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Beyond Depression: Predictors of Self-reported Cognitive Function in Adults Living with MS

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Abstract

Objective—To investigate the association between self-reported cognition and demographic/ psychosocial variables in individuals with a self-reported diagnosis of multiple sclerosis (MS).

Design—Secondary longitudinal analysis of mailed self-report surveys over a period of 2 years.

Setting—Community.

Participants—407 community-dwelling individuals from the Pacific Northwest with a self-reported diagnosis of MS.

Interventions—Not applicable.

Main Outcome Measures—Subjective general cognitive concerns and subjective executive difficulties as measured by the Neuro-QOL Applied Cognition–Executive Function–Short Form (SF) and the Applied Cognition–General Concerns–SF.

Results—Univariate and multiple linear regression analyses were used to identify statistically significant longitudinal predictors of perceived cognitive difficulties 2 years later. Fatigue and anxiety were statistically significant predictors of general cognitive concerns. Fatigue and perceived stress were statistically significant predictors of perceived executive difficulties. Fatigue was the strongest predictor in both models.

Conclusions—In MS, perceived cognitive impairment is frequently linked to depression without consideration of other possible contributors. This study suggests that in people with MS, fatigue is a stronger predictor of self-reported cognitive function two years later than depression

Keywords

multiple sclerosis; metacognition

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Introduction

Metacognition, or self-perceived cognitive functioning, has been studied in a variety of populations including aging (Jorm, Christensen, Korten, Jacomb, & Henderson, 2001; Slavin et al., 2010; R. Stewart, 2012), cancer (Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012; Poppelreuter et al., 2004; Pullens, De Vries, & Roukema, 2010), traumatic brain injury (Belanger, Kretzmer, Vanderploeg, & French, 2010; Gass & Apple, 1997; Russo, 2012; Spencer, Drag, Walker, & Bieliauskas, 2010), fibromyalgia(Suhr, 2003), chronic fatigue syndrome (Knoop, Prins, Stulemeijer, van der Meer, & Bleijenberg, 2007; Metzger & Denney, 2002), multiple sclerosis (Benedict et al., 2008; Benedict et al., 2003; Bruce, Bruce, Hancock, & Lynch, 2010; Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman, 2005; Julian, Merluzzi, & Mohr, 2007b; Kinsinger, Lattie, & Mohr, 2010; O'Brien et al., 2007), and others (Bosma & Kessels, 2002; Hinkin et al., 1996; Shin, Katz, & Julian, 2012). When self-reported difficulties are compared to objective neuropsychological data, the findings are mixed. While some studies have found a relationship between perceived and objective cognitive decline (Randolph, Arnett, & Higginson, 2001; A. Stewart et al., 2008), most have found that self-reported impairment is influenced by, and often correlated with, emotional distress (Akbar, Honarmand, & Feinstein, 2011; Hutchinson et al., 2012; Kinsinger et al., 2010; Middleton, Denney, Lynch, & Parmenter, 2006; O'Brien et al., 2007; Shin et al., 2012; Spencer et al., 2010).

This is also true of multiple sclerosis (MS) (Akbar et al., 2011; Kinsinger et al., 2010; Middleton et al., 2006; O'Brien et al., 2007). MS is a chronic heterogeneous disease characterized by central nervous system inflammation and neurodegeneration. Individuals with MS commonly have a complex constellation of physical and psychosocial symptoms. Objective neuropsychological deficits found by neuropsychological testing are common and can effect up to 34-65% of individuals (Benedict et al., 2006; Olazaran et al., 2009; Rao, Leo, Bernardin, & Unverzagt, 1991). Although there is considerable variability in cognitive symptoms among individuals with MS, the most common symptoms include: slowed processing speed and difficulty with visual and verbal memory – particularly impaired acquisition of new information (Chiaravalloti & DeLuca, 2008; Deluca, Barbieriberger, & Johnson, 1994; DeLuca, Gaudino, Diamond, Christodoulou, & Engel, 1998; Thornton, Raz, & Tucker, 2002). Medical providers may rely on patient self-report to help screen for cognitive decline. Unfortunately, metacognition can be impaired (Akbar et al., 2011), making self-reported symptoms potentially unreliable.

Likely because of its high prevalence in MS (Ehde & Bombardier, 2005), depression is the most commonly studied psychological variable influencing metacognition. Studies report that perceived neurocognitive functioning is indeed more strongly associated with depression than with objective neuropsychological findings (Benedict et al., 2008; Julian, Merluzzi, & Mohr, 2007a). However, people with MS often report a large number of symptoms concurrently, some of the most common being: fatigue, pain, depression, anxiety, and sleep disturbance (Kraft et al., 2008). Recent research, both within and outside of MS, suggests that depression is not the only predictor of perceived cognitive impairment. Elevated anxiety (Akbar et al., 2011; Bruce et al., 2010), psychosocial stress (van der Hiele, Spliethoff-Kamminga, Ruimschotel, Middelkoop, & Visser, 2012), changes in personality

(Akbar et al., 2011; Benedict, Priore, Miller, Munschauer, & Jacobs, 2001), and fatigue (Kinsinger et al., 2010) have also been reported to influence self-report in MS. Outside of MS, sleep disturbance (Weber, Mapstone, Staskiewicz, & Maki, 2012), pain and gender (female) have been associated with cognitive complaints (Roth, Geisser, Theisen-Goodvich, & Dixon, 2005).

So far metacognition studies in MS have evaluated psychosocial constructs independently or with relatively few constructs (e.g., anxiety and personality (Akbar et al., 2011), depression and fatigue (Kinsinger et al., 2010)) which calls external validity into question. Such studies have also been nearly exclusively cross-sectional in design. Longitudinal data were examined in the context of two treatment trials, one for depression (Julian et al., 2007b) and the other a behavioral treatment of cognitive impairment (Christodoulou et al., 2005). Individuals with MS were able to better estimate actual neuropsychological performance with the remittance of depression symptoms (Julian et al., 2007b). Individuals in the cognitive rehabilitation trial were able to perceive changes in cognitive functioning, but not always accurately predict actual performance at any singular time-point (Christodoulou et al., 2005).

Measures such as the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ), a 15-item self-report questionnaire (Benedict et al., 2003), and the Perceived Deficits Questionnaire (PDQ) (Sullivan, Edgley, & Dehoux, 1990), a 20-item self-report measure that is part of the Multiple Sclerosis Quality of Life Inventory (Vickrey, Hays, Harooni, Myers, & Ellison, 1995), were developed as clinical and research screening tools for MS-related cognitive change. These, like most subjective report, are highly correlated with emotional distress (O'Brien et al., 2007). Becker and colleagues (Becker, Stuifbergen, & Morrison, 2012) suggest that new-generation self-report measures may be a more suitable alternative.

The Applied Cognition–Executive Function–Short Form (NeuroQOL-EF) and the Applied Cognition–General Concerns–Short Form (NeuroQOL-GC) are two such measures. The item banks and the short forms derived from them were developed with funding from the National Institute of Neurologic Diseases and Stroke (NINDS).These item response theory based measures were developed as part of a multi-site, multi-step project to create patient reported outcomes that are brief, reliable, valid, consistent, and can be used as primary or secondary outcomes measures in clinical research. The item banks for these measures were created via extensive literature review, expert input, patient and caregiver focus groups, existing questionnaires, and various factor analytic techniques. (Cella et al., 2011; Gershon et al., 2012; "PROMIS: Dynamic Tools to Measure Health Outcomes from the Patient Perspective,").

Using the NeuroQOL metacognition measures as the primary outcome, we sought to examine the demographic and psychosocial constructs that predict perceived cognitive impairment two years after baseline. We decided to look at these relationships longitudinally because many contemporary studies have focused on cross-sectional relationships that cannot be used to identify predictors that may signal a distal outcome of interest (such as cognitive deficit) and because longitudinal studies are needed to study change. Psychosocial variables were chosen that measure common symptoms in MS and have been associated with perceived cognition in the literature. We hypothesized that the included psychosocial variables (fatigue, depression, anxiety, perceived stress, wakefulness, sleep disturbance and pain) would be significantly correlated with and predict metacognition over time.

METHODS

Participants and Procedures

This secondary analysis used data collected as a part of an ongoing longitudinal survey tracking symptoms and quality of life in people with MS. Previous publications from this dataset (Fisk et al., 1994; Gershon et al., 2012; "National Institute of Neurological Disorders and Stroke (NINDS). User Manual for the Quality of Life in Neurological Disorders (Neuro-QOL) Measures ", September 2010) have described recruitment procedures and reported on findings related to sleep, fatigue, and communication. Briefly, adults with MS were recruited from the mailing list of the Greater Northwest chapter of the National MS Society. Participants were mailed a paper survey. Participants were eligible if they were age 18 or older and self-reported being diagnosed with MS by a physician. Research from the NARCOMS data registry supports the validity of using self-reported diagnosis (Marrie, Cutter, Tyry, Campagnolo, & Vollmer, 2007). However, to discourage potential participants without MS from participating: (1) questions were asked that a person unfamiliar with the disease would have difficulty answering, (2) research staff followed up by phone if answers were unclear or inconsistent, and (3) participants were asked to provide contact information for their diagnosing or treating physician. If there was a doubt about a diagnosis of MS, the participant was excluded.

Of the participants in the baseline survey (N=1270) a randomly selected subset of participants were invited to continue in the longitudinal study. Of the selected subset, 562 participants completed T2 surveys. The surveys were administered every four to five months over a two-year period and then once a year. If participants were significantly delayed in returning (or did not return) surveys they were dropped from future mailings.

Data for this study were collected in 2008 (T5, approximately 20 months post-baseline; “baseline”) and 2010 (T8, about 42 months post baseline; “follow-up”). The 20-month follow-up survey represents the first year that the NeuroQOL measures (NeuroQOL-EF and NeuroQOL-GC) were administered (see below). Of the 470 participants who were sent the 20-month survey, 461 (98%) completed it. A total of 407 individuals completed the survey at both the 20 and 42-month timepoints and are included in this analysis. The average difference in time between the two data timepoints included in this study is 22.7 months (range: 18.7 – 26.1 months). The Human Subjects Division at the University of Washington approved all study procedures, participants provided informed consent, and were paid $25 for completing the surveys at each time point.

Measures

Cognition—The Applied Cognition–General Concerns–Short Form (NeuroQOL-GC) is an 8-item short form based on the IRT-based item bank measuring perceived cognitive dysfunction (Gershon et al., 2012). Items in the item bank ask about perceived difficulty over the past 7 days with multitasking, thinking clearly (e.g., "I had trouble thinking clearly"), attention, and concentration. The Applied Cognition–Executive Function–Short Form (NeuroQOL-EF) is an 8-item questionnaire measuring perceived dysfunction in higher order cognitive tasks such as planning, organizing, working memory, and mathematics (Gershon et al., 2012); sample question: "How much difficulty do you currently have … managing your time to do most of your daily activities?" For both measures, individual responses (e.g., 1 = Not at all, 2 = A little bit, 3 = Somewhat, 4 = Quite a bit, 5 = Very Much) are summed and converted into Item Response Theory (IRT) based scores on a T-score metric. Standardized T-scores have a mean of 50 and a standard deviation (SD) of 10. ("National Institute of Neurological Disorders and Stroke (NINDS). User Manual for the Quality of Life in Neurological Disorders (Neuro-QOL) Measures ", September 2010) Intraclass correlations (test-retest reliability) in a sample of people with stroke were good, ranging from .73-.94.

Fatigue—In MS, fatigue has been defined as a "reversible, motor and cognitive impairment with reduced motivation and desire to rest, either appearing spontaneously or brought on by mental or physical activity, humidity, acute infection and food ingestion" (Mills & Young, 2008). The Modified Fatigue Impact Scale (MFIS) is an abbreviated 21-item version of the 40-item Fatigue Impact Scale (Fisk et al., 1994). It was recommended for research and clinical practice in 1998 by the Multiple Sclerosis Council for Clinical Practice Guidelines ("Multiple Sclerosis Council for Clinical Practice Guidelines. Fatigue and multiple sclerosis: Evidence-based management strategies for fatigue in multiple sclerosis," 1998). The scale measures how fatigue impacts physical, cognitive and psychosocial functioning (Tellez et al., 2005). Items are endorsed on a Likert scale of 0 (never) to 4 (almost always) with an overall score ranging from 0 to 84 (Flachenecker et al., 2002). An example item includes: "I have been less able to complete tasks that require physical effort." Higher scores on the MFIS indicate a greater impact of fatigue on one's life (Noonan et al., 2012). In a European sample of individuals with MS the scale demonstrated internal consistency of 0.92 for the total score (Kos et al., 2005).

Depression—Depression was assessed using the PHQ-9 subscale from the Patient Health Questionnaire (PHQ). Each of the nine questions coincides with one of the nine criteria listed in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) for major depressive disorder (e.g., "Over the last 2 weeks, how often have you been bothered by … feeling down, depressed, or hopeless"). The questions are answered using a Likert scale ranging from zero to three (0 = not at all, 1 = several days, 2 = more than half the days and 3 = nearly every day). Depression symptom severity is determined using the total score of all endorsed questions. The PHQ-9 was validated on a sample of 3,000 primary care patients and 3,000 obstetrics-gynecology patients. The overall sensitivity and specificity of the questionnaire was 84% and 72% respectively (Kroenke, Spitzer, & Williams, 2001).

Stress—The Perceived Stress Scale was originally developed as a 14-item measure for use in community samples. Two additional shorter versions (10-item and 4-item) were also validated (Cohen, 1988). The present study uses the 4-item version. The measure asks participants to reflect on how overwhelming, unpredictable or uncontrollable their lives have been over the past month (e.g., "In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?") (Cohen, 1988). Total scores range from 0 to 16 with higher scores indicative of more stress. A publication providing population normative data for the 4-item version demonstrated acceptable internal consistency with a Cronbach's alpha of 0.77 (Warttig, Forshaw, South, & White, 2013).

Anxiety—The PROMIS Anxiety questionnaire measures "Unpleasant thoughts and/or feelings related to fear (e.g., fearfulness, feelings of panic), helplessness, worry and hyperarousal (e.g., tension, nervousness, restlessness)" (Pilkonis PA, 2011). An example item states, "In the past 7 days … I felt fearful". As is true with all PROMIS instruments, the IRT-based score is on a T-score metric with a mean of 50 and SD of 10. The mean represents the mean score of the US general population. A higher score indicates more anxiety.

Pain—The PROMIS Pain Interference PROMIS-PI (Amtmann et al., 2010) measures the degree to which pain limits or interferes with individuals' physical, mental and social activities (e.g., "In the past 7 days … how much did pain interfere with your day to day activities?"). A higher PROMIS-PI score indicates more pain interference. The scores are IRT-based with a mean of 50 and SD of 10. The score of 50 represents the average score of the general US population.

Sleep-Wake Disturbance—The PROMIS Sleep Disturbance item bank consists of 27 items (e.g., "In the past 7 days … I had difficulty falling asleep") assessing overall sleep quality and satisfaction (Buysse DJ, 2010). The PROMIS Sleep-related Impairment (SRI) item bank consists of 16 questions (e.g., "In the past 7 days … I had a hard time getting things done because I was sleepy") that assess daytime impairment that is the result of poor sleep (Buysse DJ, 2010). Short forms of both measures (i.e., sleep disturbance and sleep-related impairment) were used in this study. They have a 7-day time frame and higher scores indicate greater sleep disturbance or sleep-related impairment. Scores are IRT-based with a mean of 50 and SD of 10; 50 represents the average score for the US general population.

Expanded Disability Status Scale (EDSS)—Data for this study was collected via survey; therefore a self-report version of EDSS was used to assess MS-related disease progression. This version has been shown to be highly correlated with physician administered EDSS (Bowen J, 2001). Participants were divided into three categories: no use of mobility aid or minimal severity (≤ 4), use of bilateral or unilateral mobility aid or intermediate severity (4.5-6.5), and use of a wheelchair for mobility or advanced severity (≥ 7).

MS-Type—MS clinical course was assessed using a self-report measure (Bamer, Cetin, Amtmann, Bowen, & Johnson, 2007) developed for use in research where physician confirmation of course is impractical or impossible. The measure asks respondents to select from one of five graphic images with corresponding descriptions of each image, resulting in classification in to one of the following courses: relapsing remitting, secondary progressive, primary progressive, and progressive relapsing. A validation study found substantial agreement between the self-administered measure and a physician-assessed disease course (K= 0.45) (Bamer et al., 2007).

Statistical Analysis

Descriptive statistics for demographic data (percentages, mean, and standard deviation) are presented from baseline. Pearson product-moment correlation coefficients were used to examine the relationship of demographic and psychosocial variables with the outcome measures of general cognitive concerns and perceived executive difficulties. Univariate and multiple linear regression were used to evaluate potential predictors of self-reported cognitive decline two years later. Potential predictors included demographics (MS type, MS duration, EDSS, age, gender, education, race, and marital status) and psychosocial variables (fatigue, depression, anxiety, pain, perceived stress, sleep disturbance, and daytime sleep-related impairment). All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 19. Preliminary analyses were conducted to confirm there was no violation of the normality, linearity and homoscedasticity assumptions for the correlation analysis, and that the assumptions of multicollinearity, normality, linearity and homoscedasticity were not violated for the regression analyses.

RESULTS

Graphs (histograms and P-P plots) along with values of skew and kurtosis were used to assess normality. We examined VIF and considered values of 3 or greater as indication of multicollinearity. Linearity was assessed with a plot of residuals versus predicted values. The assumptions of multicollinearity, normality, linearity and homoscedasticity were not violated.

Description of the Sample—The average age of the sample was 53, most were women (83%), Caucasian (91%), married or living with a partner (70%), had a diagnosis of relapsing-remitting (57%) and about half the sample had at least a college education (47%). Over half the sample (63%) was unemployed (see Table 1).

Correlations Between Cognitive Function and Potential Predictor Variables

As shown in Table 2, for general cognitive concerns there was a small, negative correlation with sleep disturbance ($r = -.29$) and EDSS (-.17); a medium, negative correlation with sleep-related impairment ($r = -.43$), pain ($r = -.44$) and perceived stress ($r = -.46$); and a strong, negative correlation with fatigue($r = -.63$), depression ($r = -.51$) and anxiety ($r = -.5$). For perceived executive functioning there was a small, negative correlation with sleep disturbance ($r = -.27$); a medium, negative correlation with sleep-related impairment ($r = -.39$), pain ($r = -.37$), perceived stress ($r = -.49$) and anxiety ($r = -.47$); and a strong, negative correlation with depression ($r = -.54$) and fatigue ($r = -.59$). All but two of the correlations were statistically significant. Therefore only those that were not significant are marked in Table 2.

Regression

Fifteen univariate linear regression models were used to identify significant predictors of (1) general cognitive concerns, then (2) executive difficulties. The potential demographic predictors included: age, gender, education, ethnicity, duration of MS symptoms, MS-type, and EDSS. None of these demographic variables, measured at baseline, predicted self-reported general cognitive concerns or executive difficulties 2 years later, except EDSS. Conversely all considered psychosocial variables (fatigue, depression, anxiety, perceived stress, wakefulness, sleep disturbance and pain) independently and significantly predicted perceived cognition in the univariate analyses. All the significant univariate predictors were forced in a single-step multiple regression. Because the demographic variables did not significantly predict perceived cognition (neither general cognitive concerns nor executive function) they were not controlled for in the multiple linear regression models.

The final multivariate model explained 45% of the variance in general cognitive concerns, $R^2 = .447$, $F(8, 389) = 39.23$, $p < .0001$. Fatigue (beta = −.52, $p <.0001$) and anxiety (beta = −.17, $p =.003$) were statistically significant predictors of general cognitive concerns. Sleep-related impairment ($p = .059$) and EDSS ($p = .056$) just missed statistical significance in predicting NeuroQOL-GC. Similarly, the final multivariate model with the executive function as an outcome variable predicted 41% of the variance in perceived executive functioning scores, $R^2 = .407$, $F(7, 389) = 33.39$, $p < .0001$. Fatigue (beta = −.41, $p < .0001$) and perceived stress (beta = −.12, $p = .049$) significantly predicted self-reported executive functioning (Table 3). Depression just missed statistical significance ($p = .056$) in predicting NeuroQOL-EF.

DISCUSSION

The main goal of this study was to extend the existing literature on metacognition in people with MS by identifying psychosocial variables, beyond depression, predictive of perceived cognition over time. To reflect the complexity of symptoms many individuals with MS experience, we incorporated a large number of demographic, disease-related, and psychosocial variables common to the disease; no other study, to our knowledge, has examined this breadth of factors with validated, standardized measures. Furthermore, we chose to examine two constructs of self-reported cognition (executive and general) with new-generation measures developed utilizing Item Response Theory.

All of the psychosocial variables included in the study (fatigue, depression, perceived stress, anxiety, pain, day-time sleep-related impairment, and sleep disturbance) were significantly correlated with both constructs of self-reported cognition. Similarly, all of the psychosocial variables were significantly associated with general cognitive concerns and perceived executive dysfunction when each was looked at as an independent predictor. However, when placed into a single model, fatigue and anxiety significantly predicted general cognitive concerns and fatigue and perceived stress significantly predicted self-reported executive functioning. Fatigue had the strongest association with both cognitive measures (general cognitive and concerns executive functioning). For each point of increase in the fatigue score the general cognitive concerns score decreased (i.e., got worse) by about a half a point and the executive function score decreased by about .4 points.

The current literature on metacognition in MS heavily emphasizes depression. It is therefore, interesting that this study found fatigue as the strongest predictor of perceived cognitive impairment, both for general cognitive concerns and perceived executive difficulties. Anxiety was significantly related to general cognitive concerns, consistent with one other study (Middleton et al., 2006) which examined anxiety and metacognition; while perceived stress significantly predicted self-reported executive functioning. For each point of increase in the anxiety score the general cognitive concerns score decreased (i.e., got worse) by .17 points. For each point of increase in the perceived stress score the executive functioning decreased (i.e., got worse) by .12 points. It is not completely clear why the findings from this study differ from previous research in the MS literature. It may be that fatigue heavily influences a diagnosis of depression, or depression symptomology. Unlike previous research, our analyses included a large number of symptoms common to MS, a larger sample size, and a longitudinal design. It is possible that previous findings are inconsistent due to the limited number of variables assessed. There may also be mediating or moderating relationships that have yet to be examined. Furthermore, the metacognition measures used in this analysis were designed to examine more specific constructs (i.e., executive dysfunction) than previously used measures (e.g., MSNQ, PDQ). Although fatigue was the strongest predictor in both models, approximately 60% of the variance remained unexplained. While we tried to be comprehensive when including demographic and psychosocial predictors, many variables, probably most importantly objective neuropsychological data, were not included.

There are several limitations in this study. First, there was no objective neuropsychological data with which to compare or validate participant scores on the metacognition measure. Some research suggests that metacognition can be influenced by neuropsychological deficits such as executive dysfunction or severe impairment (i.e., lack of insight). Future research should assess to what extent these variables influence this study’s findings. Future studies should include objective measures of cognitive functioning and examine these same relationships.

Second, the NeuroQOL measures are relatively new. Although the cognitive measures (NeuroQOL-GC and NeuroQOL-EF) were validated with objective data including the MS Functional Composite, Symbol Digit Modalities Test (SDMT), Symbol Search and Digit Symbol Coding, additional research is needed to verify that each questionnaire measures the intended constructs. Additional studies are needed to establish reliability and validity of each measure in individuals with multiple sclerosis. Since this study was a mailed survey, MS diagnosis was provided by self-report and not confirmed by a neurological examination. However, we utilized the self-report diagnosis questions from the NARCOMS data registry. In previous research these questions were found to be a valid way of determining a diagnosis of MS (Marrie et al., 2007).

The large size and community-based nature of the sample precluded the obtaining and verifying extensive medical and mental health histories. Important factors such as medication, comorbid medical conditions, mental health history, and medical history were not included in this analysis. Future research should examine how medication and comorbid diagnoses might influence the predictor and outcome variables. Finally, the participants were part of a convenience sample and were not intended to be representative of the entire MS population.

Despite these limitations, this study presents interesting new findings suggesting that metacognition in individuals with MS is likely influenced by a number of variables (fatigue, anxiety and stress), not just depression. These findings have implications for future research. Future metacognition studies would likely benefit from utilizing a more comprehensive model of potential factors, including not only depression but also anxiety, fatigue, stress, objective cognitive functioning, sleep, and pain. This area would also be advanced if a theoretical or conceptual model of metacognition was developed and tested, as such information could inform future research and clinical care. Existing longitudinal studies in MS seem to indicate that individuals are better at self-perceiving change in functioning, rather than actual performance on any one test (Christodoulou et al., 2005). Furthermore, in the aging literature, metacognition studies have demonstrated that cognitive complaints are predictive of future decline (Dufouil, Fuhrer, & Alperovitch, 2005; Reisberg et al., 2008). Whether this may also be true of individuals with MS merits investigation in future research.

The present findings also have implications for clinical care, including how to best use patient-reported metacognition in clinical assessment and treatment planning. Although metacognition may not be the best predictor of objective neuropsychological functioning (Akbar et al., 2011), when described as poor, it may be an indicator that other factors such as fatigue, anxiety, stress, or depression warrant further assessment and, if present, treatment. Furthermore, including factors such as fatigue, anxiety and stress into individual or group treatment may help to improve perceived cognitive functioning. The fact that metacognition is associated with several factors also suggests a more dynamic and complex process at play. Future research might focus on the best way to assess and treat these symptoms in the context of metacognition. Helping people with MS understand the factors that influence perception of cognitive functioning (beyond objective decline) may alleviate some of these symptoms or facilitate their engagement in relevant treatments (e.g., fatigue self-management, psychotherapy for anxiety).

CONCLUSIONS

Self-perceived cognition has been studied in a number of patient populations including multiple sclerosis. When compared to objective data finding are mixed reflecting different constructs measured by neuropsychological and self-reported instruments. Most often, metacognition is associated with emotional distress. Much of the research in MS has focused on depression and very few studies have explored demographics, disease-related variables, or other common symptoms such as fatigue, anxiety, pain, sleep, and stress. This study sought to capture the complexity of clinical cases by exploring the association of a large collection of common symptoms to metacognition over time. Our results suggest that fatigue, not depression, is the strongest predictor of self-reported cognition in both general cognitive concerns and more specific executive functioning concerns. Furthermore, this study found that a number of symptoms are predictive of subjective cognitive complaints: fatigue, anxiety and daytime sleep-related impairment for general complaints and fatigue and depression for perceived executive functioning difficulties.

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Impact and Implications

- Multiple studies have established a relationship between depression and self-reported cognition. However, individuals with multiple sclerosis often report a large number of psychosocial and physical symptoms which could influence metacognition. This is one of the first studies to assess a large number of common symptoms (fatigue, depression, anxiety, perceived stress, wakefulness, sleep disturbance and pain) and their relationship with self-reported cognition.
- Although metacognition may not be the best predictor of objective neuropsychological functioning, when described as poor, it may be an indicator that other factors such as fatigue, anxiety, stress, or depression warrant further assessment and, if present, treatment.
- Treating factors such as fatigue may also improve perceived cognitive functioning.

Table 1

Descriptive Statistics for Demographics (Baseline), Predictor (Baseline) and Outcome Variables (2-years Post-Baseline)

	% (N) N = 407
Gender	
Female	83 (338)
Male	17 (69)
Education	
Some High School	0.5 (2)
High School Graduate/GED	13 (53)
Some College/Vocational or Technical School	39.1 (159)
College degree	28.7 (117)
Advanced degree	18.7 (76)
Race	
Non-Hispanic White	91.4 (372)
Non-Hispanic Black	2 (8)
Non-Hispanic American Indian/Alaska Native	.2 (1)
Non-Hispanic Asian	.5 (2)
Non-Hispanic Native Hawaiian/Pacific Islander	2.2 (9)
White Hispanic	.7 (3)
Hispanic and Other Race	2.5 (10)
More than One Race	.5 (2)
Marital Status	
Married/Living with a Partner	70.3 (286)
Divorced	14 (57)
Single	5.2 (21)
Never Married	4.9 (20)
Widowed	3.2 (13)
Separated	.5 (2)
Other	2 (8)
EDSS	
≤4.0	31.4 (127)
4.5 - 6.5	48.6 (197)
≥7.0	20 (81)
MS Type	
Relapsing Remitting	57.2 (233)
Secondary Progressive	20.9 (85)
Primary Progressive	11.1 (45)
Progressive Relapsing	8.6 (35)
Paid Employment	
Yes	36.9 (150)

	% (N) **N = 407**
No	62.9 (256)

	M (SD) **N = 407**
Age	52.95 (10.67)
Duration of MS	14.62 (9.8)
MFIS	38.29 (18.74)
PHQ-9	6.33 (5.03)
PSS	5.09 (3.51)
PROMIS Anxiety	49.97 (9.55)
PROMIS Pain	54.33 (9.67)
PROMIS Sleep-related Impairment	52.25 (9.22)
PROMIS Sleep Disturbance	50.5 (10)
EDSS (T8)	0.89 (0.71)
General Cognition (T8)	40.03 (7.72)
Executive Functioning (T8)	42.05 (9.14)

Table 2

. Correlates of Self-Reported Cognition

	1	2	3	4	5	6	7	8	9	10
1. General Cognition	-									
2. Executive Functioning	.74	-								
3. MFIS	-.63	-.59	-							
4. PHQ-9	-.51	-.54	.71	-						
5. PSS	-.46	-.49	.57	.69	-					
6. PROMIS Anxiety	-.5	-.47	.55	.64	69	-				
7. PROMIS Pain	-.44	-.37	.62	.52	.41	.43	-			
8. PROMIS Sleep-related Impairment	−.43	−.39	.53	.58	.46	.47	.42	-		
9. PROMIS Sleep Disturbance	−.29	−.27	.36	.54	.4	.45	.33	.65	-	
10. EDSS (T8)	−.17	−.21	.43	.19	.22	.1	.27	.06*	−.004*	-

Abbreviations: MFIS, Modified Fatigue Impact Scale; PHQ-9, Patient Health Questionnaire; PSS, Perceived Stress Scale

* ns

Table 3

Regression Analysis

General Cognitive Concerns				**Executive Functioning**			
	B	***SE B***	β		***B***	***SE B***	β
Intercept	58.24	2.88		Intercept	54.88	3.52	
EDSS	.91	.48	.08	EDSS	.25	.58	.02
MFIS	−.21	.03	−.52***	MFIS	−.2	.03	−.4***
PHQ-9	.06	.1	.04	PHQ-9	−.24	.13	−.13
PSS	−.13	.13	−.06	PSS	−.3	.16	−.12*
PROMIS Anxiety	−.14	.05	−.17**	PROMIS Anxiety	−.09	.06	−.09
PROMIS Pain	−.03	.04	−.04	PROMIS Pain	.05	.05	.05
PROMIS Sleep-related Impairment	−.09	.05	−.11	PROMIS Sleep-related Impairment	−.07	.06	−.07
PROMIS Sleep Disturbance	.05	.04	.07	PROMIS Sleep Disturbance	.06	.05	.07
	$R^2 = .45$				$R^2 = .41$		

Abbreviations: MFIS, Modified Fatigue Impact Scale; PHQ-9, Patient Health Questionnaire; PSS, Perceived Stress Scale; EDSS, Expanded Disability Status Scale

* $p < .05$;

** $p < .005$;

*** $p < .0001$