Original Research Article

The relationship between cognition, education, and employment in multiple sclerosis patients

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Abstract

Background: Processing speed decline is a common manifestation of multiple sclerosis (MS). The processing speed test (PST) is a validated electronic cognitive assessment based on the Symbol–Digit Modalities Test, which is routinely administered as part of the multi-institutional Multiple Sclerosis Partners Advancing Technology and Health Solutions (MS PATHS) initiative. The longitudinal relationship between education, processing speed, and employment is unclear.

Objectives: Determine the longitudinal impact of educational attainment on processing speed and employment.

Methods: MS PATHS data through March 2020 were analyzed. Repeat PST assessments at 1, 2, and 3 years were classified as improved, worsened, or stable. Linear regression was used to evaluate the relationship between education and baseline PST performance and logistic regression was used to determine the odds of PST worsening by educational attainment. Employment outcomes were analyzed by PST status and educational level.

Results: There were 13,732 patients analyzed. Education impacted baseline PST scores, but had a limited effect on PST performance over time. Education was protective with respect to employment in the setting of both PST worsening and improvement.

Conclusion: Greater education results in better baseline processing speed and is protective with respect to employment status. Its impact on processing speed over time is marginal.

Introduction

Multiple sclerosis (MS) impacts cognitive functioning, especially processing speed, attention, and working and episodic memory.[1] Cognitive changes are present in 34% to 65% of adults with MS,[2,3] and are even seen in patients with radiologically isolated syndrome.[4] Cognitive dysfunction is associated with loss of employment and impacts the financial and social well-being of MS patients.[5] Routine cognitive screening is recommended to identify affected individuals.[6]

Educational attainment is associated with important factors in MS, including cognition. Worsened cognitive performance is seen in less educated MS patients, especially during the first five years of the disease.[7] Several cross-sectional analyses identified education as a predictor of employment.[8,9] A large Norwegian case–control study even showed that individuals with ≥14 years of education had 41% lower odds of developing MS than those completing ≤10 years of education, despite adjustment for sex, age, and smoking.[10] The relationship between MS and education is complex, with education likely partially acting as a proxy for characteristics such as smoking, comorbidity, employability, and wealth.

The Multiple Sclerosis Partners Advancing Technology and Health Solutions (MS PATHS) multi-institutional registry offers a unique opportunity to study the relationship between education, cognition, and employment in MS patients. MS PATHS is sponsored by Biogen® and data collection began in 2016.[11] MS PATHS participants complete the processing speed test (PST), an electronic tablet-based cognitive

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assessment based on the Symbol-Digit Modalities Test (SDMT),[12] at each clinical visit. Like the SDMT, the PST requires patients to translate symbols to numbers based on a randomly generated key. The PST was validated in MS, has excellent test–retest reliability, and is highly correlated with the SDMT.[13] It also correlates with patient-reported outcome measures and magnetic resonance imaging measures such as grey matter fraction and T2 lesion volume.[14] The MS PATHS protocol has been implemented at 10 sites across the United States and Europe.

We anticipated a cross-sectional advantage for better educated MS patients in baseline cognitive functioning, as previously demonstrated in other populations.[7,15] We hypothesized this advantage would persist longitudinally and would also result in better retention of employment over time.

Methods

MS PATHS data cut 11 (March 2020) was used. To be included in the analysis, participants were required to have a diagnosis of a clinically isolated syndrome (CIS) or MS based on the McDonald criteria current at the time of MS PATHS enrolment.[16,17] At least one PST evaluation, ≥1 Patient Determined Disease Steps (PDDS) assessment,[18] age, sex, MS disease duration, MS phenotype, and data pertaining to educational attainment and employment were required. For the longitudinal analysis, all individuals with PST and/or employment data at the required time points were included.

Participants with assessments at 1 (6–18 months), 2 (19–30 months), and 3 years (31–42 months) from the baseline assessment were identified. The cohorts were characterized by descriptive statistics. Educational attainment was classified based on years of education, which patients self-reported via an electronic questionnaire. Educational attainment was classified as follows: ≥12 years = high school diploma; ≥16 years = college degree; and ≥18 years = graduate degree.

The relationship between educational attainment and baseline PST score was explored with univariable and multivariable linear regression, with adjustment for age, sex, MS phenotype, PDDS score, and disease duration. PDDS scores were broken into three categories: low or no disability (PDDS 0–2), early gait dysfunction (PDDS 3–5), and bilateral support or wheelchair (PDDS 6–7).

Repeat PST scores were classified as worsened (≥4 points drop), improved (≥4 points increase), or stable in reference to the baseline score.[19] Univariable and multivariable logistic regression were used to determine the odds of worsening on the PST versus being stable or improved based on level of education.

Employment status was classified at baseline. Participants working full- or part-time and students were considered to be employed while those on disability or not working were classified as unemployed. Individuals who were retired or homemakers were not analyzed due to uncertainty about whether these conditions were voluntary. Baseline employment percentages were assessed by PST score and stratified by education. Employment status was reassessed at 1 (6–18 months), 2 (19–30 months), and 3 years (31–42 months) from baseline. Individuals who obtained a job (e.g. switching from unemployed to employed) or who maintained a job (e.g. full-time both at baseline and at 1 year) were classified as having a good employment outcome. Participants who lost a job (e.g. switching from part-time to disabled) or who remained jobless (e.g. disabled at baseline and 1 year) were classified as having a bad employment outcome. Switches from full-time to part-time were considered a good outcome because employment was maintained.

Univariable logistic regression models were used to determine the relationship between educational attainment and the odds of a negative employment outcome in the setting of worsening processing speed. Multivariable logistic regression was also carried out with adjustments for age, sex, MS phenotype, and disease duration. The same analysis was also carried out for the subgroup of participants with PST improvement relative to baseline. These calculations were done for the 1-, 2-, and 3-year time points.

All participants give informed consent when enrolling in the MS PATHS registry. This study was approved by our local institutional review board. All analyses were carried out using R version 4.0.3 (https://www.r-project.org). Data to support these findings are accessible to MS PATHS Network investigators and collaborators. These data will be made available to qualified researchers upon request.

Results

We identified 15,837 individuals with baseline PST evaluations, of whom 13,732 had complete data. There were 5967 patients with a follow-up PST at 1 year, 3484 at 2 years, and 633 at 3 years. The average age at baseline was 49.2 years, the participants were 73.3% female and had an average of

14.3 years of education. The full characteristics of the cohort at each time point are described in Table 1.

The level of education had a clear impact on baseline PST performance in the univariable models. Relative to individuals with a high school diploma, those without a high school diploma averaged a raw PST score that was 4.6 points lower ($p < 0.001$), while individuals with a college degree averaged 5.0 points higher ($p < 0.001$) and those with a graduate degree averaged 6.6 points higher ($p < 0.001$). In the multivariable model adjusting for sex, age, MS phenotype, and disease duration, similar results were seen (Table 2).

Baseline employment percentages by PST score and education are shown in Supplemental Table 1. PST scores from 28 to 38 appeared to represent a threshold

Table 1. Characteristics of MS PATHS cohort with PST data.

Characteristic	Baseline ($N = 13,732$)	1 Year ($N = 5967$)	2 Years ($N = 3484$)	3 Years ($N = 633$)
Age, mean (SD)	49.2 (12.4)	49.2 (12.0)	49.6 (11.6)	49.6 (11.1)
Gender, *n* (%)				
Male	3670 (26.7)	1578 (26.4)	958 (27.5)	166 (26.2)
Female	10,062 (73.3)	4389 (73.6)	2526 (72.5)	467 (73.8)
Disease duration, mean (SD)	13.9 (9.6)	13.7 (9.2)	14.3 (8.9)	14.1 (8.7)
MS phenotype, *n* (%)				
Relapsing–remitting	8684 (63.2)	3907 (65.5)	2268 (65.1)	436 (68.9)
Secondary progressive	2433 (17.7)	1070 (17.9)	646 (18.5)	113 (17.9)
Primary progressive	1055 (7.7)	446 (7.5)	246 (7.1)	34 (5.4)
Progressive relapsing	1171 (8.5)	482 (8.1)	290 (8.3)	48 (7.6)
Clinically isolated syndrome	389 (2.8)	62 (1.0)	34 (1.0)	2 (0.3)
PDDS (categorical)				
No to moderate disability	8951 (65.2)	4000 (67.0)	2242 (64.4)	395 (62.4)
Early gait dysfunction	3511 (25.6)	1397 (23.4)	900 (25.8)	167 (26.4)
Bilateral support or wheelchair	1270 (9.2)	570 (9.6)	342 (9.8)	71 (11.2)
PDDS (numerical), median (IQR)	1.0 (0, 3.0)	1.00 (0, 3.0)	1.00 (0, 3.0)	1.00 (0, 3.0)
Years of education, mean (SD)	14.3 (3.1)	14.2 (3.2)	14.4 (3.1)	14.6 (2.7)
Categorical education, *n* (%)				
No high school diploma	1498 (10.9)	714 (12.0)	355 (10.2)	18 (2.8)
High school diploma or some college	6398 (46.6)	2750 (46.1)	1920 (55.1)	334 (52.8)
College degree or some graduate school	3249 (23.7)	1386 (23.2)	866 (24.9)	164 (25.9)
Graduate degree	2587 (18.8)	1117 (18.7)	704 (20.2)	117 (18.5)
Employment status, *n* (%)				
Employed	7831 (57.0)	3414 (57.2)	1920 (55.1)	337 (53.2)
Unemployed	1532 (11.2)	551 (9.2)	316 (9.1)	75 (11.8)
Retired	1619 (11.8)	804 (13.5)	474 (13.6)	57 (9.0)
Disability	2750 (20.0)	1198 (20.1)	774 (22.2)	164 (25.9)
PST number correct, mean (SD)	46.8 (13.1)	49.0 (13.6)	49.6 (13.7)	50.5 (13.7)
PST change, *n* (%)				
Improved	NA	2204 (36.9)	1436 (41.2)	240 (37.9)
Stable	NA	2631 (44.1)	1419 (40.7)	275 (43.4)
Worsened	NA	1132 (19.0)	629 (18.1)	240 (37.9)
Employment outcome, *n* (%)				
Good	NA	3337 (55.9)	1863 (53.5)	328 (51.8)
Bad	NA	1259 (21.1)	805 (23.1)	178 (28.1)
Can't analyze	NA	1371 (23.0)	816 (23.4)	127 (20.1)

MS PATHS: Multiple Sclerosis Partners Advancing Technology and Health Solutions; MS: multiple sclerosis; PST: processing speed test; SD: standard deviation; PDDS: Patient Determined Disease Steps; IQR: interquartile range; SD: standard deviation.

Table 2. Results of adjusted linear regression model predicting baseline PST scores. Adjusted $R^2 = 0.41$.

Covariate	Baseline ($N = 13,732$)		
	Beta value	95% CI	*P*-value
Education (reference group: HS diploma)			
No HS diploma	−4.88	−5.45 to −4.32	<0.001*
College degree or some graduate school	3.69	3.26 to 4.12	<0.001*
Graduate degree	5.17	4.70 to 5.63	<0.001*
Female	2.02	2.40 to 1.63	<0.001*
Age	−0.35	−0.37 to −0.34	<0.001*
Disease duration	−0.17	−0.19 to −0.15	<0.001*
PDDS (reference group: low or no disability)			
Early gait dysfunction	−4.44	−4.88 to −4.00	<0.001*
Bilateral support or wheelchair	−8.13	−8.80 to −7.45	<0.001*
Phenotype (reference group: relapsing–remitting MS)			
Secondary progressive MS	−2.58	−3.08 to −2.07	<0.001*
Primary progressive MS	−3.66	−4.35 to −2.97	<0.001*
Progressive relapsing MS	−4.82	−5.46 to −4.18	<0.001*
Clinically isolated syndrome	−1.52	−2.54 to −0.49	0.004*

* denotes a significant *P*-value of <0.05.
PST: processing speed test; CI: confidence interval; HS: high school; PDDS: patient determined disease steps; MS: multiple sclerosis.

at which <50% employment was seen in all educational groups except for those with advanced degrees. Two-thirds of individuals with a graduate degree were able to maintain employment with a PST score ≤28. Individuals unemployed at baseline had a 64.6% increased odds of PST worsening at 1 year ($p < 0.001$), 104% at 2 years ($p < 0.001$), and 53% ($p = 0.047$) at 3 years.

In the unadjusted models for the 1-year cohort, we found that individuals with a graduate degree had a 20% lower odds of worsened PST performance relative to those with a high school diploma ($p = 0.019$). Individuals with a college degree had an 8% lower odds of PST worsening while those without a high school diploma had 4% higher odds of PST worsening when compared to those with no high school diploma, but neither of these differences was significant. Similar results were seen in the multivariable model of 1-year outcomes (Table 3). In the univariable models for the 2-year cohort, those with a college degree had a 20% lower odds of PST worsening ($p = 0.045$) and those with a graduate degree had a 29% lower odds of the same ($p = 0.006$). No significant difference was seen between those with and without a high school diploma. In the adjusted model (Table 3), only patients with a graduate degree had a significant reduction in odds of PST worsening (OR = 0.77, $p = 0.037$) at 2 years. At 3 years, there was no

significant relationship between educational attainment and the likelihood of PST worsening in the univariable or multivariable models (Table 3). The evolution of PST performance over time, stratified by level of education, is depicted in Figure 1.

Among individuals with PST worsening, more education was generally protective with respect to maintaining employment through the 3-year study period (Figure 2). The univariable model predicting employment outcomes at 1 year based on education level revealed that those with a college degree (OR = 0.40, $p < 0.001$) or graduate degree (OR = 0.30, $p < 0.001$) had significantly lower odds of a negative employment outcome than those with a high school diploma. There was no significant difference between individuals with and without a high school diploma at 1 year. These results were upheld in the multivariable model with adjustment for relevant covariates, as those with a college degree had 14% lower odds of a negative employment outcome ($p < 0.001$), and those with a graduate degree had 20% lower odds of a negative employment outcome ($p < 0.001$) compared to individuals with a high school diploma (Table 4).

In the 2-year unadjusted models, individuals with a college degree had 52% lower odds ($p = 0.002$) and those with a graduate degree had 80% lower odds ($p < 0.001$) of a negative employment outcome

Table 3. Results of adjusted logistic regression models predicting worsening of PST performance by year.

Covariate	1 year (N = 5967)		2 years (N = 3484)		3 years (N = 633)	
	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Education (reference group: HS diploma)						
No HS diploma	1.05	0.617	0.92	0.582	2.02	0.192
College degree or some graduate school	0.95	0.534	0.85	0.138	1.12	0.651
Graduate degree	0.83	0.044*	0.77	0.037*	0.83	0.520
Female	1.12	0.124	1.10	0.331	1.09	0.707
Age	1.01	0.017*	1.01	0.003*	1.01	0.223
Disease duration	1.01	0.011*	1.00	0.696	0.98	0.156
PDDS (reference group: low or no disability)						
Early gait dysfunction	1.27	0.005*	1.28	0.025*	1.66	0.042*
Bilateral support or wheelchair	1.09	0.510	1.59	0.003	2.67	0.007*
Phenotype (reference group: RRMS)						
Secondary progressive MS	1.00	0.970	1.07	0.560	0.96	0.901
Primary progressive MS	1.37	0.013*	0.97	0.884	0.48	0.183
Progressive relapsing MS	1.02	0.870	1.33	0.064*	1.22	0.599
Clinically isolated syndrome	1.22	0.522	1.02	0.969	0.00	0.983

* denotes a significant P-value of <0.05.
PST: processing speed test; HS: high school; PDDS: patient determined disease steps; RRMS: relapsing–remitting multiple sclerosis; MS: multiple sclerosis.
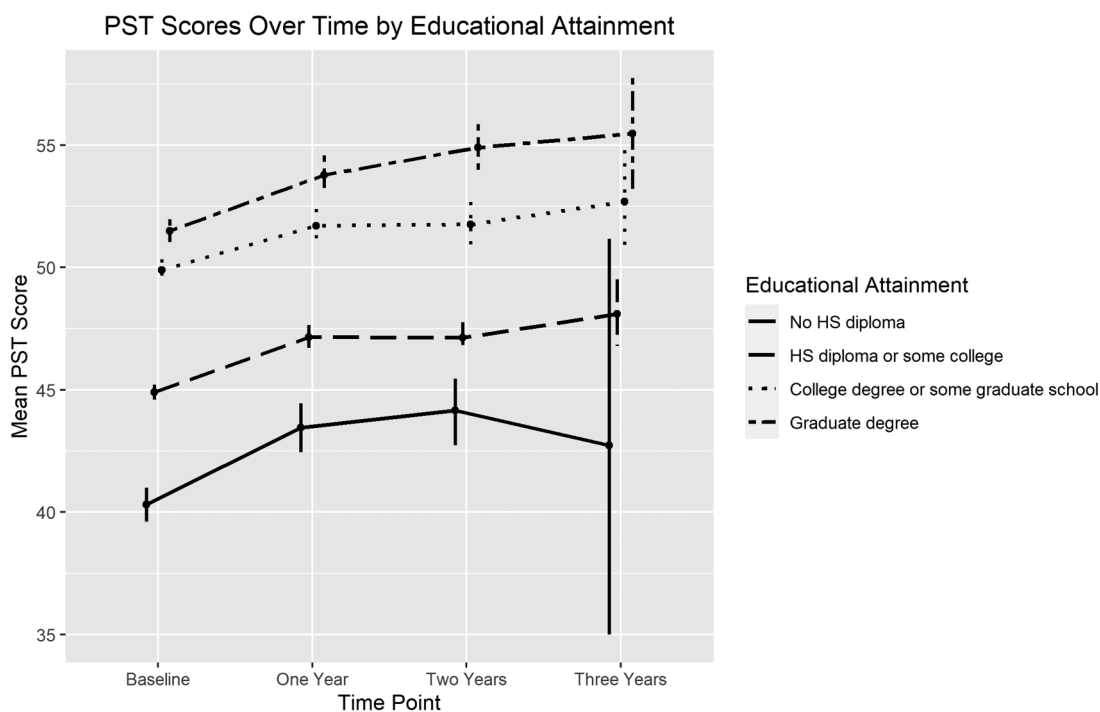
Figure 1. PST scores over time by educational attainment.
PST: processing speed test; HS: high school.
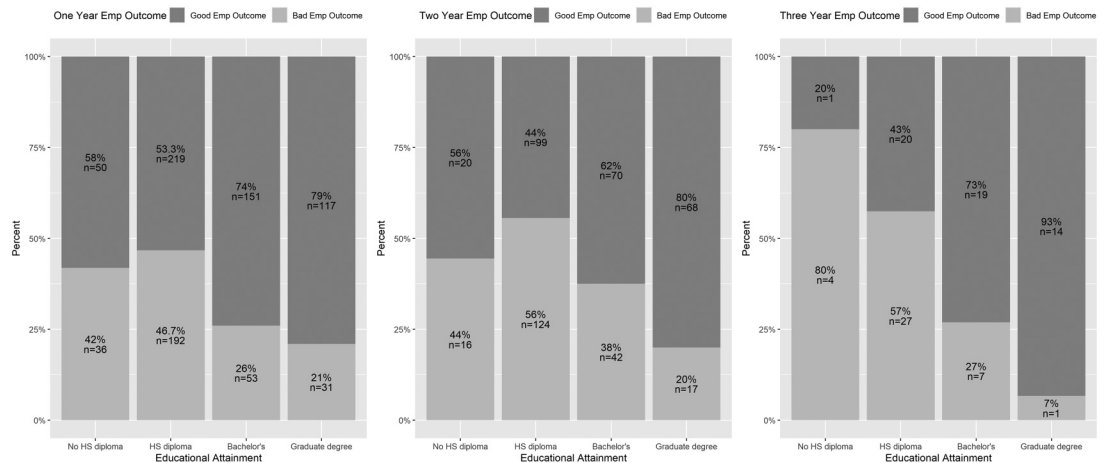
Figure 2. Employment outcomes by year among individuals whose PST score worsened from baseline.
PST: processing speed test; Emp: employment; HS: high school.

Table 4. Results of adjusted logistic regression models predicting a negative employment outcome in individuals with PST worsening from baseline.

Covariate	1 year (N = 849)		2 years (N = 456)		3 years (N = 93)	
	Odds ratio	*P*-value	Odds ratio	*P*-value	Odds ratio	*P*-value
Education (reference group: HS diploma)						
No HS diploma	1.00	0.973	0.93	0.314	1.00	0.985
College degree or some graduate school	0.86	<0.001*	0.86	0.003*	0.75	0.010*
Graduate degree	0.80	<0.001*	0.79	<0.001*	0.64	0.001*
Female	1.06	0.040*	1.02	0.683	0.93	0.472
Age	1.00	0.347	1.00	0.033*	1.00	0.993
Disease duration	1.00	0.009*	1.00	0.079	1.00	0.648
PDDS (reference group: low or no disability)						
Early gait dysfunction	1.50	<0.001*	1.32	<0.001*	1.20	0.083
Bilateral support or wheelchair	1.77	<0.001*	1.63	<0.001*	1.72	<0.001*
Phenotype (reference group: RRMS)						
Secondary progressive MS	1.07	0.092	1.16	0.005*	0.90	0.413
Primary progressive MS	1.10	0.069	1.11	0.166	1.11	0.618
Progressive relapsing MS	1.22	<0.001*	1.13	0.074	1.34	0.077
Clinically isolated syndrome	0.91	0.456	1.30	0.288	NA	NA

* denotes a significant *P*-value of <0.05.
PST: processing speed test; HS: high school; PDDS: patient determined disease steps; RRMS: relapsing–remitting multiple sclerosis; MS: multiple sclerosis.

relative to individuals with a high school diploma. The odds ratios continued to favor more highly educated patients in the adjusted models, though to a lesser degree (Table 4). In the 3-year univariable models, individuals with a college degree had 73% lower odds of a negative employment outcome (*p* =
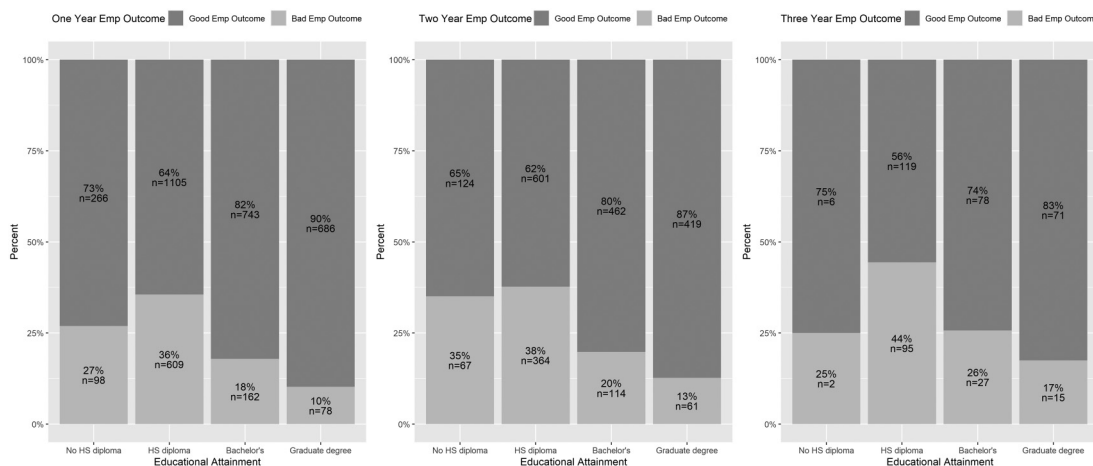
Figure 3. Employment outcomes by year among individuals whose PST score improved from baseline.
PST: processing speed test; Emp: employment; HS: high school.

Table 5. Results of adjusted logistic regression models predicting a negative employment outcome in individuals with PST improvement from baseline.

Covariate	1 year ($N=3747$)		2 years ($N=2212$)		3 years ($N=413$)	
	Odds ratio	*P*-value	Odds ratio	*P*-value	Odds ratio	*P*-value
Education (reference group: HS diploma)						
No high school diploma	0.96	0.083	1.01	0.678	0.89	0.395
College degree or some graduate school	0.88	<0.001*	0.88	<0.001*	0.90	0.030*
Graduate degree	0.83	<0.001*	0.84	<0.001*	0.84	<0.001*
Female	1.04	0.006*	1.06	0.002*	0.99	0.771
Age	1.00	<0.001*	1.00	0.003*	1.00	0.089*
Disease duration	1.00	<0.001*	1.00	0.001*	1.00	0.868
PDDS (reference group: low or no disability)						
Early gait dysfunction	1.37	<0.001*	1.33	<0.001*	1.42	<0.001*
Bilateral support or wheelchair	1.69	<0.001*	1.77	<0.001*	1.76	<0.001*
Phenotype (reference group: RRMS)						
Secondary progressive MS	1.14	<0.001*	1.11	<0.001*	1.20	0.001*
Primary progressive MS	1.06	0.020*	1.02	0.503	1.19	0.062
Progressive relapsing MS	1.12	<0.001*	1.15	<0.001*	1.05	0.518
Clinically isolated syndrome	1.04	0.517	0.90	0.292	0.80	0.570

* denotes a significant *P*-value of <0.05.
PST: processing speed test; HS: high school; PDDS: patient determined disease steps; RRMS: relapsing–remitting multiple sclerosis; MS: multiple sclerosis.

0.015) and those with a graduate degree had 95% lower odds of a negative employment outcome ($p = 0.006$). The results were again upheld in the multivariable model (Table 4).

Greater education also conferred an advantage with respect to employment outcomes in patients with PST improvement (Figure 3). At 1 year, participants with a college degree had 60% lower odds

of a negative employment outcome ($p < 0.001$) and individuals with a graduate degree had 79% lower odds of the same ($p < 0.001$) in the unadjusted models. Similar results were seen in the multivariable model, though the effect of education was less dramatic (Table 5).

In the 2- and 3-year unadjusted models, college graduates had 59% and 57% lower odds of a negative employment outcome, respectively ($p < 0.001$ for both) compared to those with a high school diploma only. Individuals with a graduate degree had a 76% lower odds of a negative employment outcome at 2 years ($p < 0.001$) and a 74% lower odds of a negative employment outcome at 3 years ($p < 0.001$) compared to those who only graduated from high school. There was no significant difference between participants who did and did not have a high school diploma at 2 ($p = 0.491$) or 3 years ($p = 0.292$). Results were similar after adjusting for important covariates except for a less pronounced benefit from greater education (Table 5).

Discussion

To our knowledge, this is the first study analyzing the longitudinal relationship between cognition, educational attainment, and employment in MS patients. As anticipated, there is a strong correlation between education and baseline PST performance. Contrary to our expectations, the longitudinal benefit of education was marginal. Individuals with a college degree were no less likely than high school graduates to have PST worsening at 1, 2, or 3 years. Holders of a graduate degree were less likely than high school graduates to have PST worsening at 1 and 2 years, but this advantage was no longer present at 3 years, despite a good representation of graduate degree holders in the 3-year cohort (n = 117).

Our findings suggest the rate of cognitive decline in MS is largely independent of educational attainment. Similar trends have been observed in other neurodegenerative diseases. For instance, several studies showed that individuals with greater educational attainment in the dementia stage of Alzheimer's disease have more rapid cognitive deterioration than their less educated counterparts.[20–22] These observations could be a function of cognitive reserve, with the notion that more highly educated patients can compensate for neural damage to a point, but past that point, the advantage of education is lost. Our study, though, does not provide direct evidence of cognitive reserve in MS because we did not specifically evaluate if education moderates the relationship between disease status and cognitive functioning.

The applicability of the cognitive reserve hypothesis to MS remains incompletely understood, with a recent study suggesting limited benefits from intellectual enrichment.[23] Another consideration is that lower education is often associated with more physically demanding employment, which may be protective from a cognitive standpoint.[24]

Cognitive functioning has been closely linked to employment status in MS patients. For instance, a prospective study of 124 relapsing–remitting patients over 2 years found that baseline executive functioning and physical disability were significant predictors of deteriorated employment status,[25] which was defined as loss of employment or a 20% decrease in work hours because of MS. Baseline physical and executive functioning were significant predictors of a negative employment outcome. A cross-sectional retrospective study of 158 persons with MS had similar findings, with an expanded disability status scale,[26] SDMT, and the Hospital Anxiety and Depression Scale[27] as significant predictors of vocational status.[28] Information processing speed is a significant predictor of the number of hours worked by MS patients[29] and also influences early retirement.[30] A recent cross-sectional study of 260 MS patients found that in addition to physical disability and cognitive impairment, female sex was a strong predictor of unemployment while years of education were protective.[31]

Our study provides a unique evaluation of the relationship between education, cognition, and employment, in that we were able to longitudinally assess the evolution of processing speed and employment status based on the level of education. We found that among individuals with worsening PST performance, education had a protective effect on employment outcomes. The effect appeared additive, as graduate degrees provided a greater advantage than college degrees at all time points. Interestingly, no significant differences were observed between those with and without a high school diploma. This could support the presence of an academic threshold that one must reach to achieve an employment advantage in the setting of declining cognitive functioning.

Although this study focused on the relationship of educational attainment to processing speed and employment status, other intriguing findings were evident. At baseline, women had significantly better processing speeds than men, which is consistent with prior research suggesting more pronounced cognitive deterioration in men.[32,33] However, in a pattern

similar to what was seen with education, this did not translate into a reduced longitudinal risk of deterioration in PST performance. In fact, women were more likely to worsen over time, and given the average age of participants was 49 years old, a hormonal contribution could be considered. Regarding MS phenotype, CIS patients had worse baseline performance than patients with relapsing–remitting MS, though there was no significant relationship over time. Cognitive changes are seen even in patients with radiologically isolated syndrome,[34] but this may have been a spurious finding given that, by definition, relapsing–remitting MS is a more advanced disease than CIS. Progressive MS patients had worse baseline scores on the PST, though there were no discernible patterns between phenotype and cognitive worsening over time. There also was not a clear pattern between phenotype and maintenance of employment over time in those with either PST worsening or improvement. It is possible that most of the progressive MS disadvantage was already accounted for by the PDDS cofactor in the model. Physical disability, as expected, was consistently associated with the ability to maintain employment.

Strengths of our study include the large and geographically diverse sample, which increases its generalizability. The study's longitudinal design also makes it more informative, although there was a substantial reduction in data availability at 3 years. However, data were still available for over 600 individuals at the 3-year time point and almost all subgroup analyses had robust sample sizes. Unfortunately, the 3-year cohort was short on patients with PST worsening as well as individuals without a high school diploma or with a graduate degree. As such, results from these subgroups should be interpreted with caution.

Limitations of the study include the lack of a healthy control group and the use of the PST rather than a complete neuropsychological battery for cognitive assessments. It should be noted, though, that while the PST and SDMT are primarily thought of as assessing information processing speed, there is evidence that other cognitive domains including memory and lexical access speed are required for the completion of the symbol–digit translation task.[35] A number of factors that may impact cognitive performance were not included in the analysis due to constraints in the data, which is an important limitation. These include relapses, depression levels, and disease-modifying therapy use. As is typical when working with long-term observational data, missing data were a shortcoming of our study. We included only individuals with complete data, which can introduce bias into the analysis. However, when comparing data for those included in and excluded from the analysis, the cohorts were fairly similar. For instance, excluded patients had an average age of 53.1 years and a mean of 13.7 years of education, as compared to 49.2 and 14.3 years, respectively, for included patients. Our data set also contained only the number of years of education, so inferences had to be made with regard to completed degrees, but the timeframes used are typical in the United States and Western Europe, from which the data were sourced.

Our results show a significant boost in baseline PST performance for more educated individuals, but longitudinal benefits from education were realized only by those with advanced degrees, and only over the first two years. Notably, more highly educated patients had better employment outcomes in the setting of declining PST performance. This may be related to a better ability to compensate for cognitive decline, or perhaps better job mobility in which an alternative job can be secured if one loses the ability to perform their current job. Ultimately, our results suggest benefits from education that may significantly impact quality of life in MS patients. Given that MS is often diagnosed when patients are still attending school, an opportunity exists to encourage a focus on education, which may prolong the ability to maintain competitive employment.

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