article itself was reviewed. This was applicable for 37 articles. Thirty two articles did not meet the inclusion criteria and were excluded from the study. The search strategy yielded five relevant studies to be included in the review. A further hand search of relevant journals bibliographies, and thesis projects, were also conducted to discover additional references not identified in the primary search. This yielded one additional study. These six studies were initially reviewed and rated for quality. Data for review were gathered from the full text copies of the studies (figure 1).

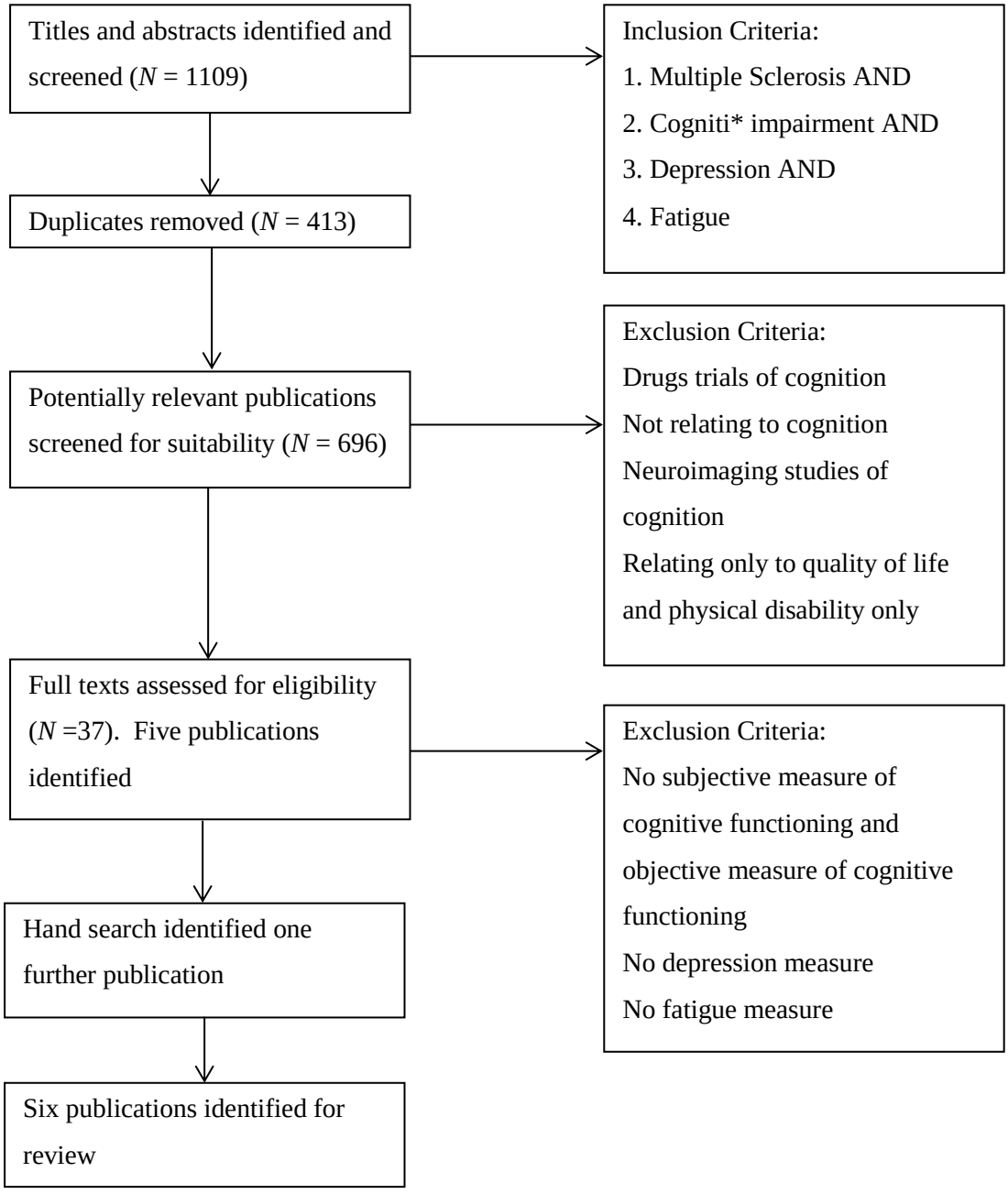

Figure 1. Flow chart demonstrating the process used to select publications for review.

Quality appraisal

The 16 item Quality Assessment Tool (QATSDD, Sirriyeh, Lawton, Gardner, & Armitage, 2012) was used to assess the quality of the studies (appendix B). The QATSDD, is designed to assess quality of methodologically diverse research. The papers included in this review were of varied methodology and the QATSDD provided a standardised approach to reviewing the literature. The QATSDD has demonstrated good reliability and validity (Sirriyeh et al., 2012). Each of the 16 items were then totalled to create an overall score, which was used as a guide when interpreting the quality of the studies. The first author rated each of the studies and discussed the quality with the other co-authors. The limitations of each study are noted in appendix B.

Results

Design and aims

Six papers met the inclusion criteria and were included in the review (appendix B). However, Roberg et al's. (2012) study reported two individual studies. Therefore, for the purpose of this review they were considered individually and referred to as study one and study two, making a total of seven individual studies. Of the seven studies, five papers were cross-sectional and two were longitudinal in design. Four studies included a control group (Deloire et al., 2006; Middleton et al., 2006; Roberg et al., 2012, study 1 & 2).

The aims of each of the studies varied. Three studies (Deloire et al., 2006; Marrie et al., 2005; Middleton et al., 2006) stated that their aim was to evaluate the relationship between subjective and objective cognitive impairment, as measured by neuropsychological tests, and identify variables that contribute to this relationship. Roberg et al. (2012), study one and two, focused on one cognitive domain, speed of processing, investigating the relationship between self-reported processing speed and objective processing speed, examining the role of fatigue and emotion. Study 1 examined this in a community sample and study 2 in a clinic sample. Jones' (2012) aim was to compare subjective and objective cognitive functioning, whilst considering the role of depression. Kinsinger et al. (2010) aimed to examine the relationship between depression, fatigue, perceived cognitive functioning and objective neuropsychological performance, in the context of a clinical trial designed to treat depression with psychological interventions.

Participants

Across all seven studies, there were 952 participants in total, 837 MS patients and 115 controls. Experimental sample sizes ranged from 40 (Roberg et al., 2012, study 1) to 221 (Middleton et al., 2006). All control groups were much smaller than experimental groups. Of the four studies that used controls, one matched controls for age, gender and years of education (Deloire et al., 2006). The majority of studies recruited from MS clinics (appendix B) The mean age of participants in the studies ranged from 37.17 (Deloire et al., 2006) to

51.60 (Jones, 2012). Of the six studies that reported gender, there were higher numbers of female participants, possibly reflecting the higher prevalence of MS in woman than men (NICE, 2014). Six studies reported disease duration, which ranged from 2.10 years (Deloire et al., 2006) to 18.33 years (Jones, 2012). The disease duration in the Deloire et al. (2006) study was much shorter than the other studies as their inclusion criteria was newly diagnosed MS patients.

Education

All studies reported education levels of participants, with three studies reporting the mean, two studies categorising years of education into two groups (Deloire et al., 2006; Marrie et al., 2005), one categorising years of education into three groups (Roberg et al., 2012, study 1) and one categorising years of education into four groups (Jones, 2012). Of the studies reporting the mean years of education, they were quite similar, ranging from 14.80 years (Roberg et al., 2012, study 2) to 15.36 years (Kinsinger et al., 2010).

Functional impairment

Functional impairment, referring to patient's physical ability, was measured in all studies. Four studies used the Expanded Disability Status Scale (EDSS, Kurtzke, 1983) (Deloire et al., 2006; Jones, 2012; Middleton et al., 2006; Roberg et al., 2012, study 2), two used the Multiple Sclerosis Functional Composite (MSFC, Fischer, Jak, Kniker, Rudick, & Cutter, 2001) (Marrie et al., 2005; Roberg et al., 2012, study 1) and one used Guys Neurological Disability Scale (GNDS, Sharrack & Hughes, 1999) (Kinsinger et al., 2010). Of the studies reporting the mean EDSS, the mean ranged from 2.0 (Deloire et al., 2006), signifying mild disability to 5.18 (Jones, 2012), indicating moderate to severe disability.

Type of MS

All studies reported MS subtype. The majority of the participants had relapsing-remitting MS. One study included only newly diagnosed participants with relapsing-remitting MS (Deloire et al., 2006) whereas the other six studies included relapsing-remitting, secondary

progressive and primary progressive, representing the most common types in the general MS population (NICE, 2014).

Depression

A variety of screening measures were used to measure depression, both Roberg et al. (2012), study two, and Jones (2012) used the Beck Depression Inventory – Fast Screen (BDI-FS, Beck, Steer, & Brown, 2000). This questionnaire has been validated for use in the MS population. Kinsinger et al. (2010) used a telephone version of the Hamilton Rating Scale for Depression (Hamilton, 1960), The Mongomery and Asberg Depression Rating Scale (MADRS, Montgomery & Åsberg, 1979) was used by Deloire et al. (2006), the Mental Health Inventory (Veit & Ware, 1983) was used in the Marrie et al. (2005) study, the Chicago Multiscale Depression Inventory (CMDI, Nyenhuis et al., 1998) was used in Roberg et al. (2012), study one, and the Centre for Epidemiological Studies-Depression Scale (CES-D, Radloff, 1977) by Middleton et al. (2006).

Four studies commented on levels of depression. Jones (2012) found 43% of MS patients in their study met the criteria for clinically significant levels of depression. Of the studies employing a control group, there were differing findings, Roberg et al. (2012), study two found there were no significant differences in depression between controls and MS patients. However, Roberg et al. (2012), study one, using a community sample, found significantly higher levels of depression in MS patients than controls, reporting a large effect size. This was corroborated by Middleton et al. (2006), who found higher levels of reported depression in MS patients than controls matched for age, gender and education level.

Fatigue

The most common measure of fatigue was the Modified Fatigue Impact Scale (MFIS, Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994) which is frequently used in MS research (Kinsinger et al., 2010; Marrie et al., 2005; Roberg et al., 2012, study 1 & 2). Two studies (Jones, 2012; Middleton et al., 2006) used the Fatigue Severity Scale (FSS, Jones, 2012; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989; Middleton et al., 2006) which is also

widely used in MS research and one study (Deloire et al., 2006) used the five graded fatigue subscale of the UK Neurological Disability Scale (Sharrack & Hughes, 1999). Middleton et al. (2006) and Roberg et al. (2012), studies one and two, compared MS patients with controls and found higher levels of fatigue in MS patients. A large effect size was reported in both Roberg studies.

Subjective measures

Five of the seven studies use self-report questionnaire measures to assess perceived cognitive functioning in multiple cognitive domains. The most common questionnaire assessing multiple domains was the Perceived Deficits Questionnaire (PDQ, Sullivan, Edgley, & Dehoux, 1990) (Jones, 2012; Kinsinger et al., 2010; Marrie et al., 2005). Two of the seven studies used a questionnaire which assessed only speed of processing, the Processing Speed Difficulties Scale (Roberg et al., 2012, studies 1 & 2). Deloire et al. (2006) assessed cognitive complaints using only four questions from an adapted French version of the MS Quality of Life Questionnaire (Vernay, Gerbaud, & Clavelou, 2001).

In addition, to self-report using the Cognitive Failures Questionnaire (CFQ, Broadbent, Cooper, FitzGerald, & Parkes, 1982), Middleton et al. (2006) also used a Performance Estimates interview, which consisted of questions assessing participants' subjective performance, immediately following neuropsychological tests.

Objective measures

All studies employed face-to-face neuropsychological testing to assess objective cognitive functioning, with the exception of Kinsinger et al. (2010) who used telephone administered neuropsychological testing. The most common cognitive domains to be assessed were speed of processing and memory. All studies employed a measure of processing speed apart from Kinsinger et al. (2010), which could be due to the feasibility of employing a processing speed measure via telephone administration. The majority of the studies assessed multiple cognitive domains, with the exception of Roberg et al. (2012), study two, who assessed only speed of processing and memory.

Two studies looked at objective cognitive functioning using composite scores, (Kinsinger et al., 2010; Middleton et al., 2006) whereas the remaining five studies examined individual cognitive domains. Although all of the studies quantified the scores into either t-scores or z-scores, which allowed for comparison against the population mean, they tended to use different measurement criteria. Two studies defined cognitive impairment as performance on one neuropsychological test below the 5th percentile, using a t-score (Marrie et al., 2005) or z-score (Jones, 2012). However, Deloire et al. (2006) defined cognitive impairment as performance on two neuropsychological tests below the 5th percentile of healthy controls, matched for age, gender and education levels. Roberg et al. (2012), studies one and two, did not define neuropsychological measurement criteria.

Middleton et al. (2006) and Roberg et al. (2012), studies one and two, compared MS patients' neuropsychological performance to controls using t-tests. They found MS patients performed more poorly than controls on tasks assessing speed of processing and delayed memory (Roberg et al., 2012, studies 1 & 2), list learning, verbal fluency, working memory (Roberg et al., 2012, study 1) and poorer on overall composite scores (Middleton et al., 2006). Deloire et al. (2006) demonstrated that 88% of MS patients performed at less than the 5th percentile of controls on at least one test. Marrie et al. (2005) and Jones (2012) found 56% and 54% of patients to be impaired in one domain, respectively. This data was not reported by Kinsinger et al. (2010).

The relationship between subjective cognitive functioning and objective cognitive functioning

Six of the seven studies found small to medium positive correlations between self-reported cognitive functioning and performance on specific tasks, finding increasing subjective cognitive complaints associated with decreasing cognitive performance, as measured by neuropsychological tests. Roberg et al. (2012), study two, found a small correlation between perceived speed of processing and performance on speed of processing tasks. Roberg et al. (2012), study one, found a large correlation between perceived speed of

processing and commission errors on an executive functioning task. Kinsinger et al. (2010) found a small to medium correlation between subjective cognitive functioning and overall cognitive performance. Jones (2012) found subjective cognitive functioning was correlated with one executive functioning task and working memory. Marrie et al. (2005) performed univariate logistic regression and found a non-linear relationship between immediate memory, processing speed and subjective complaints; slight declines in cognitive impairment were associated with increased risk of subjective cognitive impairment. This relationship was not significant when defining impairment by traditional means (less 5th percentile). However, Deloire et al. (2006) only found one cognitive domain, speed of processing, to be correlated with one question about memory complaints. Middleton et al. (2006) found no correlation between perceived global cognitive functioning and objective cognitive functioning. They did, however, find a significant correlation between 'estimates performance' and objective cognitive functioning.

The relationship between depression and fatigue, and subjective cognitive functioning

Six of the seven studies demonstrated self-reported cognitive functioning to be associated with depression, reporting positive correlations. As depression levels increased, patients reported more problems with cognition. However, this ranged from weak (r = .28, Roberg et al., 2012, study 2) to medium correlations (r = .43, Deloire et al., 2006). A multivariate logistic regression demonstrated that as depression increased so did the likelihood of reporting subjective cognitive impairment (Marrie et al., 2005) . Roberg et al. (2012), study one, did not find a significant association between depression and subjective speed of processing.

Six studies reported the association between self-reported cognitive functioning and fatigue. Five studies used a correlational design and found medium (r = .35, Deloire et al., 2006) to large correlations (r = .68, Kinsinger et al., 2010) demonstrating that subjective cognitive complaints increased as levels of self-reported fatigue increased. Marrie et al. (2005) used a multivariate logistic regression, finding increasing physical fatigue to be

associated with increased subjective cognitive impairment. Jones (2012) did not report this data.

The relationship between depression and fatigue, and objective cognitive functioning

Kinsinger et al. (2010) found that neither depression nor fatigue were associated with objective cognitive functioning. No other studies assessed the relationship between depression, fatigue and objective cognitive functioning.

Extended analysis

Five studies performed further analysis on the data, with three studies using multiple regression analysis to examine unique predictors of subjective cognitive functioning (Middleton et al., 2006; Roberg et al., 2012, study 1 & 2). Kinsinger et al. (2010) and Marrie et al. (2005) used logistic regression analysis to examine depression and fatigue as predictors of subjective cognitive functioning. Whereas, Jones (2012) used an ANOVA to examine the role of depression in patients categorised as 'impaired' or 'unimpaired' on neuropsychological tests.

Middleton et al. (2006) found disability, fatigue, anxiety and depression were the only unique predictors of subjective cognitive functioning, collectively accounting for 40% of the variance, when objective performance was removed. Depression (β = .54) and anxiety (β = .55) accounted for the greatest unique variance.

Marrie et al. (2005) demonstrated that increasing physical fatigue and depression were both associated with increased odds of subjective impairment.

Conversely, both Roberg et al. (2012), studies one and two, did not find either depression or fatigue to uniquely account for any of the variance in subjective cognitive functioning. Roberg et al. (2012), study two, found the only variables to account for the unique variance in subjective processing speed, when controlling for disease duration, age and physical disability, was extroversion (R^2 = .21) and anxiety (R^2 = .10). Roberg et al. (2012), study one, found anxiety (R^2 = .34) and a finger tapping task (R^2 = .14) to uniquely account for the variance in subjective processing speed. Unlike the Marrie et al. (2005)

study, Roberg et al. (2012), studies one and two, did not control for objective cognitive performance.

Jones (2012) found that depressed patients reported more subjective cognitive difficulties, regardless of whether they are cognitively 'impaired' or 'unimpaired' on neuropsychological tests.

Kinsinger et al. (2010) demonstrated that participants perceived fewer cognitive complaints after successful psychological treatment (t = -7.65), which improved self-reported depression and fatigue. Additionally, they found that as depression and fatigue decreased, the probability of patients becoming more accurate at perceiving their cognitive functioning increased.

Discussion

The current review aimed to investigate MS patient's accuracy at reporting their cognitive functioning when compared to their objective cognitive functioning on neuropsychological tests. Additionally, both depression and fatigue were examined to determine if they were associated with subjective reporting of cognitive functioning. To explore this, seven studies were identified and selected for inclusion. Although this is a relatively small number of studies, the focus of this review was to examine the contribution of both depression and fatigue.

The relationship between subjective and objective cognitive functioning

The literature reviewed demonstrated mixed results when examining the relationship between self-reported cognitive symptoms and objective cognitive functioning, as measured by neuropsychological tasks. Although the review generally demonstrated small to medium positive correlations between self-reported cognitive functioning and objective performance, this was confined to one or two specific neuropsychological tasks, rather than a specific cognitive domain. These correlations did not tend to be domain specific, for example Deloire et al. (2006) only found processing speed to correlate with one question assessing subjective memory complaints. Although a large correlation was demonstrated in Roberg et al. (2012), study one, this correlation was between subjective speed of processing and one particular area (commission errors), on one executive functioning task. Only one study (Roberg et al., 2012, study 2) found a domain specific correlation. However, this correlation was weak. Studies using overall neuropsychological composite scores, rather than examining individual cognitive domains, found small strength correlations (Kinsinger et al, 2010) or no relationships (Middleton et al., 2006) between subjective and objective performance. Marrie et al. (2005) found only slight declines in cognitive functioning were associated with increased reporting of subjective cognitive impairment. The findings of this review suggest that MS patients are not particularly accurate at reporting their cognitive functioning. Although some associations between subjective and objective cognitive

functioning have been found, there does not appear to be a consistent association between cognitive complaints in any particular domain and objective functioning in a specific domain.

A number of differences in the methodology in each of the reviewed studies make comparisons difficult. For instance, two studies used composite scores to measure objective cognitive functioning, whereas the other four studies examined individual cognitive domains. Although all of the studies quantified the scores into standard scores, which allowed for comparison against the population mean, studies tended to use different measurement criteria. The differences in definitions of cognitive impairment mean participants defined as 'impaired' in one study could be defined as 'unimpaired' in another study.

In addition, each study used different neuropsychological tests and focused on different cognitive domains. The cognitive domains thought to be most commonly affected in MS, memory and processing speed difficulties, were assessed by the majority of studies. However, there were differences between studies, for example studies assessing the same cognitive domain often used different neuropsychological tests. Some studies used numerous cognitive tests to assess one cognitive domain, whereas other studies only used one individual test. The procedure for collecting data also differed, most of the studies conducted face-to-face cognitive assessment, whereas Kinsinger et al. (2010) used telephone neuropsychological assessment. The use of telephone assessments means it is not possible to determine whether all participants were tested under the same conditions, for example some participants may have been using aides.

Furthermore, measures of subjective cognitive impairment were not consistent throughout the reviewed studies, and were limited to the cognitive domains they included. The majority of studies assessed subjective cognitive performance in multiple domains, including speed of processing, memory, concentration, attention. The Roberg et al. (2012) studies focused solely on processing speed. Only Jones (2012) examined at all of the cognitive domains that are thought to be affected in MS. In addition to the PDQ, Jones

(2012) provided additional questions assessing language and processing speed due to the prevalence of these cognitive difficulties in MS population.

As the aims of each of the studies were slightly different, this meant the population of MS participants differed in some studies. Deloire et al. (2006) only recruited newly diagnosed MS participants who all had relapsing-remitting MS. As Kinsinger et al. (2010) was examining treatment of depression, the sample only included MS patients who were experiencing depression. Marrie et al. (2005) used a sample of MS patients who were all experiencing cognitive difficulties. In addition, the majority of the studies were cross sectional in design, making it difficult to infer causality.

The role of depression and fatigue on subjective cognitive functioning

The second aim of the review was to examine the role of depression and fatigue on subjective cognitive functioning. At the minimum, all studies used correlational analysis to investigate the relationship between depression or fatigue and subjective cognitive functioning. With the exception of Roberg et al. (2012), study one, all of the studies demonstrated that as levels of depression increased, so did subjective cognitive complaints. However, this relationship was only marginally associated in Roberg et al. (2012) , study two. In other studies, a medium correlation was found. A stronger association was demonstrated between fatigue and subjective cognitive functioning, with all studies that assessed this demonstrating medium to large correlations.

Although further analysis was conducted in five studies, the difference in the aims and analysis makes comparisons difficult. Studies examining unique predictors of cognitive functioning found contrasting results (Marrie et al., 2005; Roberg et al., 2012, study 1 & 2). Marrie et al. (2005) found depression and fatigue to account for the greatest unique variance, whereas Roberg et al. (2012), studies one and two, did not find depression or fatigue to uniquely account for any of the variance in subjective functioning. Although different methodology was used by Middleton et al. (2006), Kinsinger et al. (2010) and (Jones, 2012) the results generally corroborate the findings of Marrie et al. (2005).

Synthesising these analyses is also complicated by the lack of reported effect sizes and confidence intervals. Effect sizes could not be calculated from the existing published data due to the limited information reported.

In addition to the limitations described previously, there are also additional considerations when examining the secondary aim. The measures used to examine depression and fatigue differ from study to study. Given the population being studied, the measures need to be sensitive to MS symptoms. Measures of depression should not include somatic symptoms of MS, such as fatigue and decreased concentration, as this may lead to falsely elevated depression. Only three studies use a suitable depression measure, using the BDI – FS (Jones, 2012; Roberg et al., 2012), which is specifically designed to assess depressive symptoms in medical populations, and has also been validated within the MS population, and the MHI, which excludes somatic symptoms of depression (Marrie et al., 2005). Furthermore, measures of fatigue varied between studies and not all had been validated in the MS population. It should be noted that measures of fatigue and depression, in all studies, were screening measures and not diagnostic tests.

In relation to the review question, three studies were found to have particular strengths (Jones, 2012; Marrie et al., 2005; Middleton et al., 2006) . There were a number of positives about these studies including large samples of participants with varying MS presentations, varying disease durations, objective cognitive measures that assessed all domains found to be affected in MS, subjective areas that assessed a number of cognitive domains, depression measures that did not include somatic symptoms (Jones, 2012; Marrie et al., 2005) and a control group (Middleton et al., 2006), However, there were also limitations to these studies with participants recruited from clinics only, potentially leading to a biased sample. All of the participants in the Marrie et al. (2005) study were recruited due to pre-existing cognitive complaints, possibly leading to a biased sample. In addition, Middleton et al. (2006) used a depression measure that included somatic symptoms of depression. Furthermore, Jones (2012) did not compare subjective cognitive functioning to fatigue. These studies demonstrated mixed findings when examining the relationship

between subjective and objective cognitive functioning, suggesting no clear relationship. These studies demonstrated similar findings when examining the relationship between depression and fatigue and subjective cognitive impairment, finding depression and fatigue influence subjective cognitive impairment.

Conclusion

This systematic review has demonstrated that there is no clear relationship between MS patients' subjective and objective cognitive functioning in any particular cognitive domain. However, the review has shown that fatigue impacts upon this relationship, with patients who report greater levels of fatigue reporting increasing cognitive difficulties. A slightly less consistent relationship has been found with depression. The findings of this review have direct implications for clinical practice, as MS patients may potentially underestimate or overestimate their cognitive functioning. This kind of discrepancy might not be identified in time-limited medical consultations that rely on MS patient's subjective report of their cognitive functioning, when no formal neuropsychological assessments are carried out. Fatigue and depression should both be considered when patients are reporting cognitive difficulties. In addition, there are potential therapeutic implications from this review, as the treatment of fatigue and depression may improve MS patient's accuracy at reporting their cognitive functioning, as demonstrated previously with psychological interventions (Marrie et al., 2005). Current interventions for self-reported cognitive difficulties in the MS population may include compensatory cognitive strategies. However, interventions may prove more effective if they focus on reframing perceptions of difficulties.

Although the studies in this review have accounted for some of the variance in subjective cognitive functioning, it is likely other variables influence the relationship. In order for effective interventions, to improve MS patient's accuracy at assessing their cognitive functioning and potentially increasing quality of life, these variables need to be accounted for. A recent study by (Schmitt, Goverover, DeLuca, & Chiaravalloti, 2014) has implicated self-efficacy as a predictor of self-reported cognitive functioning, when

controlling for depression. It therefore seems prudent to explore the relationship between self-efficacy and objective and subjective cognitive functioning, whilst taking into account the role of fatigue and depression.

This review has also highlighted that future studies in this area should use a consistent approach to methodology including a uniform approach to defining cognitive impairment, assessing all cognitive domains associated with MS, using appropriate measures that have been validated in the MS population and recruiting participants with varying MS presentations.

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Chapter 2: The predictive role of self-efficacy and objective cognitive functioning on subjective cognitive functioning and quality of life in Multiple Sclerosis[1]

[1] To be submitted to Multiple Sclerosis Journal, author guidelines can be found in Appendix H

Abstract

Background: Self efficacy, a belief in an individual's own capabilities, has previously been found to play an important role in how individuals meet the challenges of health conditions.

Objectives: The aim of this study was to investigate whether self-efficacy is associated with subjective cognitive functioning and quality of life in people with Multiple Sclerosis (MS) when controlling for objective cognitive functioning, fatigue, depression and anxiety.

Methods: Forty five MS participants completed neuropsychological tests and self-report questionnaires measuring subjective cognitive functioning, quality of life, self-efficacy, depression, anxiety and fatigue.

Results: Correlational analysis showed associations between self-efficacy, depression, anxiety, fatigue, MS duration, objective cognitive functioning and subjective cognitive functioning. Associations were also demonstrated between depression, self-efficacy, anxiety, fatigue and quality of life. Hierarchical regression analysis showed self-efficacy is a significant predictor of subjective cognitive functioning and quality of life even after controlling for age, MS duration, depression, anxiety, fatigue and objective cognitive functioning.

Conclusion: This study has demonstrated that self-efficacy is an important predictor of subjective cognitive functioning and quality of life. Important implications in relation to clinical practice are discussed.

Keywords

Anxiety, cognition, depression, fatigue, multiple sclerosis, objective cognitive functioning, quality of life, subjective cognitive functioning.

Introduction

Cognitive decline is a common symptom in Multiple Sclerosis (MS), with approximately 50% of people experiencing cognitive difficulties [1, 2]. Research has shown that cognitive dysfunction in people with MS has a significant impact on daily living, lifestyle, social functioning, overall quality of life [2] and employment status [3]. However, discrepancies have been noted between self-reported cognitive functioning and objective assessments of functioning as measured by neuropsychological assessment [4-12]. These studies have generally demonstrated that people with MS are not particularly accurate at reporting their cognitive functioning, finding either no relationship or weak relationships between subjective cognitive functioning and one or two specific cognitive tests. There does not appear to be a consistent association between cognitive complaints in any particular cognitive domain and objective functioning in a specific domain [4-12]. This kind of discrepancy is unlikely to be identified in routine medical consultations, including those in specialist MS services, when no formal neuropsychological assessments are carried out and clinicians rely on subjective reports.

Several studies have shown levels of self-reported cognitive functioning to be associated with symptoms of depression but not with objective assessments of cognitive functioning [6, 13], in that people with MS experiencing depression report greater cognitive difficulties when compared to their objective functioning. Furthermore, Kinsinger et al. [12] found fatigue, along with depression, to positively correlate with subjective cognitive complaints. However, depression and fatigue were not associated with objective cognitive performance. In addition to depression [4, 5, 7-10, 12-15] and fatigue [9, 10, 12, 14, 15], self-reported cognitive functioning has also been shown to be associated with anxiety [15] and self-efficacy [16]. These studies demonstrated that subjective cognitive complaints increased as levels of depression, fatigue and anxiety increased, and self-efficacy decreased. The implication of these results is that depression, anxiety, self-efficacy and fatigue may influence MS patients' ability to accurately perceive their cognitive performance. Increased depression and fatigue are also associated with reduced quality of life in people with MS [17].

Self-efficacy, which can be described as an individual's belief about their ability to manage specific situations or conditions [18], has been shown to play an important role in the MS population. Schmitt et al. [16] found that self-efficacy was a significant predictor of self-reported physical, cognitive and social functioning, after controlling for functional impairment and depression. Higher levels of self-efficacy were associated with better self-reported physical and cognitive functioning. In addition, self-efficacy was associated with health related quality of life. However this study did not measure or control for objective cognitive functioning or fatigue.

Previous research has demonstrated that self-efficacy is a predictor of psychological adjustment to MS, in that self-efficacy is positively associated with psychological wellbeing and predicts higher levels of social activity and self-esteem [19]. Furthermore, Riazi et al. [20] found increased self-efficacy predicted improved health status in rehabilitation settings. In addition, higher levels of self-efficacy are associated with increased motivation, psychological wellbeing, adherence with treatment and self-reported quality of life [21]. MS wellness programs have been developed to promote health and quality of life [18]. These wellness programs have included a component addressing self-efficacy. Ng et al. [18] found that over the course of one such wellness program, self-efficacy and quality of life improved.

Although previous research has identified a relationship between self-efficacy and subjective cognitive functioning, and between self-efficacy and quality of life, this research has failed to examine the role of objective cognitive functioning and fatigue. The purpose of the study was to examine the relationship between objective and subjective cognitive functioning in a group of people with MS, using a subjective questionnaire measure and neuropsychological tests. In addition, the study aimed to examine if self-efficacy predicted subjective cognitive functioning and quality of life, whilst controlling for other variables previously found to be related to subjective cognitive functioning. It is hypothesised that self-efficacy will predict subjective cognitive functioning and quality of life when objective cognitive functioning, MS duration, age, depression, anxiety and fatigue are controlled for.

Materials and method

A total of 45 patients (29 females, 16 males), with clinically definite MS were recruited from routine clinics at a North West England Neurology Hospital (Appendix D & E). Patients were excluded if they were currently experiencing an episode of relapse and if they had other chronic medical conditions that might have contributed to cognitive impairment (e.g. epilepsy). Demographic information was collected including age, gender, years in education, duration of MS and MS subtype.

Measures

Dependent variables. Subjective cognitive functioning was measured using the Perceived deficits questionnaire (PDQ [22]). It is a 20 item questionnaire, consisting of questions that assess subjective memory, attention, and planning. Total scores range from 0 - 80, with higher scores indicating greater subjective cognitive impairment. Internal consistency has been measured at $\alpha = .95$ in an MS population [23].

Quality of life was measured using the WHO Quality of Life – BRIEF (WHOQOL [24]), a 26 item questionnaire rated on a five point scale. Higher scores indicate greater quality of life. Internal consistency in an MS population has been measured at between $\alpha = .63$ and $\alpha = .81$ [25].

Independent variables. Composite objective cognitive functioning scores (COCFS) was assessed using standardised neuropsychological tests (Appendix F). The tests were selected as they measure cognitive domains frequently affected in MS [26]; digit span from the Wechsler Adult Intelligence Scale-IV (concentration and working memory), visual reproduction from the Wechsler Adult Memory Scale-IV (visual memory), Symbol Digit Modalities Test (SDMT; information processing speed), California Verbal Learning Test-II (CVLT; verbal learning and memory), Hayling from the Hayling and Brixton (Executive Functioning) and verbal fluency from the Delis-Kaplan Executive Functioning System. Raw scores were compared against

published normative population data for each test to derive age-adjusted standard scores. These were then converted into T scores to allow comparisons between different tests.

The Hospital Anxiety and Depression Scale (HADS [27]) was used to measure psychological distress. The HADS is an anxiety and depression screening measure, for people with physical ill health. Total scores range from 0 – 21 for both anxiety and depression, with higher scores indicating greater levels of depression or anxiety. The HADS does not ask questions about somatic symptoms such as fatigue and sleep, therefore avoiding falsely elevated scores in people with MS. Atkins et al. [28] report good levels of internal consistency within the MS population.

The Fatigue Severity Scale (FSS [29]) was used to assess the severity of fatigue and the impact of fatigue on activities and lifestyle. Total scores range from 9 – 63, with higher scores indicating greater fatigue. Internal consistency has been measured at $\alpha = .81$ in an MS population and $\alpha = .81$ in a healthy population [29].

Self-efficacy was measured using the General Self-Efficacy Scale (GSES [30]). It is a 30 item scale that includes a general self-efficacy subscale and a social self-efficacy subscale. For the purposes of this study, only general self-efficacy scores were used as it reflects a general overview of functioning, rather than being limited to social self-efficacy. It contains 17 items, rated on a five point scale. Higher scores indicate greater self-efficacy. Internal consistency has been measured at $\alpha = .85$ [30].

Control variables. Age and MS duration.

Procedure

Ethical approval was obtained from Greater Manchester West National Research Ethics Service. Participants were informed about the study during their routine MS clinic appointments and invited to participate. Neuropsychological testing and questionnaires were either completed at

a further clinic appointment or at the participant's home. During the appointment, participants completed the cognitive assessments and the self-report questionnaires.

Data analysis

Data analysis was conducted using SPSS (21) statistical software. Correlational analysis was used to explore the relationship between PDQ and hypothesised variables of interest. This analysis was repeated exploring the relationship between quality of life (QoL) and hypothesised variables of interest. Two hierarchical multiple regression analyses were conducted; one to examine the relationship between self-efficacy and PDQ after controlling for age, MS duration, fatigue, depression, anxiety, executive functioning (EF) and COCFS, and one to examine the relationship between self-efficacy and quality of life after controlling for age, MS duration, fatigue, depression, anxiety, EF and COCFS.

Results

A total of 45 participants with MS were included in the study. The participants were composed of predominantly females (*N* = 29), reflecting the MS population. Patients ranged in age from 23 - 73 (*M* = 46.20). In terms of MS subtypes, 78% had relapsing-remitting, 7% had secondary progressive and 15% had primary progressive. Patients years in education ranged from 11 – 21 (*M* = 14.61) and their length of illness ranged from 1-32 years (*M* = 6.84) (table 1).

Objective neuropsychological tests represented a wide range of tests examining different areas of cognitive functioning. As participants' performance could vary from test to test, it could not be assumed that a simple averaging of these tests would represent a valid and reliable measure of their overall objective cognitive functioning. However, in order to simplify the analysis of objective cognitive function, it was deemed appropriate to attempt a form of data reduction. The method chosen for this was a Principle Component Analysis (PCA) of the eight neuropsychological tests.

Prior to preforming PCA, the suitability of the data for factor analysis was assessed. Inspection of the correlation matrix revealed the majority of the coefficients were above .5. A Direct Oblimin rotation was used as it was assumed that any derived factors would be oblique rather than orthogonally related. The Kaiser Meyer-Olkin value was .844, exceeding the recommended value of .6 and Bartlett's test of Sphericity reached statistical significance supporting the factorability of the correlation matrix.

PCA revealed the presence of two factors with eigenvalues, exceeding 1, explaining 56% and 13% of the variance respectively. Seven components loaded onto factor 1, (digit span, SDMT, immediate and delayed visual reproduction, CVLT, verbal fluency, category fluency) and one component loaded on factor 2 (executive functioning). Therefore, for the purposes of the analysis the Composite Objective Cognitive Functioning Score (COCFS) was computed using

the average T-scores for the seven tests loading onto factor 1 and executive functioning scores were used unchanged.

Correlations

Pearson's R was used to conduct correlational analyses between tests of cognition, age, MS duration, measures of fatigue, emotion, self-efficacy, subjective cognitive functioning and quality of life. PDQ was significantly associated with quality of life (r = -.65, p < .001), self-efficacy (r = -.64, p < .001), depression (r = .60, p < .001), anxiety (r = .59, p < .001), fatigue (r = .42, p < .001), MS duration (r = .38, p < .001), and COCFS (r = -.35, p < .05). In addition to PDQ, quality of life was associated with depression (r = -.65, p < .001), self-efficacy (r = .61, p < .001), anxiety (r = -.54, p < .001) and fatigue (r = -.48, p < .001). Correlation coefficients can be seen in table 1.

Table 1. Correlation coefficients between tests of cognition, age, MS duration, measures of fatigue, emotion, self-efficacy, subjective cognitive functioning and quality of life

Variables	Mean	SD	1	2	3	4	5	6	7	8	9
1.Age	46.20	12.61									
2.Duration	6.84	7.22	.08								
3.FSS	42.60	14.75	.18	.18							
4.Depression	6.40	4.35	-.12	.15	.45**						
5.Anxiety	7.82	4.39	-.27	.35*	.24	.72**					
6.GSE	59.47	13.09	.11	-.09	-.20	-.63**	-.49**				
7.EF	45.73	10.07	-.17	-.17	-.29	.00	.04	.05			
8.COCFS	47.30	9.14	.01	-.37*	-.16	-.14	-.18	.06	.34*		
9.PDQ	35.29	17.64	-.14	.38**	.42**	.60**	.59**	-.64**	-.23	-.35*	
10.QoL	258.67	6.99	-.05	-.25	-.48**	-.65**	-.54**	.61**	.10	.15	-.65**

** Correlations significant at the 0.01 level (2-tailed) * Correlations significant at the 0.05 level (2-tailed)

Note. COCFS: Composite Objective Cognitive Functioning Score; Duration: MS duration; EF: Executive Functioning; FSS: Fatigue Severity Scales; GSE: General Self-Efficacy Scale; PDQ: Perceived Deficits Questionnaire; QoL: Quality of Life Questionnaire

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Subjective cognitive functioning

Preliminary analyses were conducted to ensure no violations of the assumptions of normality, linearity and homoscedasticity (Appendix G). Hierarchical multiple regression was used to assess the ability of self-efficacy to predict subjective cognitive functioning after controlling for the influence of age, MS duration, depression, anxiety, fatigue, EF and COCFS. Age and MS duration were entered into step 1, explaining 18% of the variance of subjective cognitive functioning. After entry of fatigue and HADS scores, step 2 explained 50% variance. After entry of EF and COCFS scores in step 3, the total variance explained by the model as a whole was 54%, F (7, 37) = 6.28, p <. 001. However, EF and COCFS did not make a statistically significant contribution. Self-efficacy explained an additional 11% of the variance in subjective cognitive functioning, after controlling for age, MS duration, fatigue, anxiety, depression, EF and COCFS, R squared change = .11, F change (1, 36) = 11.80, p = .002. In the final model, only self-efficacy (*beta* = -.44, p = .002) was statistically significant (table 2).

Table 2. Hierarchical Regression Analysis for PDQ (*N* = 45)

Variable	*Beta*	*SE(B)*	*β*	*Adjusted R²*
Step 1				.14*
Age	-.24	.19	-.17	
MS Duration	.97	.34	.39	
Step 2				.44**
Age	-.14	.17	-.09	
MS Duration	.58	.31	.24	
FSS	.24	.16	.20	
Depression	1.28	.75	.32	
Anxiety	.83	.75	.21	
Step 3				.46**
Age	-.15	.17	-.10	
MS Duration	.42	.32	.17	
FSS	.17	.16	.15	
Depression	1.32	.73	.33	
Anxiety	.87	.74	.22	
COCFS	-.24	.24	-.13	
EF	-.26	.22	-.15	
Step 4				.58**
Age	-.13	.15	-.09	
MS Duration	.41	.28	.17	
FSS	.23	.14	.19	
Depression	.20	.72	.05	
Anxiety	.74	.65	.19	
COCFS	-.29	.22	-.15	
EF	-.18	.19	-.10	
GSE	-.59	.17	-.44*	

** $p < .001$ * $p < .05$ Note. COCFS: Composite Objective Cognitive Functioning Score; EF: Executive Functioning; FSS: Fatigue Severity Scale; GSE: General Self-Efficacy Scale; PDQ: Perceived Deficits Questionnaire

Quality of life

Hierarchical multiple regression was used to assess the ability of self-efficacy to predict subjective quality of life after controlling for the influence of age, MS duration, depression, anxiety, fatigue and objective cognitive functioning. Age and MS duration were entered into step 1, explaining 7% of the variance of subjective cognitive functioning. After entry of fatigue and HADS scores, step 2 explained 51% variance. After entry of EF and COCFS scores in step 3, the total variance explained by the model as a whole was still 51%, F (7, 37) = 5.40, p <. 001. COCFS did not make a statistically significant contribution. Self-efficacy explained an additional 8% of the variance in subjective cognitive functioning, after controlling for age, MS duration, fatigue, HADS, EF and COCFS, R squared change = .08, F change (1, 36) = 6.61, p = .014. In the final model, only self-efficacy (*beta* = .36, p = .01) was statistically significant (table 3).

Table 3. Hierarchical Regression Analysis for QoL (N = 45)

Variable	*Beta*	*SE(B)*	*β*	*Adjusted R²*
Step 1				.02
Age	-.16	.72	-.03	
MS Duration	-2.11	1.27	-.25	
Step 2				.44**
Age	-.53	.59	-.11	
MS Duration	-.68	1.06	-.08	
FSS	-.88	.55	-.21	
Depression	-6.14	2.57	-.44*	
Anxiety	-2.34	2.57	-.17	
Step 3				.41**
Age	-.52	.61	-.11	
MS Duration	-.67	1.15	-.08	
FSS	-.86	.58	-.21	
Depression	-6.18	2.64	-.44	
Anxiety	-2.36	2.65	-.17	
COCFS	-.04	.88	-.01	
EF	.13	.79	.02	
Step 4				.49**
Age	-.56	.57	-.12	
MS Duration	-.65	1.08	-.08	
FSS	-1.03	.55	-.25	
Depression	-2.99	2.76	-.21	
Anxiety	-1.99	2.47	-.14	
COCFS	.09	.82	.02	
EF	-.09	.74	-.02	
GSE	1.68	.66	.36*	

** $p < .001$, * $p < .05$ Note. COCFS: Composite Objective Cognitive Functioning Score; EF: Executive Functioning; FSS: Fatigue Severity Scale; GSE: General Self-Efficacy Scale; QoL: Quality of Life

Discussion

The results of this study demonstrated significant relationships between subjective cognitive functioning and self-efficacy, depression and anxiety, with a large effect size. In addition, significant relationships, with a medium effect size, were demonstrated between subjective cognitive functioning and fatigue and objective cognitive functioning (COCFS). MS participants who reported more subjective cognitive difficulties also reported greater levels of depression, anxiety and fatigue. They also performed poorer on objective cognitive tests and reported lower levels of self-efficacy. In addition, self-efficacy, depression, anxiety and fatigue were shown to be associated with quality of life in our sample of participants with MS. Participants reporting greater self-efficacy and fewer symptoms of depression, anxiety and fatigue, reported better quality of life. Furthermore, self-efficacy was shown to be a significant predictor of self-reported cognitive difficulties and quality of life even after controlling for age, MS duration, depression, anxiety, fatigue and objective cognitive functioning.

The results of this study corroborate the findings of a number of studies demonstrating associations between subjective cognitive functioning and depression, anxiety [10, 12, 14, 15, 31] fatigue [15, 31] and self-efficacy [16]. Previous studies have demonstrated mixed findings when examining the relationship between subjective cognitive functioning and objective cognitive functioning, using composite scores. The findings of this study are contrary to the findings of Middleton et al. [10], who found no relationship. This study supports the findings of Kinsinger et al. [12] who found a weak relationship.

This study corroborates the findings of previous studies showing self-efficacy to be associated with subjective cognitive functioning [16] and quality of life [16, 18, 21]. This study found that self-efficacy, fatigue, anxiety and depression were all significant predictors of subjective cognitive functioning and quality of life. However, self-efficacy was the only variable to make a unique contribution to both dependant variables when all the other variables were controlled for. Although objective cognitive functioning was associated with subjective cognitive functioning,

this did not make a significant contribution in the regression model and was not associated with quality of life.

This study has demonstrated that self-efficacy is a greater predictor of subjective cognitive functioning and quality of life than objective cognitive functioning, depression, anxiety or fatigue. This has important implications for clinical practice. This research has further demonstrated the importance of a number of variables that are associated with self-appraisal of cognitive functioning, that are not strongly associated with objective cognitive performance. Clinically, this highlights the need for specialist assessments of cognitive functioning and further assessments of self-efficacy, mood and fatigue. Specialist assessments will enable clinicians to develop meaningful formulations about factors underlying inaccurate self-appraisals of cognitive functioning, allowing clinicians to provide feedback to clients about what factors, other than objective functioning, may contribute to perceived cognitive difficulties. People with MS may be reassured to know that their subjective cognitive difficulties could be attributed to other factors, such as low self-efficacy, and not necessarily due to MS related neurological change.

Additionally, self-efficacy could be targeted for intervention. A previous study [12] has demonstrated that interventions aimed at improving depression and fatigue show some success at improving MS patients' accuracy at perceiving their cognitive functioning. However, the findings of this study would suggest that targeting self-efficacy for intervention might be more effective as it was a greater predictor of both subjective cognitive functioning and quality of life, rather than mood or fatigue. Interventions aimed at improving self-efficacy could potentially improve MS patients' accuracy at appraising and reporting their cognitive functioning and improve their quality of life. Self-efficacy has previously been found to be a predictor of psychological adjustment to MS [19], and has been targeted for intervention [18, 20]. Improvements in self-efficacy, using self-management programs [18, 32] and social cognitive wellness programs [33], have been associated with improvements in quality of life. These improvements have been maintained at six month follow up. Additionally, increasing self-

efficacy has also been found to be associated with lower levels of depression, anxiety [34, 35] and fatigue [34]. To the author's knowledge, no longitudinal research studies have examined whether targeting self-efficacy for intervention is related to MS patients' improved accuracy at reporting cognitive functioning.

There are a number of limitations to the present study. There was a small sample size in this study, in order to increase power, the sample size would need to be increased (Appendix E). Additionally, participants were only recruited from MS clinics and there was a short disease duration (M =6.95) potentially leading to a biased sample. This study was also a quasi-experimental design and used correlational analysis, making it difficult to ascertain causality. Future research would benefit from longitudinal research to address the issue of causality.

In sum, this study has demonstrated that self-efficacy is a significant predictor of subjective cognitive functioning and quality of life, even after controlling for objective cognitive functioning, age, MS duration, depression, anxiety and fatigue. Future research would benefit from longitudinal studies targeting self-efficacy in intervention studies. This would help determine whether improvements in self-efficacy lead to improved accuracy at appraising cognitive functioning and improved quality of life in people with MS.

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Appendix

Appendix A

Participant information sheet - People with Multiple Sclerosis

Title of Project: Investigating thinking and memory impairment and wellbeing in people with Neuromyelitis Optica (NMO), Multiple Sclerosis and healthy controls

You are being invited to take part in a research study investigating memory, thinking and wellbeing in people with Neuromyelitis Optica (NMO), Multiple Sclerosis (MS) and people with no neurological condition.

The study consists of completing several thinking and memory tasks and some questionnaires. The study will take between approximately one hour and one hour thirty minutes to complete.

Before you decide to take part it is important that you understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

What is the purpose of this study?

Neuromyelitis Optica is a degenerative condition that may cause blindness and paralysis. For many years it was considered as a type of MS but as there is now a better understanding of differences in symptoms and treatments then it is now important to further investigate how these conditions differ and what life is like for people living with them. A symptom mentioned commonly in both MS and NMO is thinking and memory difficulties; including language, concentration, attention, memory and also changes in mood.

This study will examine these symptoms in a group of people with MS, a group of people with NMO and a group of people with no neurological condition to act as a control group and help better understand differences in thinking and memory and mood symptoms in people with MS or NMO.

The study aims to involve both people who are experiencing difficulties and people who are not, so that we can develop a better understanding of the types of difficulties that different people experience and how common these difficulties are. In addition, we will be asking questions related to your quality of life and how you view your MS, as this can sometimes be linked to how people experience and manage any difficulties they may have.

Do I have to take part?

It is up to you to decide to join the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will happen if I consent to take part?

You will be asked to complete a set of tests that will take approximately an hour and a half.

You will be asked to complete a series of thinking and memory tasks that investigate your thinking, memory, concentration and language. You will also be asked to complete questionnaires that relate to symptoms you might experience and broader aspects of your wellbeing such as mood and symptoms.

These tasks take place at the Walton Centre or we can try to arrange to see you at home if this is preferable to you. Travel expenses will not be paid as it is hoped that these visits can be completed on the same day as your regular clinic appointments at the Walton Centre. If this is not possible then a researcher can visit you at your home.

Why is this research useful?

There is currently little research that helps to inform our understanding of the relationships between thinking processes, and emotional and social wellbeing of people with MS and NMO. Understanding more about this can then help in the management of MS and NMO and inform how health care services can be improved.

What will happen if I don't want to carry on?

You are free to withdraw at any time from the study without giving a reason and without it affecting your future care. If you begin to complete the tests and decide you no longer wish to continue then you can stop at any time. If you chose to withdraw from the study any identifiable data will be destroyed and all non-identifiable data will be retained in the study.

Complaints

If you have a concern about any aspect of this study, you should contact the researchers on the details below and they will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do so in accordance with the NHS complaints procedure by contacting Research Officer Rebecca McDonald on 01515298006.

What are the possible disadvantages and risks of taking part?

We are aware that people with MS often experience fatigue (both thinking and memory and physical). If you feel fatigued at any point then you can take a break or postpone the testing until another time. If you do not feel up to taking part in testing due to ill health then please just let the researcher know and testing can be postponed.

If you are currently experiencing a relapse then you will not be able to participate until you are no longer having a relapse.

It is possible that you may find it upsetting to think about your quality of life or feelings and emotions. Should you wish to stop the study you can do so immediately. Should you wish to skip a question on a questionnaire this is also fine.

What are the benefits of taking part?

Many people with neurological conditions report that there is a lack of information for both patients and health care professionals on the experience of living with these conditions and specifically on thinking and memory difficulties. This study aims to add information on this under-researched area and contribute to the improvement of care for people affected by neurological conditions.

There are however no direct benefits to taking part. You will not receive personalised feedback from this testing as it is not a complete clinical assessment, however general information on cognition and mood can be provided.

Will my taking part be kept confidential?

All information you provide will be treated and stored confidentially, however if you told us anything that raised concerns about your safety or the safety of a vulnerable other then we would have to break confidentiality and pass this information on to the appropriate organisation. In this situation you would be made aware of what information would be reported and to whom.

Some data may be used from your medical records so that we do not ask you to answer questions that we already have information on. This data will only be accessed by members of your clinical care team and will remain confidential.

The consent form containing personal information will be locked in a secure place, and only the research team will have access to it. Any data and written results will be anonymised in accordance with the Data Protection Act 1998.

What will happen to the results of the study?

The results of the study will be used to inform future research and to inform the management of MS and NMO and the types of services that would best support people's needs.

The data will be collected and anonymised so that your results cannot be identified and analysed to write up for peer reviewed journals and for presentation at international conferences. The findings will also be written up in a newsletter and available to all patients.

Who is organising and funding this research?

This research is organised and funded by The Walton Centre for Neurology and Neurosurgery.

Who has reviewed this study?

This study has been reviewed by NRES Committee North West-Greater Manchester West 12/NW/0763.

Finding out more before deciding

If you would like more information on taking part in research in general please contact Patient Advice and Liason Services (PALS) in the Customer Care Team:

Customer Care Team,

The Walton Centre NHS Foundation Trust,

Lower Lane,

Fazakerley,

Liverpool

L9 7LJ

0151 529 5530 or 0151 529 6100

Customer.CareTeam@thewaltoncentre.nhs.uk

If you would like to discuss this study further or if there are any questions you would like to ask, please contact the lead Clinical Neuropsychologist Dr Phil Moore at

The Walton Centre NHS Foundation Trust,

Jubilee House,

Longmoor Lane,

Fazakerley

L9 7LJ

Telephone: 0151 529 5693

Thank you for taking the time to read this information sheet.

CONSENT FORM for people with Multiple Sclerosis

Title of Project: Investigating cognitive function and wellbeing in people with Neuromyelitis Optica, Multiple Sclerosis and healthy controls

Name of Lead Researcher: Dr Phil Moore **Please initial box**

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that relevant data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to this data.	☐
4. I agree that if I disclose information regarding my safety and the safety of vulnerable others then this information will have to be disclosed to the relevant authorities.	☐
5. I agree to take part in the above study.	☐

Name of Participant	Signature	Date
_____	_____	_____
Researcher	Signature	Date
_____	_____	_____

Appendix B

Table 1

Summary of studies included in the review

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
Delorie, Bonnet, Salort, Arimone, Boudineau Petry & Brochet (2006)	Cross-sectional Case control	57	Age: *M* = 37.17 Gender: 75% female MS duration (years): *M* = 2.10	RR: 100%	Community	Yes *N* = 44	SRT SPART SDMT PASAT WLG Stroop Similarities (WAIS-R) BNT RFF	SEP-59	MADRS UKNDS	One cognitive domain, speed of processing correlated with one question about memory complaints on MSQOL (r = .31, p < .02) UKNDS correlated significantly with SEP-90 (r = .35, p < .001) MADRS correlated significantly with UKNDS (r = .43,	Newly diagnosed MS patients only All participants had RR MS Not all subjective domains assessed Depression measure, includes somatic symptoms All RR French participants – generalisable?

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
										$p < .01$)	
Jones (2012)	Cross-sectional	82	Age: *M* = 51.60 Gender: 60% female MS duration (years): *M* = 18.33	RR: 43% SP: 45% PP: 3.7%	Clinic	No	CVLT II Digit Span (WAIS IV) SDMT Animal fluency Stroop BJLOT	PDQ with additional domains assessed	BDI-FS FSS	Significant relationship between PDQ and Stroop (r = -.36, $p < .001$) and PDQ and digit span (r = -.26, $p < .01$) Relationship between fatigue and PDQ is not reported BDI-FS correlated significantly with PDQ (r = .42, $p <$ .001)	No control group Fatigue not included in the analysis Long MS duration Comparatively high mean EDSS scores, indicating moderate to severe disability
Kinsinger & Lattie	Longitudinal	127	Age: *M* = 47.96	RR/SP/PR:	Community and clinic	No	COWAT Digit Span &	PDQ	HDRS (telephone	PDQ correlated with objective cognitive	MS patients with severe cognitive

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
(2010)	RCT		Gender: 77% female MS duration (years): *M* = 11.24	89%, PP: 10%,			Letter-Number sequencing (WAIS-III) CVLT-II		version) MFIS	performance at pre (*r* = -.23, *p* < .01) and post treatment (*r* = -.37, *p* < .01) PDQ correlated with MFIS at pre (*r* = .67, *p* < .001) and post treatment (*r* = .68, *p* < .001) PDQ correlated with HDRS at pre (*r* = .37, *p* < .001) and post treatment (*r* = .45, *p* < .001)	impairment were excluded All patients experiencing depression Neuropsychological tests were administered via telephone No objective measure of processing speed Depression measure - includes somatic symptoms
Marrie, Chelune, Miller &	Cross-sectional Correlation	136	Age: *M* = 45.65	RR: 71%	Clinic	No	WAIS WMS	PDQ	MHI MFIS	Multivariate logistic regression demonstrated subtests	All participants had subjective cognitive complaints

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
Cohen (2005)			Gender: 69% female MS duration: not stated	SP/PP: 29%						of WAIS and WMS are associated with being subjectively impaired independent of emotional status, physical disability, fatigue and age Increasing physical fatigue was associated with increased odds of subjective impairment Poor emotional status was associated with increased odds of subjective impairment	Depression measure – very short screening measure (4 questions)

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
Middleton, Denny, Lynch & Parmenter (2006)	Cross-sectional Case control	221	Age: *M* = 44.8 Gender: 74% female MS duration (years): *M* = 6.5	RR: 65% SP: 21% PP: 12% PR: 2%	Clinic	Yes *N* = 31	TOL CVLT-II PASAT SRT WLG	CFQ Performance estimates	CES-D FSS	No correlation was found between CFQ and objective cognitive functioning. CFQ significantly correlated with FSS (r = .41, p < .001) CES-D significantly correlated with CFQ (r = .52, p < .001)	CFQ does not assess all cognitive domains associated with MS Depression measure, includes somatic symptoms
Roberg Bruce, Lovelace & Lynch (2012) – study 1	Cross-sectional Correlation	40	Age: *M* = 48.58 Gender: 85 % female MS duration	RR: 80% SP: 18% PP:	Community	Yes *N* = 25	SDMT Stroop PASAT LNS AVLT COWAT CPT II	PSDS	CMDI MFIS	PSDS associated with commission errors on CPT II (r = .51, p < .001) and motor slowing on FTT (r = -.35, p < .05)	Only subjective cognitive domain assessed was speed of processing Depression measure – includes somatic

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
			(years): *M* = 11.53	2%			FTT			PSDS significantly associated with fatigue (r = .54, p < .001) No association between PSDS and depression	symptoms Large proportion of females
Roberg, Bruce, Lovelace & Lynch (2012) – study 2	Cross-sectional Correlation	79	Age: *M* = 47.1 Gender: 90 % female MS duration (years): *M* = 10.96	RR: 90% SP: 10%	Clinic	Yes *N* = 20	SDMT Stroop LNS AVLT (modified)	PSDS	BDI-FS MFIS	More self-reported processing speed difficulties only marginally associated with Stoop (r = -.27, p = .016) and SDMT (r = -.28, p = .014) PSDS significantly associated with fatigue (r = .57, p <	All participants recruited for medication-adherence study, presumably all taking medication Only subjective cognitive domain assessed was speed of processing

Study	Study type and design	*N*	Characteristics	Type of MS	Recruited from	Control group	Objective cognitive tests	Subjective cognitive measure	Depression and fatigue measure	Findings	Limitations
										.001) PSDS marginally associated with depression (r = .28, p = .013) Stepwise regression demonstrated only extroversion (R^2 = .21, p = <.001) and trait anxiety (R^2 = .10, p = <.001) accounted for unique variance in PSDS	Large proportion of females Limited objective cognitive domains assessed.

Note. AVLT = Auditory Verbal Learning Test; BJLOT = Benton Judgement Line Orientation Test; BNT = Boston Naming Test; BDI – FS = Beck Depression Inventory – Fast Screen; CES-D = Centre for Epidemiologic Studies – Depression Questionnaire; CFQ = Cognitive Failures Questionnaire, CMDI = Chicago Multiscale Depression Inventory; COWAT = Controlled Oral Word Association Test – FAS Version; CPT II = Connors' Continuous Performance Test II, CVLT = California Verbal Learning Test, FTT = Finger Tapping Test; FIS = Fatigue Impact Scale, FSS = Fatigue Severity Scale; LNS = Letter Number Sequencing from Wechsler Adult Intelligence Scale III, HDRS = Hamilton Rating Scale for Depression; MADRS = Montgomery and Asberg Depression Rating Scale; MFIS = Modified Fatigue Impact Scale; MHI = Mental

Health Inventory; MSQOL = Multiple Sclerosis Quality of Life Scale; PASAT = Paced Auditory Serial Addition Test; PDQ = Perceived Deficits Questionnaire; PSDS = Processing Speed Difficulties Scale; RFF = Ruff Figural Fluency Test; SDMT = Symbol Digit Modalities Test; SEP - 59 = Self-Administered Health Related Quality of Life Questionnaire; SPART = Spatial Recall Test; SRT = Selective Reminding Test, TOL = Tower of London; UKNDS = UK Neurological Disability Scale; WAIS = Wechsler Adult Intelligence Scale; WAIS-R = Wechsler Adult Intelligence Scale – Revised; WLG = Word List Generation, WMS =Wechsler Memory Scale

Table 2

Quality review table

	Delorie, Bonnet, Salort, Arimone, Boudineau, Petry & Brochet (2006)	Jones (2012)	Kinsinger & Lattie (2010)	Marrie, Chelune, Miller & Cohen (2005)	Middleton, Denny, Lynch & Parmenter (2006)	Roberg Bruce, Lovelace & Lynch (2012) – Study 1	Roberg Bruce, Lovelace & Lynch (2012) – Study 2
Explicit theoretical framework	3	3	3	3	3	3	3
Aims/objectives in main body of report	3	3	3	3	3	3	3
Clear description of research setting	3	3	2	3	2	2	2
Evidence of sample size considered in terms of analysis	0	3	0	0	0	0	0
Representative sample of target group of reasonable size	2	2	2	2	2	1	2
Description of procedure for data collection	1	3	3	1	3	1	1

	Delorie, Bonnet, Salort, Arimone, Boudineau, Petry & Brochet (2006)	Jones (2012)	Kinsinger & Lattie (2010)	Marrie, Chelune, Miller & Cohen (2005)	Middleton, Denny, Lynch & Parmenter (2006)	Roberg Bruce, Lovelace & Lynch (2012) – Study 1	Roberg Bruce, Lovelace & Lynch (2012) – Study 2
Rationale for choice of data collection tools	2	3	1	2	2	2	2
Detailed recruitment data provided	1	2	3	2	2	1	1
Statistical assessment of reliability/validity of data collection tools	1	3	3	0	0	1	1
Fit between stated research question and method of data collection	3	3	2	3	3	3	3
Fit between research question and method of analysis	3	3	3	3	3	3	3
Good justification for analytical method selected	3	3	3	3	1	2	2
Evidence of user involvement in design	0	0	0	0	0	0	0

	Delorie, Bonnet, Salort, Arimone, Boudineau, Petry & Brochet (2006)	Jones (2012)	Kinsinger & Lattie (2010)	Marrie, Chelune, Miller & Cohen (2005)	Middleton, Denny, Lynch & Parmenter (2006)	Roberg Bruce, Lovelace & Lynch (2012) – Study 1	Roberg Bruce, Lovelace & Lynch (2012) – Study 2
Strengths and limitations critically discussed	2	3	2	2	1	2	2
Total	27	37	30	27	25	24	25

Appendix C

Author guidelines: Health Psychology Review

Full guidelines:

www.tandfonline.com/action/authorSubmission?journalCode=rhpr20&page=instructions#.U4IkUfldVNM

General guidelines

- Manuscripts are accepted in English. British English spelling and punctuation are preferred. Please use single quotation marks, except where 'a quotation is "within" a quotation'. Long quotations of 40 words or more should be indented without quotation marks.
- The editorial team acknowledge that review articles are usually longer than empirical articles. However, it is also recognised that articles should be concise and pithy so that the main focus of the article is not lost and the argument is not encumbered by unnecessary detail. Articles to *Health Psychology Review* should therefore be no longer than 30 double-spaced manuscript pages in length with 2.4cm margins (minimum) including abstract, main text, references, footnotes, figures and tables. Authors can include additional figures and tables not directly germane to the main argument of the manuscript as online supplemental materials. For meta-analyses and systematic reviews, references for studies included in the review should be only appear in a separate supplemental list that the journal will make available as an online supplement. These materials will not count toward the page length of the manuscript, but will be included as a permanent record of supplemental materials alongside the online version of the manuscript (see later). Manuscripts should be compiled in the following order: title page; abstract; keywords; main text; acknowledgements; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figure caption(s) (as a list).
- Abstracts of 200 words are required for all manuscripts submitted.

- Each manuscript should have 3 to 6 keywords .
- Search engine optimization (SEO) is a means of making your article more visible to anyone who might be looking for it. Please consult our guidance.
- Section headings should be concise.
- All authors of a manuscript should include their full names, affiliations, postal addresses, telephone numbers and email addresses on the cover page of the manuscript. One author should be identified as the corresponding author. Please give the affiliation where the research was conducted. If any of the named co-authors moves affiliation during the peer review process, the new affiliation can be given as a footnote. Please note that no changes to affiliation can be made after the manuscript is accepted. Please note that the email address of the corresponding author will normally be displayed in the article PDF (depending on the journal style) and the online article.
- All persons who have a reasonable claim to authorship must be named in the manuscript as co-authors; the corresponding author must be authorized by all co-authors to act as an agent on their behalf in all matters pertaining to publication of the manuscript, and the order of names should be agreed by all authors.
- Biographical notes on contributors are not required for this journal.
- Please supply all details required by any funding and grant-awarding bodies as an Acknowledgement on the title page of the manuscript, in a separate paragraph, as follows:
- *For single agency grants:* "This work was supported by the [Funding Agency] under Grant [number xxxx]."
- *For multiple agency grants:* "This work was supported by the [Funding Agency 1] under Grant [number xxxx]; [Funding Agency 2] under Grant [number xxxx]; and [Funding Agency 3] under Grant [number xxxx]."

- Authors must also incorporate a Disclosure Statement which will acknowledge any financial interest or benefit they have arising from the direct applications of their research.
- For all manuscripts non-discriminatory language is mandatory. Sexist or racist terms must not be used.
- Authors must adhere to SI units . Units are not italicised.
- When using a word which is or is asserted to be a proprietary term or trade mark, authors must use the symbol ® or TM.

Appendix D

My role in the research

This study was a component of a larger study investigating cognitive functioning and subjective wellbeing in Neuromyelitis Optica (NMO), Multiple Sclerosis (MS) and healthy controls. The primary aim in the larger study is to investigate the prevalence of cognitive impairment in patients with NMO, MS and healthy controls. The secondary aim, in the larger study, is to investigate quality of life, emotion well-being, and self-efficacy. This study already had ethical approval.

The research question for this study was developed from the secondary aim of the larger study. This was developed by me, in conjunction with my supervisors. Based on the research question, an ethical amendment was submitted and approved, permitting the recruitment of additional participants. I personally recruited and assessed 35 participants. I also scored, input and analysed all of the MS data.

Appendix E

Power calculation

Faul et al. [1] provide guidelines for using G*Power to determine sample size and power. A medium and large effect size was demonstrated for the quality of life and the perceived deficits hierarchical regression respectively. The R^2 values for the quality of life regression (.51 for step 3 and .58 for step 4) were converted to an f^2 value (0.18). This f^2 value was entered into G*Power to determine whether there was an adequate sample size. Based on a medium effect size using an $\alpha = 0.05$, with one tested predictor variable (self-efficacy) and eight total predictor variables (age, MS duration, fatigue, anxiety, depression, composite objective cognitive functioning, executive functioning and self-efficacy) and an 80% chance of power being detected, 45 participants were required for this study.

References

1. Faul F, Erdfelder E, Buchner A and Lang A. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods,*. 2009; 41: 1149-60.

Appendix F

Neuropsychological tests

Visual Reproduction

A visual memory test from the Wechsler Memory Scale WMS IV, [1] examining immediate, delayed recall and delayed recognition. Test retest reliability has been measured at r=0.93 for the immediate recall task and r=0.97 for the delayed recall task [1].

Symbol Digit Modalities Test SDMT, [2]

The SDMT is a measure of information processing speed. The test can be used with participants with motor impairments as it requires verbal responses. The test-retest reliability has been measured at between r = 0.82 and r=0.95 within a MS population [3].

California Verbal Learning Test-II [4]

A test of verbal learning and memory, and is the most commonly used measure of memory within the MS population. The CVLT-II has been found to have high test-retest reliability (r=0.80 to r=0.89) for the immediate recall tasks, and adequate reliability for the long delay task (r=0.70 to r=0.79) [4].

Hayling [5]

A clinical test of executive functioning, specifically measuring response ignition and suppression, that is suitable for people with visual and motor impairments. Test retest reliability has been demonstrated between r=0.62 to r=0.78 [5].

Verbal fluency

The verbal fluency is a component of the Delis-Kaplan Executive Functioning System [6]. A test of verbal, category and switching fluency used to assess executive functioning. Test-retest reliability, for adults aged 18-89, ranges from r=0.77 to r=0.90, r=0.60 to r=0.76 and r=0.51 to r=0.72 for verbal, category and switching fluency respectively [6].

Digit Span

The Digit Span task is a subtest that forms part of the Wechsler Adult Intelligence Scale fourth Edition WAIS-IV, [7]. It is a measure of auditory attention and working memory. The measure has been found to have test-retest reliability at r=0.93 [8]

References

1. Wechsler D, Holdnack J and Whipple Drozdick L. *WMS-IV technical and interpretive manual*. San Antonio, USA: Pearson Inc, 2009.

2. Smith A. *Symbol digit modalities test (SDMT)*. Los Angeles, USA: Western. Psychological Services, 1991.

3. Benedict R, Duquin J, Munschauer F, et al. Repeated assessment of neuropsychological deficits in multiple sclerosis using the symbol digit modalities test and the MS neuropsychological screening questionnaire. *Multiple Sclerosis*. 2008; 14: 940-6.

4. Delis D, Kaplan E, Kramer J and Ober B. *California verbal learning test–II*. San Antonio, USA: The Psychological Corportation, 2000.

5. Burgess P and Shallice T. *The hayling and brixton tests*. Suffolk, UK: Thames Valley Test Company Ltd, 1997.

6. Delis D, Kaplan E and Kramer J. *Delis-Kaplan executive functioning system: Technical manual*. San Antonio, USA: Pearson Inc, 2001.

7. Wechsler D. *Wechsler memory scale: Fourth edition*. San Antonio, USA: Pearson Inc, 2008.

8. Wechsler D, Coalson D and Rngi Raiford S. *WAIS IV technical and interpretive manual*. San Antonio, USA: Pearson Inc, 2008.

Appendix G

Data screening analysis

Prior to conducting statistical analysis, preliminary analyses were performed to ensure parametric assumptions were met.

Multicollinearity

Tolerance and VIF values were produced to check the assumption of multicollinearity. Pallant [1] suggests that low tolerance values, under .10, and high VIF values, over 10, suggests the possibility of multicollinearity. The tolerance value for each independent variable was below .10 and the VIF values were above 10 for both regression analyses.

Outliers, normality, linearity, homoscedasticity and independence of residuals

P-P plots were produced with data points falling close to the diagonal line, suggesting no major deviations from normality. Scatterplots were also produced and the standardised residuals were roughly rectangularly distributed. The scatterplot was also examined for the presence of outliers. Additionally, the presence of outliers was assessed by examining the Mahalanobis distance and Cook's distance. Pallant (2013) recommends a Mahalanobis value of less than 24.32 with seven predictor variables, and a Cook's distance of less than 1. Manhalanobis and Cook's distance were in the recommended range for both regression analyses.

Missing Data

Three participants were unable to complete the visual memory drawing task due to motor and sensory difficulties in their arm or hand. A further participant was unable to complete the visual memory task, category fluency and verbal fluency due to unexpected time constraints. This represented less than 3% of the total objective cognitive functioning data. Schafer [2] suggests this is in within the recommended range of fewer than 5%. There was no missing data for any other variables.

References

1. Pallant J. *SPSS survival manual: 6th edition*. New York: McGraw-Hill Companies, 2010.

2. Schafer JL. Multiple imputation: a primer. *Statistical Methods in Medical Research*. 1999; 8: 3-15.

Appendix H

Author guidelines: Multiple Sclerosis Journal

Full guidelines: http://www.uk.sagepub.com/msg/msj.htm

Article Type	Abstract	Main text	References	Figures/Tables
Research paper	200	3000*	Up to 35	As necessary

*excludes references, tables and legends

Original research papers should be no more than 3,000 words and contain the following sections: Title page, Abstract, Introduction, Materials (or patients or animals) and Methods, Results, Discussion, Acknowledgements, References, Tables, Figure legends, Figures (see 'Sections of the manuscript' for further details).

Journal Style

Multiple Sclerosis Journal conforms to the SAGE house style. Click here to review guidelines on SAGE UK House Style

In addition to the details in the above style guide, please note the following:

Units, symbols and abbreviations

For detailed advice please refer to the guidelines in Baron, DN (1988). Units, symbols and abbreviations, 4th edn. (Obtainable from The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE, UK). Note that the SI system of units is preferred. Because of the multidisciplinary nature of the readership and to avoid confusion, the number of abbreviations in the text should be kept to a minimum. Standard abbreviations acceptable without definition are limited to the following:

CNS (central nervous system); CSF (cerebrospinal fluid); DNA (deoxyribonucleic acid); HLA (human leukocyte antigen; MRI (magnetic resonance imaging); CT (computerized tomography); MS (multiple sclerosis); RNA (ribonucleic acid). Nonstandard definitions

must be defined in full at their first usage in the abstract and again at their first use in the text.

Reference Style

Multiple Sclerosis Journal adheres to the SAGE Vancouver reference style. Click here to review the guidelines on SAGE Vancouver to ensure your manuscript conforms to this reference style.

If you use EndNote to manage references, download the SAGE Vancouver output file by following this link and save to the appropriate folder (normally for Windows C:\Program Files\EndNote\Styles and for Mac OS X Harddrive:Applications:EndNote:Styles). Once you've done this, open EndNote and choose "Select Another Style..." from the dropdown menu in the menu bar; locate and choose this new style from the following screen. Alternatively visit the EndNote website and search the Styles section for 'SAGE Vancouver'.

Manuscript Preparation

Submitting a new manuscript through the online system:

When making a submission, the following *separate*, *unpaginated* documents should be uploaded. Please do not submit one combined document. The separate files will be combined into a pdf in the online system.

1. Title page (title, names of authors, affiliations, keywords, corresponding author)
2. Main document (includes structured abstract, main text, acknowledgements, references)
3. Tables (each as a *separate* Word document)
4. Figure legends (Word document)
5. Figures (as *separate* tiff, jpg or eps files)
6. Any supplementary files

Title page

The title should be concise with no abbreviations. Please provide the surname, initials, department, institution, city and country of each author, and the name, email address, full mailing address, telephone number and fax number of the corresponding author to whom proofs should be sent. List six to eight keywords (chosen from Index Medicus, Medical Subject Headings if possible).

Abstract

The second page of the manuscript must contain only the abstract, which should be of no more than 200 words and must be clearly written and comprehensive to readers before they have to read the paper. The abstract should be structured according to the following sub headings: Background, Objective, Methods, Results and Conclusion. Abbreviations should be avoided and reference citations are not permitted.

Any manuscripts submitted without a structured abstract will be returned to the author immediately without peer review, thus delaying the evaluation process of the manuscript.

Introduction

The introduction should assume that the reader is knowledgeable in the field and be as brief as possible.

Materials and Methods

Methods that have been published in detail elsewhere should not be described in detail. Avoid unnecessary detailed descriptions of widely used techniques. SI Units should be used throughout the text. Reports of experiments involving patients and healthy volunteers must describe the steps taken to obtain consent and to maintain confidentiality. Experiments involving animals must conform to accepted ethical standards.

Tables

Tables should be submitted in Word, typed on separate pages. Tables should be numbered

consecutively with Arabic numerals, and cited as such in the manuscript. The preferred placing of tables in the main text should be indicated. Tables should include a brief descriptive title and be self-explanatory. Footnotes to tables indicated by lower-case superscript letters are acceptable, but they should not include extensive experimental details.