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# Motor function in the elderly

## Evidence for the reserve hypothesis

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### ABSTRACT

**Objective:** The reserve hypothesis accounts for the lack of direct relationship between brain pathology and its clinical manifestations. Research has mostly focused on cognition; our objective is to examine whether the reserve hypothesis applies to motor function. We investigated whether education, a marker of reserve, modifies the association between white matter lesions (WMLs), a marker of vascular brain damage, and maximum walking speed (WS), an objective measure of motor function. We also examined the cross-sectional and longitudinal association between education and WS.

**Methods:** Data are from 4,010 participants aged 65–85 years in the longitudinal Three-City-Dijon Study with up to 4 WS measures over 10 years. We examined the interaction between education and WMLs for baseline WS. We studied the association between education and repeated WS measures using linear mixed models, and the role of covariates in explaining the education-WS association.

**Results:** Education was strongly associated with baseline WS; the difference in mean WS between the high and low education groups (0.145 m/s, 95% confidence interval = 0.125–0.165) was equivalent to 7.4 years of age. WMLs were associated with slow WS only in the low education group ( $p$  interaction = 0.026). WS declined significantly over time (–0.194 m/s/10 years, 95% confidence interval = –0.206, –0.182), but education did not influence rate of decline. Anthropometric characteristics, parental education, general health, and cognition had the strongest role in explaining the baseline education-WS association.

**Conclusions:** Participants with more education were less susceptible to WMLs' effect on motor function. Higher education was associated with better motor performances but not with motor decline. These results are consistent with the passive reserve hypothesis. *Neurology*® 2013;81:417–426

### GLOSSARY

**BMI** = body mass index; **MMSE** = Mini-Mental State Examination; **OR** = odds ratio; **PR** = percentage reduction; **SE** = standard error; **SES** = socioeconomic status; **WML** = white matter lesion; **WS** = walking speed.

The concept of brain reserve accounts for the lack of direct relationship between brain pathology and its clinical manifestations.<sup>1–3</sup> High reserve, assessed via anatomical features of the brain or markers of enriched environments (e.g., education, socioeconomic status [SES]), has been associated with reduced clinical manifestations of neuropathologic changes.<sup>4–6</sup> Risk factors have also been found not to be related to the same extent to functional measures among those with high and low reserve.<sup>7,8</sup> Recent evidence suggests that higher education is strongly associated with better cognitive performances but not with a slower rate of cognitive decline.<sup>9–12</sup> These findings are interpreted as supporting a “passive reserve” hypothesis: higher education is associated with better performances because of the persistence of earlier differences rather than differential rates of cognitive decline. In longitudinal studies, this translates into baseline

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differences between education groups with parallel decline over time. This model is generally opposed to an “active” model that posits education to be associated with higher function but also with less pronounced decline through active compensation; this translates into baseline differences that increase over time.<sup>1</sup>

Research on reserve has mainly focused on cognitive function. Motor decline is another key aspect of aging and is highly heterogeneous across people. Our objective was to examine whether the reserve hypothesis applies to motor function, assessed using objectively measured maximum walking speed (WS). First, we tested whether more-educated persons were less susceptible to the effects of brain vascular lesions on motor function by examining the interaction between education and white matter lesions (WMLs), a marker of vascular brain damage associated with poor motor function.<sup>13,14</sup> Second, although there is cross-sectional evidence of an association between lower education and poorer motor function,<sup>15–17</sup> few studies have examined the association of education with motor decline.<sup>18–20</sup> To distinguish active from passive reserve models, we examined cross-sectional and longitudinal associations of education with WS. Finally, we investigated the role of a wide range of covariates in explaining the education-WS association.

**METHODS Subjects.** The 3C Study is a cohort study of community-dwelling persons aged 65 years and older in 3 French cities (Bordeaux, Dijon, Montpellier).<sup>21</sup> Data reported here were collected in Dijon ( $n = 4,931$ ). At baseline (wave 0, 1999–2001), eligible Dijon inhabitants were invited to participate. Participants were then seen approximately every 2 years; 6 waves of data collection took place until 2010. Participants aged 85 years and younger were invited to the study center at each wave to be interviewed and for additional investigations, including WS measures. From wave 2 onward, participants were offered the opportunity of being seen exclusively at home. Wave 3 consisted of a self-administered questionnaire.

**Study protocol approvals, registrations, and patient consents.** The study protocol was approved by the Ethics Committee of Kremlin-Bicêtre University Hospital. Participants signed an informed consent form.

**Walking speed.** WS was measured in participants aged 85 years and younger who visited the study center at baseline and after 4 years (wave 2, 2003–2004), 8 years (wave 4, 2007–2008), and 10 years (wave 5, 2009–2010). WS was measured using 2 photoelectric cells (6 m apart) connected to a chronometer. Participants were asked to walk at “usual” and “fast” (without

running) speed. WS was computed as 6 m divided by time (seconds). Short-term reproducibility was assessed by taking 2 measures 5 minutes apart in a random sample ( $n = 51$ , mean age = 80.1 years, SD = 3.4). Intraclass correlation coefficients (standard error [SE]) were as follows: usual WS = 0.84 (0.02); maximum WS = 0.92 (0.02).<sup>22</sup> Given similar results for both measures and higher reproducibility of maximum WS, we present results using this measure.

**White matter lesions.** WML volumes (total, periventricular, deep) were measured at baseline in participants aged 80 years and younger on brain MRI scans using an automated method (e-Methods on the *Neurology*<sup>®</sup> Web site at [www.neurology.org](http://www.neurology.org)).<sup>23</sup> We previously showed that higher WML volume was associated with slower baseline WS and change in WS based on 2 measures.<sup>13</sup>

**Covariates.** Data were collected during face-to-face interviews using standardized questionnaires administered by trained psychologists. Education was self-reported at baseline as the highest degree obtained. For our main analyses, we categorized education as a 3-level variable in order to have sufficient power for interaction analyses: primary school degree or less (low), secondary school degree (intermediate), high school or university degree (high). In sensitivity analyses, we used a more detailed definition (6 levels). Other covariates are described in e-Methods.

**Statistical analysis.** Participants with conditions that cause gait impairment (Parkinson disease, dementia, stroke, recent hip fracture) were excluded. Baseline participants' characteristics were described overall and by education and sex-specific tertiles of WS.

To assess the interaction between education and WMLs on the risk of slow WS, we used logistic regression stratified by education with WS below the sex-specific median as the dependent variable and WML volume as the explanatory variable. The interaction term allowed testing for differences in odds ratios (ORs) of slow WS by education. Analyses were adjusted for age, sex, height, body mass index (BMI), cognitive function (Mini-Mental State Examination [MMSE]), and total white matter volume. Because the relation between WS and WMLs may not be linear,<sup>13</sup> we repeated these analyses by dichotomizing WMLs at the 90th percentile.

To investigate the association of education with baseline WS and change in WS, we used a linear mixed-effects model with random effects for the intercept and slope, allowing individuals to have different baseline WS and rates of decline. Time since baseline (years) was included as a continuous linear term and divided by 10; regression coefficients correspond to a 10-year increment. Adding a quadratic term did not improve the models' fit ( $p = 0.54$ ). Models were adjusted for the 2 main correlates of WS (sex and continuous baseline age). Education's main effect corresponds to its association with baseline WS; the education  $\times$  time term represents its effect on WS change over time. WS measures over the follow-up were missing because of death, participants becoming older than 85 years, incident causes of gait impairment, home examination (where WS was not measured), and nonresponse. To investigate the influence of missing data, we replicated the analyses using multiple imputation (e-Methods).

To assess the role of confounders and mediators in explaining the education–baseline WS association, we used linear regression serially adjusted for covariates. Model A included education, age (continuous), and sex. We assessed the extent to which the association was explained by covariates (models B–J): anthropometric measures, health behaviors, cardiovascular risk factors, chronic conditions, cognitive function, depressive symptoms, psychosocial factors, parental education, and general health. Model K includes all covariates. The percentage reduction (PR) of the

education-WS association was computed as  $100 \times (\beta_{\text{Model } i} - \beta_{\text{Model } A}) / \beta_{\text{Model } A}$ .

The  $p$  values were 2-tailed and  $p \leq 0.05$  was considered statistically significant. Statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

**RESULTS Study population characteristics.** At baseline, 4,421 participants (aged 65–85 years) were seen at the study center. After excluding 136 participants with conditions that cause gait impairment, 4,285 were eligible and 4,012 had at least one WS measure over the follow-up. Participants without any WS measure ( $n = 273$ ) were older ( $p < 0.0001$ ), more disabled ( $p < 0.0001$ ), had higher BMI ( $p < 0.0001$ ), lower MMSE scores ( $p < 0.0001$ ), tended to be less physically active ( $p = 0.08$ ), and male ( $p = 0.13$ ) at baseline than those included in analyses. Education was similar in the 2 groups (OR low vs high/intermediate = 1.02, 95% CI = 0.77–1.34). Data on education were missing for 2 participants; the analytic sample comprised 4,010 persons. Over the follow-up, 619 participants died, 424 reached 86 years (and were no longer invited to the study center), 1,356 preferred home interviews, and 249 were excluded because of incident conditions causing gait impairment. Overall, 961 participants (24.0%) had 4 WS measures, 754 (18.8%) had 3, 944 (23.5%) had 2, and 1,351 (33.7%) had 1; 3,709 had a baseline measure. Highly educated participants were less likely to have missing WS measures (table e-1); however, this difference was lost after adjustment for characteristics associated with missingness (greater age and BMI, disability, low physical activity, lower MMSE score).

Table 1 describes participants' characteristics. Approximately one-third had high education. More-educated participants were taller and in better health. Men walked faster than women. Ten years' greater age was associated with a WS difference of  $-0.196$  m/s (95% CI =  $-0.215, -0.178$ ). In age- and sex-adjusted analyses, faster WS was associated with better physical and mental health and higher education.

**Interaction between WMLs and education.** Mean (SE) WML volume ( $\text{cm}^3$  adjusted for age, sex, total white matter volume) was similar ( $p = 0.93$ ) across education groups: low = 5.60 (0.22); intermediate = 5.48 (0.22); and high = 5.51 (0.20). Analyses of the interaction between education and WMLs are based on 1,621 participants (61% women, mean age = 72.3 years) with MRI data (table 2). Increasing WML volume was associated with greater ORs of slow WS only in the low education group; this association weakened as education increased ( $p$  interaction = 0.026). Results remained unchanged after adjustment for height, BMI, and MMSE score. Similar patterns were observed for periventricular and deep WMLs. High WML volumes were not associated with slow WS

among highly educated participants (OR = 0.72), but were associated with a 2-fold-increased risk of slow WS among those with low education (OR =  $3.19/1.61 = 1.99$ ). The association between low education and slow WS was stronger among those with high volumes (OR =  $3.19/0.72 = 4.43$ ) compared to those with low volumes (OR = 1.61) (table e-2).

**Longitudinal association between education and WS.** WS decreased in a fairly linear way (figure e-1). Between-subject heterogeneity was significant, more pronounced for baseline WS (0.074, SE = 0.002,  $p < 10^{-4}$ ) than decline (0.023, SE = 0.003,  $p < 10^{-4}$ ), and decreased after adjustment for age, sex, and education (intercept 0.048, SE = 0.002; slope 0.020, SE = 0.003).

Higher education was associated with faster baseline WS (table 3); the age- and sex-adjusted difference in WS between high and low education groups (0.145 m/s) represents 0.47 SD of the WS distribution, and is equivalent to an age effect of 7.4 years. On average, WS declined over time: the average 10-year decline was  $-0.194$  m/s (95% CI =  $-0.206, -0.182$ ). Decline was slightly more pronounced in more-educated participants, but the difference did not reach statistical significance ( $p = 0.08$ ). This pattern was not modified by sex ( $p$  value time  $\times$  sex  $\times$  education = 0.80) or age ( $p$  value time  $\times$  age  $\times$  education = 0.20) (figure 1). In sensitivity analyses based on a 6-level definition of education, education did not influence WS decline ( $p = 0.37$ ). Analyses with multiple imputation of missing values yielded similar conclusions (table 3), and the trend toward faster decline in more-educated participants disappeared ( $p = 0.70$ ).

**Characteristics explaining the baseline association between education and WS.** Health behaviors, cardiovascular risk factors, chronic diseases, depressive symptoms, and psychosocial factors had a small role in explaining the education-WS association (table 4;  $0.0\% \leq \text{PR}_{\text{High education}} \leq -8.2\%$ ). Anthropometric characteristics, parental education, cognition, and general health had a stronger role ( $-12.2\% \leq \text{PR}_{\text{High education}} \leq -14.3\%$ ) (table 4). All covariates together explained approximately 40% of the association.

**DISCUSSION** Our main objective was to examine whether the concept of reserve, thus far explored mainly in relation to cognition, also applies to motor function. In analyses adjusted for age, sex, cognition, and other covariates, we found an interaction between education, a marker of reserve, and WMLs, a marker of brain damage: the adverse effect of WMLs on WS was observed only in the low education group, and the association between low education and slow WS was stronger among those with

**Table 1** Baseline characteristics of the participants by education and maximum walking speed

Characteristics	Overall (n = 4,010)	Education <sup>a</sup>			Maximum walking speed <sup>b</sup>		
		Low (n = 1,391)	Intermediate (n = 1,284)	High (n = 1,335)	Low (n = 1,254)	Intermediate (n = 1,258)	High (n = 1,197)
Mean age, y (SD)	73.4 (4.6)	73.7 (4.5)	73.1 (4.6)	73.3 (4.8) <sup>c</sup>	75.3 (4.7)	73.2 (4.5)	71.7 (4.2) <sup>d</sup>
Women, %	61.6	66.0	66.6	52.3 <sup>d</sup>	60.9	65.5	58.6 <sup>d</sup>
Married, %	40.4	42.9	41.9	36.5	42.8	41.9	35.9
High education, %	33.3	—	—	—	23.6	32.8	43.6 <sup>d</sup>
Father's education, high, % <sup>e</sup>	26.3	8.8	18.1	49.5 <sup>d</sup>	23.6	24.9	31.1 <sup>d</sup>
Mother's education, high, % <sup>f</sup>	22.5	6.9	16.7	42.9 <sup>d</sup>	16.8	22.0	28.4 <sup>d</sup>
Mean height, cm (SD)	162 (9)	160 (9)	161 (8)	164 (9) <sup>d</sup>	160 (9)	161 (9)	164 (8) <sup>d</sup>
Mean BMI, kg/m <sup>2</sup> (SD)	25.7 (4.0)	26.3 (4.2)	25.6 (4.1)	25.2 (3.7) <sup>d</sup>	26.7 (4.4)	25.4 (3.8)	24.9 (3.5) <sup>d</sup>
Intake of fruits and vegetables, %							
Low	7.4	8.5	6.6	7.1 <sup>c</sup>	9.3	7.0	6.4 <sup>g</sup>
Intermediate	26.9	27.7	26.3	26.7	27.0	26.9	26.2
High	65.6	63.8	67	66.2	63.7	66.1	67.4
Low physical activity, %	23.7	22.7	24.7	23.9	30.3	20.7	19.5 <sup>d</sup>
Current alcohol consumption, %	79.0	75.4	79.1	82.6 <sup>g</sup>	77.8	78.4	81.0 <sup>c</sup>
Current or ex-smoker, %	38.6	33.4	35.8	46.7 <sup>d</sup>	37.6	36.4	41.6
Psychotropic drug use, %	25.0	28.1	26.1	20.8 <sup>g</sup>	33.4	24.0	18.6 <sup>d</sup>
NSAIDs for joint pain, %	15.0	16.8	14.7	13.4	19.5	14.5	10.6 <sup>d</sup>
CAD/PAD, %	12.4	14.1	9.9	13.0 <sup>c</sup>	17.1	10.8	9.3 <sup>d</sup>
Dyspnea, %	13.2	15.3	13.7	10.4 <sup>g</sup>	21.0	11.9	7.5 <sup>d</sup>
Hypercholesterolemia, %	40.0	44.1	39.6	36.1 <sup>d</sup>	41.6	40.8	37.2 <sup>d</sup>
Diabetes, %	7.5	7.8	8.0	6.7	9.9	6.7	6.0 <sup>d</sup>
Hypertension, %	79.0	82.9	77.9	76.1 <sup>d</sup>	85.6	77.9	73.9 <sup>d</sup>
Mean homocysteine, μmol/L (SD)	14.9 (5.5)	15.1 (5.7)	15.1 (5.8)	14.5 (5.0) <sup>d</sup>	15.8 (5.9)	14.6 (5.1)	14.3 (5.5) <sup>d</sup>
Depressive symptoms, %	12.7	13.1	12.8	12.4	18.1	11.4	9.5 <sup>d</sup>
Mean MMSE score (SD)	27.5 (1.9)	26.8 (2.1)	27.5 (1.7)	28.1 (1.4) <sup>d</sup>	27.0 (2.1)	27.6 (1.8)	27.8 (1.7) <sup>d</sup>
Feeling of loneliness, %	14.5	16.0	15.2	12.1	19.1	13.2	11.2 <sup>d</sup>
Mean social activities score (SD)	6.5 (2.9)	6.2 (2.9)	6.3 (2.8)	7.0 (2.9) <sup>d</sup>	6.1 (2.8)	6.5 (2.8)	7.0 (2.9) <sup>d</sup>
Self-rated health, %							
Poor or very poor	3.5	4.1	3.5	2.8	2.7	4.6	9.3 <sup>d</sup>
Average	36.0	39.3	36.0	32.7	45.4	56.0	63.3
Good	54.9	52.1	56.2	56.6	45.5	36.7	25.9

Continued

**Table 1** Continued

Characteristics	Overall (n = 4,010)	Education <sup>a</sup>			Maximum walking speed <sup>b</sup>		
		Low (n = 1,391)	Intermediate (n = 1,284)	High (n = 1,335)	Low (n = 1,254)	Intermediate (n = 1,258)	High (n = 1,197)
Very good	5.6	4.5	4.3	7.9 <sup>d</sup>	6.4	2.7	1.5
<b>Medical contacts per year, %<sup>h</sup></b>							
≥5	24.9	27.2	26.8	20.8	35.0	22.9	17.5 <sup>d</sup>
3-4	49.8	54.3	51.5	43.5	51.2	52.2	45.9
≤2	25.3	18.5	21.7	35.7 <sup>d</sup>	13.9	24.9	36.6
<b>Hierarchical disability index, %</b>							
0	54.2	53.3	55.6	53.7	40.4	52.7	69.1 <sup>d</sup>
1	41.0	40.5	40.0	42.6	49.8	44.0	29.3
2 or 3	4.8	6.2	4.4	3.7	9.7	3.4	1.7
Falls in the preceding year, %	16.4	16.3	17.8	15.1	19.6	17.0	12.2 <sup>d</sup>
Mean walking speed, m/s (SD) <sup>a</sup>	1.5 (0.3)	1.4 (0.3)	1.5 (0.3)	1.6 (0.3) <sup>d</sup>	1.2 (0.2)	1.5 (0.1)	1.8 (0.2) <sup>d</sup>

Abbreviations: BMI = body mass index; CAD = coronary artery disease; MMSE = Mini-Mental State Examination; NSAID = nonsteroidal anti-inflammatory drug; PAD = peripheral artery disease.

<sup>a</sup> Education was defined according to the highest degree obtained and categorized into 3 levels: primary school degree or less (low), secondary school degree (intermediate), high school or university degree (high). The *p* values were computed using the Mantel-Haenszel trend test for categorical variables and analysis of variance (linear contrasts) for continuous variables, adjusted for age and sex where appropriate.

<sup>b</sup> Maximum walking speed was measured at baseline and categorized according to sex-specific tertiles (men: tertile 1 = ≤1.50 m/s, tertile 2 = 1.51-1.82 m/s, tertile 3 = >1.82 m/s; women: tertile 1 = ≤1.30 m/s, tertile 2 = 1.31-1.50 m/s, tertile 3 = >1.50 m/s). Because maximum walking speed was not available at baseline in all 4,010 participants (301 participants had no baseline measure but had at least one measure during the follow-up), analyses of the relation between participants' characteristics and baseline walking speed are based on 3,709 participants. For clarity of the presentation, we present percentages and means by sex-specific tertiles of walking speed, but *p* values were computed using analysis of covariance with walking speed as the dependent continuous variable and were adjusted for age and sex where appropriate.

<sup>c</sup> *p* Value < 0.05.

<sup>d</sup> *p* Value < 0.001.

<sup>e</sup> Father's education was dichotomized as high school or university degree (high) vs lower and was not available for 530 participants.

<sup>f</sup> Mother's education was dichotomized as high school or university degree (high) vs lower and was not available for 346 participants.

<sup>g</sup> *p* Value < 0.01.

<sup>h</sup> Usual number of contacts with a general practitioner per year.

**Table 2** Association between the volume of brain WMLs and slow maximum walking speed stratified by education

Education	Model 1 <sup>a</sup>			Model 2 <sup>b</sup>			Model 3 <sup>c</sup>			Model 4 <sup>d</sup>		
	OR <sup>e</sup>	95% CI	p <sup>f</sup>	OR <sup>e</sup>	95% CI	p <sup>f</sup>	OR <sup>e</sup>	95% CI	p <sup>f</sup>	OR <sup>e</sup>	95% CI	p <sup>f</sup>
<b>Total WMLs</b>												
Low (n = 509)	1.43	1.08, 1.89		1.43	1.09, 1.89		1.38	1.05, 1.83		1.39	1.05, 1.84	
Intermediate (n = 513)	1.26	0.91, 1.39		1.10	0.89, 1.36		1.13	0.91, 1.39		1.10	0.89, 1.36	
High (n = 598)	0.97	0.82, 1.15	0.025	0.97	0.82, 1.14	0.034	0.96	0.82, 1.14	0.027	0.96	0.81, 1.13	0.037
<b>Periventricular WMLs</b>												
Low (n = 509)	1.39	1.04, 1.86		1.38	1.03, 1.85		1.34	1.00, 1.80		1.34	1.00, 1.79	
Intermediate (n = 513)	1.12	0.91, 1.39		1.09	0.88, 1.36		1.12	0.91, 1.39		1.10	0.88, 1.37	
High (n = 598)	0.97	0.83, 1.14	0.043	0.97	0.82, 1.15	0.069	0.96	0.82, 1.13	0.049	0.96	0.82, 1.14	0.076
<b>Deep WMLs</b>												
Low (n = 509)	1.26	1.04, 1.51		1.27	1.05, 1.53		1.24	1.03, 1.49		1.26	1.04, 1.52	
Intermediate (n = 513)	1.07	0.92, 1.25		1.05	0.90, 1.23		1.07	0.92, 1.25		1.05	0.90, 1.23	
High (n = 598)	1.00	0.87, 1.16	0.079	0.97	0.84, 1.13	0.055	1.00	0.86, 1.16	0.068	0.97	0.83, 1.12	0.049

Abbreviations: BMI = body mass index; CI = confidence interval; MMSE = Mini-Mental State Examination; OR = odds ratio; WML = white matter lesion.

<sup>a</sup>Model 1 is adjusted for age, sex, and total white matter volume.

<sup>b</sup>Model 2: model 1 + height and BMI.

<sup>c</sup>Model 3: model 1 + MMSE score.

<sup>d</sup>Model 4: full model.

<sup>e</sup>ORs and 95% CIs computed using logistic regression with walking speed below the sex-specific median (1.50 m/s in women, 1.71 m/s in men) as the dependent variable and the volume of brain WMLs (continuous variable divided by its sex-specific SD) as the explanatory variable. ORs represent the change in the probability of walking slower than the median for an increase in 1 SD of the volume of brain WMLs. Sex-specific means (SDs) of WMLs were as follows: total WMLs = 5.17 (4.93) cm<sup>3</sup> in women and 6.07 (5.14) cm<sup>3</sup> in men; periventricular WMLs = 3.77 (4.19) cm<sup>3</sup> in women and 4.40 (4.23) cm<sup>3</sup> in men; deep WMLs = 1.40 (1.16) cm<sup>3</sup> in women and 1.67 (1.45) cm<sup>3</sup> in men. All variables were measured at baseline.

<sup>f</sup>The p values for the difference in ORs across strata of education level were computed by including an interaction term between education and the volume of WMLs in the models.

high WML volumes. The corollary, that more-educated persons are less susceptible to the deleterious effects of brain vascular lesions on motor function, is in favor of the reserve hypothesis. Our results show robust cross-sectional education-WS associations; the WS difference between high and low education is clinically meaningful because a 0.1 m/s higher

WS is estimated to be associated with a 12% reduced mortality risk.<sup>24</sup> Finally, our results show that WS decline was similar across education groups. Analyses using other SES markers (income, main occupation) yielded similar findings (data not shown). Taken altogether, these results provide evidence for the passive reserve hypothesis.

**Table 3** Association of education with baseline maximum walking speed and change in maximum walking speed

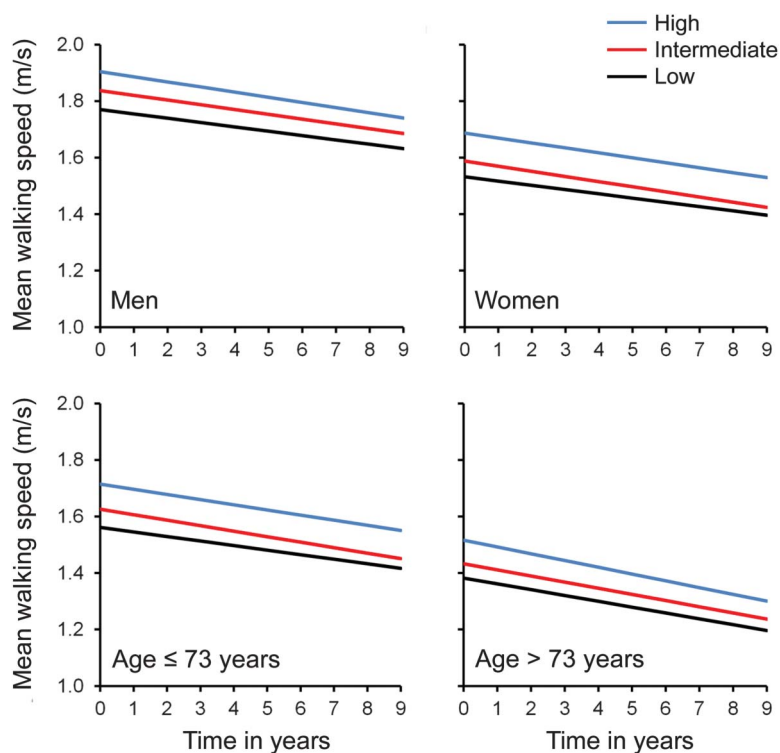
Education	Complete-case analysis				Multiple imputation analysis			
	β <sup>a</sup>	95% CI	p	p Trend	β <sup>a,b</sup>	95% CI	p	p Trend
<b>Association with baseline walking speed in m/s</b>								
Low	Ref.				Ref.			
Intermediate	0.060	0.040, 0.080	<0.001		0.058	0.038, 0.078	<0.001	
High	0.145	0.125, 0.165	<0.001	<0.001	0.143	0.123, 0.164	<0.001	<0.001
<b>Association with change in walking speed in m/s (per 10 y)</b>								
Low	Ref.				Ref.			
Intermediate	-0.027	-0.057, 0.003	0.083		-0.001	-0.004, 0.002	0.56	
High	-0.027	-0.056, 0.003	0.075	0.085	-0.001	-0.004, 0.002	0.70	0.70

Abbreviations: CI = confidence interval; Ref. = reference.

<sup>a</sup>Regression coefficients (β) and 95% CIs from a linear mixed model adjusted for age at baseline (continuous variable centered at 65 years), sex, and their 2-way interactions with time. Time (in years, divided by 10) and the intercept are included as random effects with an unstructured covariance matrix.

<sup>b</sup>Twenty datasets generated using Proc MI were pooled and analyzed using Proc MIANALYZE in SAS 9.2.

**Figure 1** Predicted trajectories of mean maximum walking speed (m/s) over the follow-up by education, sex, and median age at baseline



In sex-stratified analyses, the graph represents the mean decline in walking speed in individuals aged 65 years at baseline. In analyses stratified by age, the graph represents mean decline in walking speed in women (blue line = high; red line = intermediate; black line = low).

The reserve concept is based on the observation of an inconsistent relationship between the degree of brain damage and cognitive function. Persons with high reserve do not show clinical manifestations of neuropathology to the same extent as persons with low reserve. This concept has been extended beyond brain injury through research on the association of reserve markers, education in particular, with cognitive function. Passive and active reserve models are generally distinguished, although the demarcation is not clear-cut.<sup>1,25</sup> There is consistent epidemiologic evidence in favor of a role of reserve in aging, but its neural substrate remains under investigation.<sup>26,27</sup>

To our knowledge, the reserve concept has not been applied to motor function, but there are several parallels between motor and cognitive function. First, the education-WS association is similar in strength to the education-cognition association: the difference in MMSE scores between the high and low education groups in our data corresponds to 0.69 SD of the MMSE distribution, and the corresponding figure for WS is 0.47. Second, determinants of motor function are multifactorial. Although there is clearly a peripheral component (e.g., musculoskeletal, sensory), motor function is also under brain control with vascular lesions known to affect motor performances.

WMLs, particularly in the periventricular region, have been associated with worse motor performances,<sup>13,14</sup> and lie on the pathway between cardiovascular risk and motor function. Our finding that the WMLs-WS association weakened with increasing education is comparable to findings for cognition,<sup>28</sup> supporting the view that more-educated persons are able to sustain more brain damage without experiencing adverse outcomes. Provided that enriched environments, of which education is a marker, influence neuronal circuits involved in motor control, we hypothesize that reserve may contribute to explaining the association of education with motor function. In animals, motor stimulation and physical activity are associated with changes in brain neurochemistry and physiology that may be relevant for the reserve theory.<sup>26,29</sup> Third, our findings support a passive reserve hypothesis; studies on cognition show comparable findings as education has a robust cross-sectional association with cognition but not with cognitive decline.<sup>11,12,30,31</sup>

Several studies have shown markers of low SES (including education) to be associated with poorer physical functioning assessed using subjective measures.<sup>32,33</sup> Few studies used objective measures and most were cross-sectional.<sup>15–17</sup> Longitudinal data based on more than 2 measures are scarce and showed that education is associated with motor function in cross-sectional analyses but did not influence change over time (maximum follow-up, 5 years).<sup>19,20</sup>

We extend findings on the SES–motor functioning association in several ways. We showed that persons with lower education had slower WS and this association was not modified by sex or age. In addition, based on 4 WS measures over a longer follow-up (10 years) than previous studies, we found no evidence that education influences WS decline. There was some indication that participants in the high/intermediate education groups tended to decline more than less-educated participants but this trend completely disappeared when using a more detailed education definition or taking missing values into account. This is because those with missing WS measures during the follow-up were older, heavier, more disabled, and less physically active (all associated with low education) and therefore at higher risk of motor decline.

Education has a major influence on physical and mental health and the education-WS association was partially explained by a number of covariates,<sup>15,16</sup> among which anthropometric measures, cognition, parental education, and general health had an important role. The association of education with BMI and height is well documented; both have a strong “mechanical” impact on WS. Cognitive and motor function are known to be associated but effect sizes



**Table 4** Association of education with baseline maximum walking speed: The role of covariates<sup>a</sup>

Model	Education level							
	Low	Intermediate			High			p Trend
		$\beta^b$	95% CI	PR, % <sup>c</sup>	$\beta^b$	95% CI	PR, % <sup>c</sup>	
A = adjusted for baseline age and sex	Ref.	0.058	0.037, 0.079	—	0.147	0.127, 0.168	—	<0.0001
B = model A + height and BMI	Ref.	0.049	0.029, 0.070	-15.5	0.127	0.107, 0.148	-13.6	<0.0001
C = model A + health behaviors <sup>d</sup>	Ref.	0.058	0.037, 0.079	0.0	0.146	0.125, 0.167	-0.7	<0.0001
D = model A + cardiovascular risk factors <sup>e</sup>	Ref.	0.057	0.036, 0.078	-1.7	0.140	0.119, 0.161	-4.8	<0.0001
E = model A + cognition <sup>f</sup>	Ref.	0.048	0.027, 0.069	-17.2	0.129	0.108, 0.151	-12.2	<0.0001
F = model A + depressive symptoms <sup>g</sup>	Ref.	0.057	0.037, 0.078	-1.7	0.147	0.127, 0.168	0.0	<0.0001
G = model A + chronic diseases <sup>h</sup>	Ref.	0.052	0.031, 0.072	-10.3	0.135	0.115, 0.156	-8.2	<0.0001
H = model A + psychosocial factors <sup>i</sup>	Ref.	0.059	0.038, 0.080	1.7	0.139	0.118, 0.160	-5.4	<0.0001
I = model A + parental education level <sup>j</sup>	Ref.	0.051	0.030, 0.072	-12.1	0.128	0.105, 0.151	-12.9	<0.0001
J = model A + general health <sup>k</sup>	Ref.	0.054	0.034, 0.074	-6.9	0.126	0.106, 0.146	-14.3	<0.0001
K = fully adjusted <sup>l</sup>	Ref.	0.037	0.017, 0.058	-36.2	0.081	0.057, 0.105	-44.9	<0.0001

Abbreviations: BMI = body mass index; CI = confidence interval; PR = percentage reduction; Ref. = reference.

<sup>a</sup> Analyses are based on 3,709 subjects with baseline walking speed and education data available.

<sup>b</sup> Regression coefficients ( $\beta$ ) and 95% CIs were computed using linear regression with baseline walking speed as the dependent variable. They represent the difference in baseline walking speed associated with the corresponding group of education level compared with the reference group (low education). All regression coefficients  $\beta$  are significant at the  $p < 0.001$  level.

<sup>c</sup> PR in the regression coefficient for models B-K.

<sup>d</sup> Smoking, alcohol consumption, diet, and physical activity.

<sup>e</sup> Hypertension, diabetes, hypercholesterolemia, and homocysteine level.

<sup>f</sup> Assessed through the Mini-Mental State Examination.

<sup>g</sup> Assessed through the Center for Epidemiologic Studies Depression Scale.

<sup>h</sup> History of coronary or peripheral artery disease; self-report of dyspnea for minor efforts, daily activities, or at rest; regular use of nonsteroidal anti-inflammatory drugs for joint pain; psychotropic drug use.

<sup>i</sup> Marital status, feeling of loneliness, and engagement in social activities.

<sup>j</sup> Father's and mother's education level was missing for some participants (table 1) and we included an indicator variable to retain them in the analyses. Analyses excluding subjects without information for parental education level yielded identical results.

<sup>k</sup> Assessed through a question on self-rated health and the number of contacts with a general practitioner per year.

are modest at best. A recent review reported standardized  $\beta$  regression coefficients comprised between 0.05 and 0.15<sup>34</sup>; the authors concluded that the observed associations were not sufficiently strong or consistent to provide conclusive evidence for common causes.<sup>34</sup> Cognition appears not to have a major role in the education-WS association: in our study, MMSE explained 15% of the association; using alternative tests (Isaac Test, Benton Visual Retention Test, Trail Making Test) yielded similar conclusions (data not shown). Finally, because childhood and adult SES are independently associated with slower WS in old age,<sup>35</sup> parental education was used as a surrogate for childhood SES and attenuated the education-WS association by approximately 12%.

This study's main strengths include repeated WS measures over 10 years in a large sample of community-dwelling elderly persons. In addition, we used a highly reproducible WS measure that is not affected by ceiling effects. Nonresponse over the follow-up represents its main limitation. We dealt with missing values by using multiple imputation and including

data on surrogates of motor function, and found results similar to those from the main analysis. We did not include a standardized assessment of peripheral neuropathy, but we took important risk/protective factors (alcohol, diabetes, diet) of peripheral neuropathy into account.

In conclusion, more-educated persons were less susceptible to the effect of WMLs on motor function and higher education was associated with better motor performances but not with slower decline. We hypothesize that the concept of reserve extends to motor function and show evidence for the concept of passive reserve.

#### AUTHOR CONTRIBUTIONS

Dr. Elbaz: study concept and design, analysis and interpretation, statistical analysis, study supervision or coordination, drafting/revising the manuscript. Dr. Vicente-Vytopilova: drafting/revising the manuscript, statistical analysis, analysis and interpretation. Dr. Tavernier: drafting/revising the manuscript, data acquisition. Dr. Sabia and Dr. Dumurgier: drafting/revising the manuscript. Dr. Mazoyer: drafting/revising the manuscript, data acquisition. Dr. Singh-Manoux: drafting/revising the manuscript. Dr. Tzourio: drafting/revising the manuscript, study supervision or coordination, funding.

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