Self-reported Memory Problems in Multiple Sclerosis: Influence of Psychiatric Status and Normative Dissociative Experiences

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Abstract

Multiple sclerosis (MS) patients' self-reported cognitive difficulties do not typically correlate well with objective neuropsychological assessment. The relationship between self-reported memory, dissociation, emotional problems, and objective cognitive functioning was examined in 79 MS patients. Increased self-reported memory problems were significantly associated with higher levels of normative dissociation. Self-reported memory problems were also associated with more reports of depression, anxiety, and neuroticism. Consistent with expectations, self-reported memory was not significantly associated with performance on any of the neuropsychological variables. The present study then evaluated a theoretical causal model with normative dissociation mediating the relationship between emotional problems and perceived cognitive problems. Increased depression, anxiety, and neuroticism were all significantly correlated with more dissociative cognitive failures, which, in turn, were strongly associated with perceived memory problems. Findings have significant theoretical implications for understanding the relationship between perceived and objective cognitive difficulties. Findings are also clinically relevant and suggest that dissociative experiences should be evaluated when MS patients report memory problems.

Keywords: Multiple sclerosis; Meta-memory; Self-reported memory; Dissociation; Cogniform disorder; Depression; Anxiety

Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system that is often associated with physical, emotional, and cognitive difficulties (Arnett, 2003; Benedict et al., 2006; Bruce & Arnett, 2006; Crayton, Heyman, & Rossman, 2004; Diaz-Olavarrieta et al., 1999). Approximately 40%–65% of MS patients experience cognitive difficulties (Rao et al., 1991). Deficits in attention, speed of information processing, memory, mental flexibility, and executive functioning are common (Winkelmann, Engel, Apel, & Zeitl, 2007). Studies examining the association between self-reported memory and neuropsychological performance in MS are somewhat mixed. Although some studies have found significant relationships between self-reported memory and objective testing (Randolph, Arnett, & Freske, 2004; Randolph, Arnett, & Higginson, 2001); other studies have found that MS patients’ self-reported cognitive problems are not correlated with performance on neuropsychological measures (Benedict, Munschauer, et al., 2003; Christodoulou et al., 2005; Middleton, Denney, Lynch, & Parmenter, 2006). Taken together, these mixed results suggest that perceived deficits appear to have, at best, a minimal association with objective cognitive test results.

The terms “meta-memory” and “everyday memory” are used to describe one’s self-report of cognitive ability and memory skills (Randolph et al., 2004). Meta-memory in MS patients has primarily been studied in its relationship to depression. Approximately half of all MS patients report current problems with syndromal or subsyndromal depression (Feinstein &
Although cognitive measures are not consistently associated with self-reported cognitive functioning, considerable research indicates negative mood is associated with increased self-reported memory problems (Benedict, Munschauer, et al., 2003; Bruce & Arnett, 2004; Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman, 2005; Julian et al., 2007; Middleton et al., 2006). Despite this, few studies have investigated the mechanism by which depression may lead to perceived memory failures. One current theory proposes that depressed patients’ perceived memory problems may stem from a globally negative worldview (Beck, 1963; Bruce & Arnett, 2005). This theory appears to adequately capture mildly depressed MS patients’ exaggerated reports of memory disturbance. In contrast, moderately depressed MS patients may accurately endorse depression-related cognitive difficulties when compared with non-depressed MS patients who overestimate their cognitive abilities (Bruce & Arnett, 2004). These findings support the theory of depressive realism (Allan, Siegel, & Hannah, 2007). A weakness in both frameworks is the assumption that neuropsychological tests are an infallible measurement of everyday cognitive failures. Previous research shows a relationship between depression and neuropsychological dysfunction in MS, especially when patients exhibit maladaptive coping styles (Arnett, 2003). It is also possible that depression in MS is associated with additional cognitive failures that are not adequately assessed by neuropsychological tests. For instance, depression and other psychiatric disorders are associated with dissociative symptoms (Maaranen et al., 2008). Normative dissociative symptoms tend to be difficult to assess by traditional means of neuropsychological assessment. It is possible that depressed patients experience increased dissociation and, as a result, report genuine memory difficulties that are not adequately measured during a traditional neuropsychological evaluation.

Dissociation can be defined as the disruption of an individual’s usually integrated cognitive processes, such as consciousness, memory, identity, or perception (American Psychiatric Association, 2000). Dissociative experiences, which are present to a greater or lesser degree in everyone, can take many forms (Bernstein & Putnam, 1986; Ray, 1996; Waller et al., 1996). Between 80% and 90% of individuals report dissociative symptoms at least some of the time (Gershuny & Thayer, 1999). While the majority of adults report mild dissociative experiences such as “highway hypnosis” (losing awareness while driving, then suddenly discovering some distance has been traveled), few adults report more extreme dissociative experiences (assuming multiple identities; Freyd, Martorello, Alvarado, Hayes, & Christman, 1998).

Research in normal populations has shown that dissociative symptoms are associated with both psychiatric disturbance and perceived cognitive difficulties. In contrast, dissociation is not typically associated with objective measures of cognitive performance (Bruce et al., 2007). In the present study, we first examined the prevalence of normative dissociative symptoms in MS patients. We then broadly examined the association between emotional functioning, dissociation, neuropsychological performance, and self-reported memory problems in MS. We hypothesized that more frequent normative dissociative experiences would mediate the relationship between emotional difficulties and self-reported memory problems.

**Materials and Methods**

**Participants and Procedures**

MS patients were recruited through a large MS specialty clinic at the University of Kansas Medical Center as part of a larger treatment adherence study. Patients were given a thorough psychiatric interview, self-report questionnaires, and a brief neuropsychological evaluation. As compensation for their participation, participants were paid $125. Eligibility criteria included (a) no current history of alcohol/drug abuse; (b) no nervous system disorder other than MS; (c) no sensory impairments that might interfere significantly with cognitive testing; (d) no relapse and/or corticosteroid use within 4 weeks of assessment; (e) absence of severe physical/neurological impairment that would make participation in the study insurmountable; and (f) use of a self-injected disease modifying therapy for at least 2 months. Each patient was diagnosed as having MS based on established criteria (Polman et al., 2005) by a board-certified neurologist who also assessed disease course based on established criteria (Lublin & Reingold, 1996), and rated patients on the Expanded Disability Status Scale (EDSS; Kurtzke, 1983).

Age- and education-matched controls with no history of neurologic illness were recruited using flyers and the University of Missouri-Kansas City’s mass emailing system. Controls were given a brief neuropsychological evaluation and were paid $50 for their participation.

**Measures**

**Questionnaires**

**Prospective and Retrospective Memory Questionnaire.** The Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford, Smith, Maylor, Della Sala, & Logie, 2003) is a 16-item self-report measure designed to measure self-reported memory problems. Example items include “Do you forget something you were told a few minutes before?” and “Do you
decide to do something in a few minutes time and then forget to do it?" The PRMQ can be broken into prospective and retrospective self-reported memory factors. However, given a very high correlation between these factors ($r > .80$), for the purpose of the present study only the total score for the PRMQ was used. Higher scores on the PRMQ indicate worse self-reported memory.

**Dissociative Experiences Scale-II.** The Dissociative Experiences Scale-II (DES) is a 28-item self-report measure of dissociation that was developed by Bernstein and Putnam (1986). On the questionnaire, participants are asked to indicate what percentage of the time they experience various dissociative phenomena. Research has demonstrated reliability and validity for the DES in both clinical and non-clinical populations (Bernstein & Putnam, 1986; Carlson & Putnam, 1993; Holtgraves & Stockdale, 1997; Ray & Faith, 1995). Test–retest reliabilities range between .79 and .96 and internal reliability ranges from .83 to .93 (Bernstein & Putnam, 1986; Frischholz et al., 1990; Pitblado & Sanders, 1991). One large factor analytic study in a normal population found four separate types of dissociation measured by the DES: absorption, depersonalization, segment amnesia, and in situ amnesia (Ray & Faith, 1995). Examples of absorption include staring into space and becoming absorbed in TV or movies. Examples of depersonalization include not recognizing oneself in the mirror and feeling that other people are not real. Examples of segment amnesia include not recognizing friends and not remembering important events. Examples of in situ amnesia include “spacing out” while driving and during conversation.

**Neuroticism Subscale from the NEO Five Factor Inventory.** The Neuroticism Subscale from the NEO Five Factor Inventory measures one of the “big five” personality traits (Costa & McCrae, 1992). High scores on the neuroticism subscale of the NEO are associated with long-standing patterns of negative emotional functioning, including increased depression and anxiety.

**Beck Depression Inventory–Fast Screen.** The Beck Depression Inventory – Fast Screen (BDI; Beck, Steer, & Brown, 2000) is a self-report questionnaire designed to quickly assess common symptoms of depression. This questionnaire contains seven items specifically designed to assess depression in medical populations, and its validity has been established for use with the MS population (Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003). The variable of interest was total score, with higher scores indicating more depression.

**Trait Subscale of the State-Trait Anxiety Inventory.** The State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, and Vagg, 1983) is a self-report questionnaire designed to assess both the transient state anxiety and the more permanent trait anxiety. Because we were not interested in transient anxiety states in the present study, we only administered the trait version of the questionnaire. Higher scores indicate more anxiety.

**Neuropsychological tests**

**Symbol Digit Modalities Test, Oral Form.** The Symbol Digit Modalities Test (SDMT) is a test of information processing speed that asks participants to quickly say a number that matches a corresponding symbol (Smith, 1982). The dependent variable was the total number of correct responses in 90 s.

**Wisconsin Card Sorting Test.** The Wisconsin Card Sorting Test (WCST) is a test of executive functioning that asks participants to solve a novel problem and demonstrate flexible thinking (Grant & Berg, 1948). A computerized 64-card version of the task was employed. For the purpose of the present study, the number of correct responses was used as the dependent variable.

**Stroop Color–Word Trial.** The Stroop Color–Word Trial is a test of executive functioning that requires participants to inhibit a natural response (reading a word) and replaces it with another response (saying a color; Stroop, 1935). Participants completed 45-s word naming, color naming, and color–word naming trials of a computer-based Stroop task. The dependent variable in this study was the number of correct responses in the color–word trial.

**Auditory Verbal Learning Test.** The Auditory Verbal Learning Test (AVLT) is a test of verbal memory during which a person is asked to learn and recall a list of unrelated words (Taylor, 1959). An abbreviated version of the test was employed for the present study that included three learning trials and a delayed recall trial.

**Letter–Number Sequencing (Wechsler, 1997).** The Letter–Number Sequencing (LNS) test is a measure of working memory that asks a person to simultaneously recall and arrange a series of orally presented numbers and letters.
Data Analysis

Analyses were conducted with SPSS 15. T-tests were used to evaluate between group differences in self-reported memory, dissociation, emotional functioning, and cognitive abilities. Among patients with MS, Pearson product moment correlations and scatter plots were used to examine the relationship between self-reported memory and dissociation, emotional, and neuropsychological functioning. If violations for the use of parametric statistics were observed using standard criteria, subsequent nonparametric Spearman correlations were also conducted. Stepwise regression (entrance criteria $= .05$ and exit criteria $= .1$) was used to examine which variable predicted unique variance in self-reported memory. The Sobel test was then employed to determine whether dissociation mediates the relationship between emotional functioning and self-reported memory problems in MS.

Results

Preliminary Analyses

Seventy-one patients with relapsing–remitting and eight patients with secondary progressive MS were included in the study. MS patients were predominantly females (90%). The group was primarily Caucasian (87%) with a small number of African Americans (6%), Latinas (4%), and people of unspecified ethnicity (3%). The mean $\pm$ SD age was 47.2 $\pm$ 10.82 years with 14.85 $\pm$ 1.96 years of education. The mean $\pm$ SD diagnosis duration was 10.56 $\pm$ 8.53 years and the mean EDSS was 2.72 $\pm$ 1.52 SD.

Twenty neurologically normal age- and education-matched controls were included in this study. The control group was predominantly Caucasian (90%) and African American (10%) females (90%). The mean $\pm$ SD age was 45.40 $\pm$ 10.91 years with 15.75 $\pm$ 1.94 years of education. No significant gender, age, or education differences were observed between MS patients and controls.

Kolmogorov–Smirnov tests uncovered violations of normality for measures of dissociation and depression ($p < .05$). With the exception of depression as measured by the Beck Depression Inventory (BDI) and DES depersonalization, square root transformations corrected these violations. Lack of normality on the BDI was not considered problematic because correlation between the BDI and variables of interest produced normally distributed standardized residuals. In contrast, relatively few participants reported symptoms of depersonalization. As a result, this variable was dichotomized (no report of depersonalization/some report of depersonalization).

Between Group Analyses

Descriptive information is shown in Table 1. As expected, MS patients (41.23 $\pm$ 10.01) reported significantly more memory problems than controls (33.20 $\pm$ 7.08; $t(97) = 3.37, p < .01$). MS patients also performed worse on the SDMT, Stroop test, and delayed list recall from the AVLT. No significant differences were found between the MS and control group performance on LNS, WCST, or AVLT list learning. MS patients (38.59 $\pm$ 9.50) reported more anxiety than controls (32.75 $\pm$ 6.54; $t(96) = 2.59, p < .05$). In contrast, no significant differences were found between the MS and control group on measures of dissociation, depression, and neuroticism.

MS Patient Correlational Analyses

As shown in Fig. 1, dissociation was significantly associated with increased self-reported memory problems ($r = .59, p < .001$). Patients who reported more memory problems were more likely to endorse dissociative absorption ($r = .55, p < .001$), in situ amnesia ($r = .63, p < .001$), and segment amnesia ($r = .40, p < .001$). No significant difference in self-reported memory was found between patients who reported some symptoms of depersonalization ($n = 24$) and patients who reported no symptoms of depersonalization ($n = 54; t(76) = 1.87, p < .1$).

Self-reported memory problems were associated with more reports of depression ($r = .32, p < .01$), anxiety ($r = .50, p < .001$), and neuroticism ($r = .39, p < .001$). In contrast, consistent with expectations, self-reported memory was not significantly associated with performance on any of the neuropsychological variables. Female MS patients reported more memory difficulties (42.26 $\pm$ 9.73) than males (33.22 $\pm$ 8.94; $t(77) = 2.64, p = .01$). Patients with less formal schooling also reported more memory problems ($r = -.28, p < .05$). Stepwise regression was conducted with self-reported memory as the dependent variable and total dissociation, anxiety, depression, neuroticism, age, and education as the independent variables. Only total
dissociation ($R^2_D = .36$, $p < .001$) and education ($R^2_D = .05$, $p < .05$) accounted for unique variance in self-reported memory.

Higher total dissociation was significantly associated with more depression ($r = .42$, $p < .001$), anxiety ($r = .59$, $p < .001$), and neuroticism ($r = .44$, $p < .001$). As seen in Table 2, more dissociative absorption, in situ amnesia, and segment amnesia were also significantly associated with worse depression, anxiety, and neuroticism. No significant relationships were found between self-reported dissociation and cognition.

**Mediation modeling**

It was hypothesized that dissociation would mediate the relationship between psychiatric difficulties and self-reported memory in MS. That is, patients with more psychiatric distress would experience more dissociation and, in turn, report more memory problems. As shown in Fig. 2, dissociation fully mediated the relationship between depression and self-reported memory.
Table 2. Correlations among self-reported memory, emotional variables, and neuropsychological functioning

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<th>SR memory</th>
<th>Dissociation</th>
<th>Absorption</th>
<th>Segment amnesia</th>
<th>In situ amnesia</th>
<th>Depersonalization</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Neuroticism</th>
<th>SDMT</th>
<th>Stroop Test</th>
<th>AVLT recall</th>
<th>AVLT learn</th>
<th>WCST</th>
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Notes: SR memory = self-reported memory as measured by the Prospective and Retrospective Memory Questionnaire; Dissociation = total dissociation as measured using the Dissociative Experiences Scale (DES); Segment = segment amnesia as measured by the DES; In situ = in situ amnesia as measured by the DES; SDMT = Symbol Digit Modalities Test; AVLT = Auditory Verbal Learning Test; WCST = Wisconsin Card Sorting Test total correct; LNS = Letter Number Sequencing from the Wechsler Adult Intelligence Scale-III. One participant filled out the DES incorrectly and was not included in these analyses. Similarly, one participant filled out the STAI incorrectly and was not included in analyses involving the STAI.

*p < .05.

**p < .01.
memory ($Z = 3.26, p = .001$). Dissociation also fully mediated the relationship between neuroticism and self-reported memory ($Z = 3.18, p = .001$) and partially mediated the relationship between anxiety and self-reported memory ($Z = 3.42, p < .001$). Of note, indirect effects of mediation accounted for as much as 22% of the variance in self-reported memory.

**Exploratory analyses**

To examine whether the obtained findings were due to overlapping content between our measures of dissociation and self-reported memory, we conducted follow-up analyses with a modified version of the DES. Items from the DES that could potentially measure aspects of both dissociation and common neurologic cognitive symptoms were removed. As seen in the appendix, the modified DES (mDES) was composed of 16 items that measured relatively “pure” dissociation (see Supplementary material online, Appendix). This measure had good internal reliability (Cronbach’s alpha = .82) and was significantly correlated with the DES ($r = .93, p < .001$), PRMQ ($r = .47, p < .001$), BDI ($r = .40, p < .001$), STAI ($r = .54, p < .001$), and neuroticism subscale of the NEO ($r = .43, p < .001$). Similar to the primary hypothesis testing analyses, the mDES fully mediated the relationship between depression and self-reported memory ($Z = 2.62, p < .01$). The mDES also partially mediated the relationship between neuroticism and self-reported memory ($Z = 2.61, p < .01$) and partially mediated the relationship between anxiety and self-reported memory ($Z = 2.31, p < .05$). Results confirmed that primary findings are not due to item or construct overlap.
Discussion

Mediation modeling produced results that were consistent with the hypothesized causal relationship between emotional dysfunction and perceived memory problems. Depression, anxiety, and neuroticism were all significantly related to dissociation, which, in turn, was strongly associated with perceived memory problems. The results lend support to an alternative theoretical framework that helps further explain the established relationship between emotional difficulties and self-reported cognitive problems in MS. Previous research highlighted the impact of depressed patients’ negative worldview on perceived cognitive functioning. According to this framework, depressed MS patients over-report memory problems when compared with objective neuropsychological testing because of their depressive globally negative worldview. However, this theory fails to fully explain the relationship between depression and self-reported memory problems in several ways. First, there is evidence to suggest that nondepressed patients overestimate their cognitive skills and that moderately depressed patients may accurately assess their memory abilities (Bruce & Arnett, 2004). Furthermore, the present study found significant relationships between self-reported memory problems and emotional difficulties other than depression. For instance, anxiety does not typically create a globally negative worldview. Nevertheless, contrary to expectations, the relationship between anxiety and self-reported memory was stronger than the relationship between depression and self-reported memory. This novel finding suggests that additional research should be conducted examining how anxiety influences patient perceptions of cognitive functioning. MS patients frequently experience excess worry and anxiety (Bruce & Arnett, 2009). It is possible that anxious MS patients are particularly prone to worry about the potential neurologic complications of relatively harmless, normative dissociative experiences.

As predicted, MS patients reported more memory problems than neurologically normal controls. In contrast, MS patients reported normative levels of dissociation. It is possible that MS patients perceive normal dissociative processes to be part of their neurologic disease. For instance, neurologically normal people sometimes “space out” during conversation or become preoccupied with a daydream, thus forgetting to run an errand. Patients with MS may wrongly view these relatively benign, common cognitive lapses as evidence of memory problems caused by progressive central nervous system dysfunction.

A recent commentary proposed the classification “cogniform disorder” for individuals who report excessive cognitive complaints beyond those that can be assessed by neuropsychological tests (Delis & Wetter, 2007). Though the authors discussed pathological forms of dissociation, they excluded any discussion of how more normative dissociative experiences might affect one’s self-reported cognitive functioning. The present results suggest that misinterpretation of normative dissociative experiences may partially account for commonly observed discrepancies between perceived cognitive problems and measured cognition. This finding has significant implications for practice in clinical neuropsychology. Currently, concerned patients with normal neurocognitive profiles are commonly told that they do not have “real” cognitive problems or, if they are depressed, they may be told that they are magnifying their symptoms due to a depressive worldview. The current results suggest that these patients may indeed be experiencing genuine cognitive dissociative symptoms that are distressing and may not be easily measured by neuropsychological testing. More research is needed to fully understand how misinterpretation of normative dissociative experiences may contribute to the presentation of the proposed cogniform disorder.

Clinically, MS patients who report significant distress associated with perceived memory problems may benefit from the administration of a dissociation questionnaire. If these patients perform normally on neuropsychological testing, but endorse various dissociative symptoms, patient education highlighting normative cognitive lapses and dissociative processes should be provided. In contrast to feedback approaches that negate patients’ perceptions of cognitive change (“Even though you think you have memory problems, you don’t.”), the above approach validates everyday experiences, educates about normal dissociative cognitive lapses, and reassures patients that there does not appear to be a pathological memory problem.

Results from this study provide further evidence that the relationship between self-reported memory problems and neurocognitive testing is often nonexistent or weak. Similarly, consistent with previous research (Bruce, Ray, Bruce, Arnett, & Carlson, 2007), no significant relationship was found between normative dissociation and neurocognitive functioning. It is worth noting, however, that the present MS sample had relatively mild disability and few patients with secondary progressive disease. Similarly, the MS patients in this sample exhibited relatively mild cognitive and emotional changes when compared with controls. These findings should be replicated in a more disabled sample of patients with prominent cognitive and emotional difficulties. Other limitations of the current study include the use of a correlational design. Though mediation modeling can inform possible causal relationships, the direction of these relationships can be debated. In the present study, however, it is theoretically implausible that depression causes self-reported memory problems and that self-reported memory problems subsequently cause dissociation. It is similarly implausible that self-reported memory problems cause dissociation which causes depression. Nevertheless, future studies with larger sample sizes and additional measures may wish to employ structural equation modeling or path analysis to further elucidate rival causal models. Finally, MS patients and controls did not differ on the DES. However, it is worth noting that this null finding could be due in part to the use of a relatively small control sample.
In summary, the present study found support for the hypothesis that dissociation mediates the relationship between emotion difficulties and self-reported memory problems in MS. Findings of the present study have significant theoretical and clinical implications. Theoretically, results point to a possible causal means by which depression and other emotional difficulties may contribute to perceived memory problems in the absence of objective neuropsychological impairment. Emotional problems cause increased dissociation. In turn, dissociative cognitive failures cause an increased report of memory problems. Clinically, a better understanding of this process can inform practice and validate patients’ perceptions of cognitive decline while simultaneously offering reassurance that dissociative events are normal. Additional studies that examine the impact of normative dissociation on self-reported cognitive symptoms in other patient populations may also further inform the developing classification criteria for cogniform disorder.

Supplementary material

Supplementary material is available at Archives of Clinical Neuropsychology online.

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Conflict of Interest

None declared.

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