Factors Associated with Employment Status in Individuals with Multiple Sclerosis

Cognition, Fatigue, and Motor Function

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Background: ***Unemployment is common in individuals with multiple sclerosis (MS) and is associated with substantial socioeconomic burden. Several MS-related factors have been found to be associated with employment status, including fatigue, depression, cognitive problems, and motor difficulties. However, few studies have examined these factors collectively in predicting employment. The present study aimed to explore these variables together in predicting employment status in MS.***

Methods: ***Fifty-three individuals with MS participating in a research study of cognitive, emotional, and social factors related to MS were examined. Composite scores were created using factor analysis that represented cognition, fatigue, depression, and motor function. These composite scores, along with the Expanded Disability Status Scale score, were explored as predictors of employment status (working, not working) via logistic regression. Models of mediation were also investigated.***

Results: ***A model including composite scores of motor function, cognition, depression, and fatigue significantly distinguished those who are unemployed versus employed. However, only the cognitive, motor, and fatigue composite scores were found to be significantly associated with unemployment individually. Results of a mediation analysis using 1000 bootstrap samples indicated that the cognitive and fatigue composite scores significantly mediated the effect of disability on work status.***

Conclusions: ***Cognitive function and fatigue mediate the effect of MS disability on employment status. Interventions targeting cognitive difficulties and fatigue in MS may be effective in helping individuals maintain employment.*** ***Int J MS Care.*** **2015;17:284–291.**

Unemployment is common in individuals with multiple sclerosis (MS) and is associated with substantial socioeconomic burden. The relationship between MS and unemployment has been well documented, with the rate of unemployment in MS falling between 22% and 80%.[1] This large range is most likely due to variation in disability of the study samples and year of publication (with individuals in recent studies presumably having access to more effective disease-modifying medications). A recently published large-scale study found that employment rates in an MS population are affected up to 8 years before diagnosis compared with a control population and continue to drop steadily after diagnosis is confirmed.[2] A longitudinal study found that only 50% of individuals with MS were employed at baseline; in addition, after approximately 2.5 years, 22% of those previously employed became unemployed.[1] Unfortunately, once an individual becomes unemployed, he or she may struggle to regain full-time employment for fear of losing vital disability benefits. This predicament is known as the disability trap.[3] It has been documented that employment status and household income are closely related to quality of life measures in individuals with MS.[4,5] Further research on possible areas of intervention that might keep patients employed longer is clearly needed.

Several demographic and illness-related factors have been found to be associated with employment status in MS, including disease duration, course type, age, years

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of education, sex, and general disability.[6-11] Other MS symptom–related factors have also been found to predict employment status, including fatigue,[10,12] depression,[6-8] motor difficulties,[13] and cognitive problems.[14,15] More specifically, regarding cognitive problems, scores on tests of processing speed, verbal fluency, working memory, and long-term memory are typically lower in unemployed versus employed individuals with MS.[8,16,17]

With all this said, research on cognition and depression has produced inconsistent findings. Regarding cognition, although most studies have found it to be associated with employment status, some have not.[10] In addition, important relationships between executive function and employment have sometimes been shown to be mediated by fatigue.[15] Depression research has also yielded inconsistent findings, with one study finding the opposite result of what has been typical, with the employed group having higher depression scores than the unemployed group.[10] Some of these inconsistencies may have been due to different operationalizations of these factors across studies. In addition, it is possible that these inconsistencies can be explained by variations across studies in the factors that were statistically controlled for in the researchers' models. It is evident that a more comprehensive look at these four key MS symptom–related factors (ie, depression, cognition, fatigue, and motor function) in predicting employment status is needed because they very likely covary with each other and with overall disease burden. To our knowledge, there are no published studies that have examined these four key symptoms together, as constructs, in predicting employment status. Therefore, the present study aimed to create reliable composite scores for depression, cognition, fatigue, and motor symptoms and to explore these composite scores, along with illness variables, in predicting employment status in MS.

Patients and Methods

Participants

Participants were recruited from neurologists' practices and MS society newsletters in greater Pennsylvania. A positive diagnosis of MS based on the 2001 McDonald et al.[18] criteria by a board-certified neurologist was the only inclusion requirement for this study. Before enrolling in the research study, potential participants were administered a structured telephone interview to screen for eligibility. Individuals were excluded for any of the following reasons: 1) a significant history of alcohol or drug abuse (eg, a history of or current consumption of 4–6 drinks daily for 1 year); 2) a nervous system disorder other than MS (eg, stroke, encephalitis); 3) sensory impairment that would substantially interfere with testing (eg, loss of vision); 4) a developmental history of learning disability or attention-deficit/hyperactivity disorder; 5) a major medical condition, other than MS, that could interfere with cognitive or motor function (eg, myocardial infarction); 6) relapse or corticosteroid use within 4 weeks of participation in the study; or 7) physical or neurologic impairment that would make testing impossible (eg, if the participant was bed bound or physically unable to move hands, speak, etc.). Neurologic disability was evaluated using the Expanded Disability Status Scale (EDSS). The study was approved by the institutional review board at The Pennsylvania State University (University Park), and all the participants signed an informed consent form before partaking in the study.

Procedure

All the participants completed the neuropsychological measures in addition to a larger battery of neuropsychological tests as part of a longitudinal research study of cognitive, emotional, and social factors related to MS. Analyses for this study were run exclusively on data collected during the second phase of the study, which occurred between 2004 and 2008, and, thus, are cross-sectional in nature. A psychosocial interview was administered at the beginning of the testing session to collect demographic information. Cognitive tasks, motor tasks, and measures of fatigue and depression were administered by a clinical psychology doctoral student during a 3- to 4-hour session. Frequent breaks were offered throughout the testing session to counter the effects of fatigue.

Measures

Neuropsychological measures from Rao's Brief Repeatable Battery of Neuropsychological Tests, the Minimal Assessment of Cognitive Function in Multiple Sclerosis, and the Multiple Sclerosis Functional Composite (MSFC) were selected to be included in the analyses to establish composite scores for cognitive and motor functions. The Judgment of Line Orientation (from the Minimal Assessment of Cognitive Function in Multiple Sclerosis) and the Selective Reminding Test (from the Brief Repeatable Battery of Neuropsychological Tests) were not administered in this study and, thus, are not included in the analyses. All other tests from the aforementioned batteries were included. Maximum Repetition Rate of Syllables and Multisyllabic Combinations (MRRSMC), the Finger Tapping Test, and

the Grooved Pegboard Test were also included in the analyses to capture a broad range of motor function. Self-report measures of depression and fatigue, validated for use in MS, were selected to be included in analyses to establish composite scores for depression and fatigue.

Cognition

Digit Symbol–Coding. Digit Symbol–Coding is a processing speed subtest from the Wechsler Adult Intelligence Scale-III.[19] The dependent variable was the number of correct substitutions in 120 seconds.

Symbol Digit Modalities Test. The Symbol Digit Modalities Test is a test of visual processing speed, attention, and memory.[20] It has both written and oral conditions. The dependent variable was the number of correct substitutions in 90 seconds in the oral and written conditions.

Paced Auditory Serial Addition Test. The Paced Auditory Serial Addition Test is a speeded serial addition task that is used to assess information processing speed, attention, and working memory.[21] Both 2- and 3-second-interval versions were used in the present study, with the dependent variable for both being the total number of correct additions of a possible 60.

California Verbal Learning Test–Second Edition.[22] The California Verbal Learning Test–Second Edition is a measure of verbal learning and memory that includes immediate and short- and long-delayed recall trials.[22] The measures of interest in the present study were the number of correct words recalled in the immediate and long-delayed conditions.

10/36 Spatial Recall Test. The 10/36 Spatial Recall Test is a measure of visuospatial memory.[23] Examinees are presented with a 6 × 6 checkerboard with ten markers placed in a specific pattern and are asked to remember and replicate the pattern three times at various delays. The variables of interest in the present study were the total numbers of correct replications during the immediate and delayed trials.

Brief Visuospatial Memory Test–Revised. The Brief Visuospatial Memory Test–Revised is a measure of visual learning and memory.[24] The examinee is presented with six simple geometric designs and is asked to re-create them immediately and after a 30-minute delay. The total number correct across the first three learning trials, as well as the total recall at the delayed recall trial, were used as variables of interest.

Controlled Oral Word Association Test. The Controlled Oral Word Association Test is a measure of verbal fluency.[25] Examinees are presented aurally with a letter and are asked to generate as many words as they can that begin with that letter. The CFL version was used in the present study. The variable of interest was the total number of correct words generated in 60 seconds across all three letter cues.

Animal Naming. The animal naming test is another measure of verbal fluency.[26] Examinees are presented aurally with the semantic cue "animals" and are asked to generate as many animals as they can. The dependent variable was the total number of correct animals given in 60 seconds.

Delis-Kaplan Executive Function System–Sorting Task. The sorting task subtest from the Delis-Kaplan Executive Function System is a measure of problem solving, concept formation, and cognitive flexibility.[27] The examinee is asked to individually sort cards according to different rules. The variable used was the total number of correct sorts.

Motor Function

Grooved Pegboard Test. The Grooved Pegboard Test is a measure of fine motor coordination.[28] Examinees are instructed to insert grooved metal pegs into a metal board as quickly as possible. Mean time to completion for both hands was used as the dependent variable.

Finger Tapping Test. The Finger Tapping Test is a measure of fine motor speed.[29] Examinees are instructed to place their index finger on a specially designed "tapper" and to tap as fast as they can with that finger for 10 seconds. The variable of interest was the mean number of taps in 10 seconds across hands.

Nine-Hole Peg Test. The Nine-Hole Peg Test is a subtest from the MSFC that measures fine motor skill and dexterity.[30] The examinee is asked to insert all nine smooth pegs into a pegboard and subsequently remove them as quickly as possible. The variable of interest was mean time to completion across hands.

Timed 25-Foot Walk Test. The Timed 25-Foot Walk test is a subtest from the MSFC that measures leg function and mobility.[30] Examinees are instructed to walk the length of a marked 25-foot course as quickly as possible, with mean time to complete the course used as the key variable.

The MRRSMC. The MRRSMC is a measure of oral motor speed.[31] Examinees are instructed to repeat the monosyllables "pa," "ta," and "ka" as quickly as possible after taking a good breath. The syllables "pa," "ta," and "ka" are administered in separate trials. A fourth trial is administered in which the examinee is asked to

repeat the sequence "pa-ta-ka" as quickly as possible. The dependent variable was mean phonemes per second across all four trials.

Depression

Beck Depression Inventory–II. The Beck Depression Inventory–II is a commonly used self-report measure of depression.[32] It consists of 21 items in which the examinee picks one statement per item that best describes the way he or she has been feeling during the past 2 weeks. Each item has four statements assigned a value of 0 through 3, with higher scores indicating higher depression symptoms.

Chicago Multiscale Depression Inventory. The Chicago Multiscale Depression Inventory is a 42-item self-report questionnaire designed to evaluate depressive symptoms in individuals with neurologic and other medical conditions, including MS.[33] This questionnaire has three subscales: mood, evaluative, and vegetative. Each subscale is represented by 14 words or phrases in the larger questionnaire. Examinees are asked to rate on a scale from 1 ("not at all") to 5 ("extremely") how well each describes them during the past week. For this study only the evaluative and mood subscales were used in analyses because they are thought to be the most accurate means of examining depression in medical patients.[33,34]

Fatigue

Fatigue Impact Scale. The Fatigue Impact Scale is a 40-item self-report measure of the extent to which fatigue affects cognitive, psychosocial, and physical functioning.[35] Examinees are asked to rate a statement starting with "Because of my fatigue . . ." on a scale from 0 ("no problem") to 5 ("extreme problem") as to how much fatigue has caused them problems in certain domains of life (ie, "I feel less alert").

Fatigue Severity Scale. The Fatigue Severity Scale is a self-report questionnaire designed to evaluate fatigue severity, with examinees rating themselves on a 7-point Likert scale (1 = strongly disagree, 7 = strongly agree) about how well nine statements about fatigue describe them.[36]

Data Analysis

Composite Scores

All measures of interest were transformed into *z* scores using the mean and standard deviation from this study's MS sample. Four principal components analyses were conducted to establish which tests would be included in the cognitive, motor, fatigue, and depression composite scores. In addition, the cognitive composite was comprised of three subcomposites: memory, processing speed, and executive function. Principal components analyses were conducted that included only tests that were relevant to the domain of interest. It was decided a priori that all test indices with component loadings on the first factor greater than 0.4 would be retained in the respective composite scores.[37] The Cronbach alpha was assessed to confirm the internal consistency of the indices entered into each composite score. A cutoff score of 0.7 was used.[38] Remaining tests' *z* scores were combined into a mean *z* score for each composite score. Measures included in the final composite scores can be found in Table 1.

Logistic Regression

The four composite scores (cognitive, motor, fatigue, and depression) were entered into a logistic regression model, with unemployment status (1, 0) as the dependent variable. The same analysis was also conducted replacing the cognitive composite score with its three subcomposite scores. In addition, each composite score was entered individually into a logistic regression model, with unemployment status (1, 0) as the dependent variable. Given that previous literature[15] has found the relationship between cognition and employment to be mediated by fatigue, analyses that found individual composite scores that predicted employment status were conducted again with fatigue as a covariate. The Hosmer-Lemeshow test of goodness of fit was run for each logistic regression to ensure adequate fit of each model to the data.

Mediation

Bootstrapping mediation analyses were conducted using the PROCESS procedure for SPSS software,[39] version 22, with unemployment status (1, 0) as the outcome variable and the EDSS score as the independent variable. Composite scores found to be significant from earlier analyses were entered individually as mediator variables. Model 4, 1000 bootstrap samples, and a 95% bias-corrected confidence interval (CI) were used as the parameters for these analyses.

Results

Participants

Fifty-nine individuals with MS (10 men and 49 women) were examined. Six participants were excluded from logistic regression analyses because they indicated that their unemployment status was due to factors unrelated to their MS. Thus, 53 participants (8 men and 45

Table 1. Tests included in the composite scores based on the results of the principal components analysis and internal consistency reliability calculations

Composite score	Tests included in composite score
Motor	Grooved Pegboard (mean time across hands), FTT (mean taps per trial across hands), NHPT (mean time bilaterally), Timed 25-Foot Walk test (mean time), MRRSMC (pa-ta-ka combined mean phonemes per second)
Depression	CMDI-evaluative, CMDI-mood, BDI-II total
Fatigue	FIS-psychosocial, FIS-cognitive, FIS-physical, FSS-total
Cognition	Digit Symbol–Coding (total correct in 120 s), SDMT (written total correct in 90 s), PASAT (2 s correct + 3 s correct), CVLT-II (total correct trials 1–5), CVLT-II (long-delayed cued recall), COWAT (grand total across 3 phonetic cues), animal naming (number correct), D-KEFS (total correct sorted)
Cognition subcomposite scores	
Processing speed	Digit Symbol–Coding (total correct in 120 s), SDMT (written total correct in 90 s), SDMT (oral total correct in 90 s)
Executive function	COWAT (grand total across 3 phonetic cues), animal naming (number correct), D-KEFS (total correct sorted), PASAT (2 s correct + 3 s correct)
Memory	SPART (recall total correct immediate recall), SPART (recall total correct delayed recall), CVLT-II (total correct trials 1–5), CVLT-II (long-delayed cued recall), BVMT-R (total correct trials 1–3), BVMT-R (delayed recall score)

Abbreviations: BDI-II, Beck Depression Inventory-II; BVMT-R, Brief Visuospatial Memory Test–Revised; CMDI, Chicago Multiscale Depression Inventory; COWAT, Controlled Oral Word Association Test; CVLT-II, California Verbal Learning Test–Second Edition; D-KEFS, Delis-Kaplan Executive Function System; FIS, Fatigue Impact Scale; FSS, Fatigue Severity Scale; FTT, Finger Tapping Test; MRRSMC, Maximum Repetition Rate of Syllables and Multisyllabic Combinations; NHPT, Nine-Hole Peg Test; PASAT, Paced Auditory Serial Addition Test; SDMT, Symbol Digit Modalities Test; SPART, 10/36 Spatial Recall Test.

women) were included in all of the regression analyses. There were 30 individuals with relapsing-remitting, 17 with secondary progressive, 3 with primary progressive, and 3 with progressive relapsing course types. Thirty-three individuals were employed and 20 were unemployed at the time of the study. Of the 20 unemployed individuals, 13 were receiving disability, 4 were not receiving disability, and 3 were missing this information. Additional demographic and composite score information is available in Table 2. Four participants could not be included in some analyses because their data from four individual tasks were lost due to experimental error.

Regression and Mediation

A model including composite scores of motor function, cognition, depression, and fatigue distinguished those who are unemployed versus employed ($\chi^2_4 = 13.8$, $P = .008$, Nagelkerke $R^2 = 0.334$). However, none of the composite scores were found to be significantly associated with unemployment after controlling for all other variables in the model. Individually, the composite scores for motor function, cognition, and fatigue were significantly associated with unemployment: odds ratio (OR) = 0.31 (95% confidence interval [CI], 0.13-0.76), OR = 0.32 (95% CI, 0.13-0.79), and OR = 2.90 (95% CI, 1.22-6.90), respectively. The depression composite score was not significantly associated with unemploy-

Table 2. Characteristics of people living with multiple sclerosis by employment status

Characteristic	Employed (n = 33)	Unemployed (n = 20)	Total sample (N = 53)
Age, y (mean [SD])	48.0 (8.0)	57.8 (8.5)	51.7 (9.4)
Education, y (mean [SD])	14.8 (2.1)	14.3 (2.1)	14.7 (2.1)
EDSS score (mean [SD])	3.8 (2.0)	5.0 (2.0)	4.2 (2.1)
Disease duration, y (mean [SD])	12.5 (7.3)	19.1 (8.8)	15.0 (8.5)
Cognitive composite score (mean [SD])	0.18 (0.76)	–0.38 (0.57)	–0.02 (0.75)
Motor composite score (mean [SD])	0.19 (0.77)	–0.40 (0.57)	–0.02 (0.75)
Fatigue composite score (mean [SD])	–0.13 (0.78)	0.40 (0.60)	0.07 (0.75)
Depression composite score (mean [SD])	–0.02 (0.93)	0.15 (0.95)	0.04 (0.93)
Female sex, %	78	95	85
Course type, %			
Relapsing-remitting	64	45	57
Secondary progressive	24	45	32
Primary progressive	6	5	5.5
Progressive relapsing	6	5	5.5
Receiving disability, %	0	65	25

Note: Owing to random missing data, n = 19 for unemployed cognitive composite score and n = 18 for unemployed motor composite score. Composite scores are in *z* score units.

ment. See Table 3 for more details about these regression analyses. Even after including fatigue as a covariate, the cognitive (OR = 0.37 [95% CI, 0.15-0.92], P = .032) and motor (OR = 0.37 [95% CI, 0.15-0.95], P = .039) composite scores remained significantly associated with unemployment status. The influence of fatigue in both aforementioned cases became nonsignificant when including the cognitive or motor composite score. When run as a group, the three cognitive subcomposite scores significantly distinguished those who are unemployed versus employed (χ^2_3 = 11.7, P = .008, Nagelkerke R^2 = 0.287). The processing speed subcomposite score remained significantly associated even after controlling for all other cognitive variables (memory and executive function) in the model (OR = 0.26 [95% CI, 0.07-0.93], P = .039). All Hosmer-Lemeshow tests of goodness of fit were not significant, indicating that all the models had adequate fit.

The EDSS score, as expected based on previous work, was significantly associated with unemployment status (OR = 1.37 [95% CI, 1.01-1.86]). Results of a mediation analysis using 1000 bootstrap samples indicated that the fatigue (indirect effect = 0.10093 [95% CI, 0.0043-0.3166]) and cognitive (indirect effect = 0.1012 [95% CI, 0.0020-0.2983]) composite scores independently and significantly mediated the effect of EDSS score on employment status. When further examined, the processing speed (indirect effect = 0.1418 [95% CI, 0.0092-0.3711]) and memory (indirect effect = 0.1011 [95% CI, 0.0071-0.3566]) subcomposite scores independently and significantly mediated the effect of EDSS score on employment status; however, the executive function subcomposite score did not mediate this relationship. In addition, neither the motor nor the depression composite score mediated the relationship between EDSS score and employment.

***Table 3.* Summary of logistic regression models evaluating factors distinguishing unemployed versus employed patients with multiple sclerosis**

Predictor variable	OR (95% CI)	*P* value
Analysis 1: All four symptom-related composite scores		
Cognitive composite score	0.50 (0.18-1.40)	.19
Motor composite score	0.44 (0.14-1.33)	.15
Fatigue composite score	2.73 (0.77-9.70)	.12
Depression composite score	0.78 (0.34-1.83)	.57
Analysis 2: Cognitive composite score	**0.32 (0.13-0.79)**	**.01**
Analysis 3: Motor composite score	**0.31 (0.13-0.76)**	**.01**
Analysis 4: Fatigue composite score	**2.90 (1.22-6.90)**	**.02**

Abbreviations: CI, confidence interval; OR, odds ratio.
Note: Bold text indicates statistically significant at $\alpha < .05$. In the case of the cognitive and motor composite scores, the values reflect better cognitive and motor functioning in employed individuals. With the fatigue composite score, the value reflects higher fatigue in unemployed individuals. n = 20 unemployed, n = 33 employed.

Discussion

Unemployment is common in patients with MS, so the identification of constructs that contribute to unemployment is needed. Although a variety of studies have examined predictors of employment status in isolation or have evaluated a limited number of predictors, little published research has comprehensively examined this issue. In the present study, we examined composite scores for depression, cognition, fatigue, and motor symptoms and explored these composite scores, along with the EDSS score, in distinguishing employment status in patients with MS. As a group, all four composite scores distinguished those who are unemployed versus employed. However, individually, only cognition, motor symptoms, and fatigue were significant individual associates. Surprisingly, depression was not a significant associate.

Although the EDSS score was significantly associated with unemployment status, the results of this study indicate that fatigue, slowed processing speed, and impairments in memory more proximately distinguish unemployment. Most physicians use the EDSS score, a measure heavily weighted on ambulation, to advise patients about when they should leave work.[40] The results of the present study indicate that it may also be useful to use patients' fatigue level and cognitive functioning when making vocational suggestions, given that both seem to mediate the relationship between disability (ie, EDSS score) and employment status. In addition, health-care providers and vocational rehabilitation counselors could inform patients about techniques that help them compensate for difficulties in these domains (ie, repetition for memory impairment, allowing ample time to complete tasks for slowed processing speed, and increasing daily exercise and taking frequent breaks for fatigue) or guide them toward positions of employment that rely less on these domains. Recent research has found that improving physical fitness may also help improve cognitive functioning.[41] According to the Americans with Disabilities Act Amendment Act of 2008, individuals with MS are entitled to certain workplace accommodations, should they disclose their disease, which may help compensate for difficulties in these areas as well.

In addition, the results of this study imply that impairments in memory and processing speed are more influential, at least on employment status, than measures of executive functioning. This finding suggests that measures of these two cognitive domains should be considered for inclusion in comprehensive measures of MS. Recent studies have suggested replacing the Paced Auditory Serial Addition Test in the MSFC with the Symbol Digit Modalities Test, and the results of the present study are consistent with this suggestion.[42,43]

A potential limitation of this study is the small sample size (N = 53), a factor that may limit the ability to detect small effect sizes. In addition, this study sample was predominantly women (85%), and, thus, its findings may not generalize to men. Furthermore, we examined predominantly relapsing-remitting patients (56%), and, thus, these results may not generalize to other course types. Reliability and validity of employment status may be diminished due to the fact that this variable was self-reported. In addition, due to the small sample size, part-time and full-time employed individuals were grouped in the "employed" category. This may add error to the models because some individuals in the "employed" group may have cut down their working hours due to their MS symptoms. If a larger sample were available, analyses could be performed with three working groups: full-time employed, part-time employed, and unemployed. In addition, given the small sample size and correlational nature of this study, caution should be used when interpreting these results in clinical practice.

Perhaps most importantly, the results of this study point to more specific possible areas for intervention. More research and clinical trials for cognitive rehabilitation in the areas of memory, processing speed, and fatigue are needed. So far, the literature is promising, with a recent literature review indicating that cognitive and neuropsychological training has measurable cognitive benefits in MS.[44] Unfortunately, the generalizability of these benefits is questionable, further emphasizing the need for more research to be conducted in this area. □

PracticePoints

- Employment in MS is predicted by cognition, fatigue, and motor skills but not by depression.
- Fatigue and cognitive skills—specifically, processing speed and memory—mediate the relationship between disability and employment status.
- Health-care providers should assess fatigue and cognition when giving vocational advice.
- Health-care providers should inform patients about techniques that can help them compensate for fatigue, memory problems, and processing speed deficits to help them maintain employment.

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