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Cognitive reserve and working memory in cognitive performance of adults with subjective cognitive complaints: longitudinal structural equation modeling

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ABSTRACT

Objective: To study the influence of cognitive reserve (CR) on cognitive performance of individuals with subjective cognitive complaints (SCCs) within a period of 36 months.

Design: We used a general linear model repeated measures procedure to analyze the differences in performance between three assessments. We used a longitudinal structural equation modeling to analyze the relationship between CR and cognitive performance at baseline and at two follow-up assessments.

Setting: Participants with SCCs were recruited and assessed in primary care health centers.

Participants: A total of 212 participants older than 50 years with SCCs.

Measurements: Cognitive reserve data were collected with an ad hoc questionnaire administered to the subjects in an interview. General cognitive performance (GCP), episodic memory (EM), and working memory (WM) have been evaluated. The Mini-Mental State Examination and the total score of Spanish version of the Cambridge Cognitive Examination evaluated the GCP. Episodic memory was assessed with the Spanish version of the California Verbal Learning. Working memory was evaluated by the counting span task and the listening span task.

Results: The satisfactory fit of the proposed model confirmed the direct effects of CR on WM and GCP at baseline, as well as indirect effects on EM and WM at first and second follow-up. Indirect effects of CR on other cognitive constructs via WM were observed over time.

Conclusion: The proposed model is useful for measuring the influence of CR on cognitive performance over time. Cognitive response acquired throughout life may influence cognitive performance in old age and prevent cognitive deterioration, thus increasing processing resources via WM.

Key words: episodic memory, prevention, cognitive impairment, education, lifestyle, aging

Introduction

Cognitive reserve (CR) is an active process whereby the brain adapts to a situation of deterioration by using cognitive processing resources to compensate for the deficits (Stern *et al.*, 2018). It has been defined as a hypothetical construct that can be studied by latent variables or proxies (years of schooling, job complexity or occupational attainment, crystallized intelligence measured through vocabulary level scores, literacy, engagement in leisure activities, and social or cultural participation) (Jones *et al.*, 2011) that have shown protective effects against cognitive impairment (Chapko *et al.*, 2017; Ferreira *et al.*, 2016; Garibotto *et al.*, 2008; Giogkaraki *et al.*, 2013; Lojo-Seoane, Facal, Juncos-Rabadán *et al.*, 2014). Lojo-Seoane, Facal, Guàrdia-Olmos *et al.* (2014) used structural equation modeling (SEM) to examine the relationship between CR and cognitive performance in a sample of people older than 50 years with subjective memory complaints. The CR construct, formed by interrelated latent variables denominated educational level and lifestyle, significantly affected episodic memory (EM), working memory (WM), and

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general cognitive performance (GCP), highlighting an indirect effect on EM via WM. Thus, CR positively affected performance of WM span tasks and thereby indirectly affected other cognitive domains, especially EM, which probably benefited from the greater availability of processing resources (Constantinidou *et al.*, 2014; Facal *et al.*, 2014; Salthouse, 1991; Sandry *et al.*, 2015; Sandry and Sumowski, 2014).

Performance of WM tasks has been demonstrated to be a sensitive measure for differentiating between normal cognitive aging and mild cognitive impairment (MCI) and between MCI and Alzheimer's disease (AD) (Belleville *et al.*, 2008; Economou *et al.*, 2007; Gagnon and Belleville, 2011). The mediating effect of WM on the relationship between CR and cognitive performance has received support from studies with different clinical samples such as traumatic brain injury (Sandry *et al.*, 2015) and multiple sclerosis (Sandry and Sumowski, 2014). This mediating effect has been examined in people with SCCs by Lojo-Seoane, Facal, Guàrdia-Olmos *et al.* (2014) and Lojo-Seoane *et al.* (2018), revealing that CR positively influences EM and GCP, both baseline and follow-up, through WM.

In cognitive impairment research, subjective cognitive complaints (SCCs) have been suggested to be an early sign of clinical relevance in determining early symptoms of cognitive decline (Dufouil *et al.*, 2005). Subjective cognitive complaints constitute an important criterion for the diagnosis of MCI (Albert *et al.*, 2011; Petersen, 2004; Petersen *et al.*, 1999), and individuals with SCCs are more likely to develop dementia than those without SCCs (Mitchell *et al.*, 2014; Reisberg and Gauthier, 2008). The effect of CR on this process of cognitive deterioration is key because, according to the CR hypothesis, individuals with greater CR would tolerate a greater pathological burden affecting the brain, which would be compensated for by a greater amount of neural resources. Thus, the study of the longitudinal influence of CR on cognitive performance in people with SCC is very important because these individuals may be at the first stage of the cognitive continuum, ranging from normal aging to dementia (Jack *et al.*, 2018), and a higher level of CR may mask the cognitive impairment (Van Oijen *et al.*, 2007).

Although some longitudinal studies have been conducted to investigate the protective effect of CR against cognitive decline (Mungas *et al.* 2018; Reed *et al.*, 2010; Sumowski *et al.*, 2014; Vaughan *et al.*, 2014), specific research on people with SCCs is scarce. Van Oijen *et al.* (2007) estimated the association between subjective memory complaints and risk of dementia (during a mean follow-up of 9 years) with a cohort study of 7983 participants aged more than 55 years, considering the level of education at baseline. These researchers observed that the risk of AD associated with subjective memory complaints was higher in highly educated people than in people with low levels of education. This finding could be explained in the context of the CR hypothesis, as a high level of education may mask the pathological burden affecting the brain. In a recent study, Lojo-Seoane *et al.* (2018) directly analyzed the relationship between SCC and CR as a latent construct formed by different proxies. The study examined the influence of CR at baseline on cognitive performance at follow-up (18 months) in a sample of 266 participants with SCCs, and different longitudinal models were tested. In the best-fit model, CR affected EM and GCP at follow-up. In this line, Facal *et al.* (2019) explored the role of CR in the conversion from MCI to dementia, comparing converter and nonconverter in a sample of 169 participants with SCCs. They corroborated the protective role of CR as a mediator of conversion to dementia, whereby participants with more years of education and higher vocabulary scores survived longer without developing dementia.

In light of the previous research findings, the aim of the present study was to examine the influence of CR, as a latent construct formed by the main proxies analyzed in the literature, on cognitive performance of individual with SCCs during a period of 36 months in which the participants were assessed three times. The application of the CR model to longitudinal data currently will provide new information about the impact of CR on the process of decline in the cognitive continuum from SCCs toward AD. We analyzed the effect of CR measured at baseline on GCP and on EM and WM at three different times. The specific objectives of the study were as follows: 1) to examine the effect of CR on cognitive performance individuals aged more than 50 years with SCCs, and 2) to determine the effect of CR mediated by WM in other cognitive domains at consecutive follow-ups.

Method

Participants

A total of 398 participants were recruited from the ongoing Compostela Aging Study (Juncos-Rabadán *et al.*, 2012) and assessed at baseline. Of these, 104 did not participate in the first follow-up evaluation (reasons: 53.8% motivation, 11.5% morbidity, 30.8% mobility, and 3.8% mortality). At the second follow-up, 232 patients were assessed (62 dropouts, reasons: 50% motivation, 24.2% morbidity, 24.2% mobility, and 1.6% mortality). Finally, the study included 212 participants (20 were excluded because they did not complete some tests): 145 women (68.4%) and 67 men (31.6%). All participants were at least 50 years old; they attended to primary care centers with SCCs (participants spontaneously reported that their memory and/or attention was not as good as before), and they were referred to the project by general practitioners. The educational levels of the participants ranged from basic schooling (0-4 years of education) to university studies (+ 13 years of education) (mean 9.64 ± 4.58). In addition, the participants did not fulfil any of the following exclusion criteria at baseline: prior diagnosis of depression or other psychiatric disturbances (according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] criteria), according to the medical records provided by general practitioners; prior diagnosis of neurological disease, including probable AD or other types of dementia (according to National Institute of Neurologic, Communicative Disorders and Stroke - Alzheimer's Disease and Related Disorders Association and DSM-IV criteria); previous brain damage or brain surgery; undergoing chemotherapy; prior diagnosis of diabetes type II; sensorial or motor disturbances; and previous consumption of substances that could affect normal performance of the tasks.

Instruments

To collect the CR data, an ad hoc questionnaire was constructed and administered to the subjects in an interview to obtain measures of the main proxies analyzed in the literature. The following measures, determined at baseline, were considered observable indicators of CR: a) total number of years of formal schooling; b) occupational attainment, which evaluates the complexity of the profession to which the participants have dedicated most of their working life, according to the protocol outlined in the project entitled "Network for efficiency and standardization of dementia diagnosis" (Garibotto *et al.*, 2008) on a scale of 1 to 6 (where 1 = no occupation; 2 = unqualified worker; 3 = housewife; 4 = qualified worker, shopkeeper, low-ranking civil servant, employee, small business employee, office worker, or sales person; 5 = middle-ranking civil servant or manager, small-business owner, teacher, or specialist in subordinate position; and 6 = high-ranking civil servant or director, university lecturer, or self-employed with high level of responsibility); c) reading habits, a measure that evaluates the frequency of reading during the last 3 years via one question, with responses on a scale of 0 to 4 (where 0 = never, 1 = occasionally, 2 = once a week, 3 = twice a week, 4 = every day); d) frequency of social and cultural activities, which evaluates participation in these types of activities during the last 3 years via two questions, with responses on a scale of 0 to 4 (where 0 = never, 1 = rarely, 2 = occasionally, 3 = often, and 4 = always). The level of vocabulary knowledge was evaluated by the vocabulary test of the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1988), and the Peabody picture vocabulary test (Dunn and Dunn, 1981). The total scores obtained by participants in each of the vocabulary tests were considered observable indicators of CR.

Episodic memory, acquisition, and recall were evaluated with the Spanish version of the California Verbal Learning Test (CVLT) with norms for age groups (Delis *et al.*, 1987, Spanish version by Benedet and Alejandre, 1998). The scores for free and cued recall in short and long terms were used as EM measures. Working memory was evaluated by two span tasks: a) the counting span task (Case *et al.*, 1982) and b) the listening span task (Pickering *et al.*, 1999), which is an adaptation of the reading span task developed by Daneman and Carpenter (1980). For both WM span tasks, the measures total number of correct items and the total number of completed series were considered measures of WM. The GCP was evaluated by the following tests: a) the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975; Spanish version by Lobo *et al.*, 1999) and b) the Spanish version of the Cambridge Cognitive Examination (CAMCOG-R) (Roth *et al.*, 1986; Spanish version by López-Pousa, 2003) with norms for age and education groups (Pereiro *et al.*, 2015).

Procedure

Participants were recruited by general practitioners from patients who attended primary care centers with complaints of cognitive failure. Those individuals who agreed to participate were informed that they would take part in a longitudinal study with three evaluations over time, with an interval of about 18 months between each assessment: at baseline (T1), first follow-up (T2), and second follow-up (T3). After the baseline assessment, participants were informed that they would be called for the follow-up assessments by phone. The time (in months) between assessments varied slightly depending on the availability of the participants. The mean interval between assessments was 18.67 ± 2.73 months. All the 212 participants included in the study completed the three evaluations.

Each evaluation involved three sessions, each of around 90 minutes' duration. The sessions included interviews to obtain sociodemographic information relevant to the study and information on indicators of CR, as well as extensive neuropsychological assessment, as already mentioned. The same procedure was followed in the first and second follow-up assessments.

The study met with the approval of the Clinical Research Ethics Committee of the Xunta de Galicia

(Spain) and was conducted in accordance with the provisions of the Declaration of Helsinki (as revised in Fortaleza, 2013). The participants (volunteers) were informed of the objectives of the study and procedures involved and were required to sign an approved informed consent before each assessment.

Statistical analysis

A general linear model repeated measures procedure (IBM SPSS Statistics, version 21) was used to analyze the differences in performance between the three assessments.

To analyze the effects of CR on EM, WM, and GCP over time, we used a longitudinal structural equation model (LSEM) based on that proposed in an earlier study (Lojo-Seoane, Facal, Guàrdia-Olmos *et al.*, 2014). The CR macroconstruct was defined from an exogenous measurement model composed of a second-order factor formed by two latent variables: a) educational level, which includes the observable variable years of education, occupational attainment, and reading habits as the main variables related to education (Giogkaraki *et al.*, 2013; Lojo-Seoane, Facal, Guàrdia-Olmos *et al.*, 2014; Stern *et al.*, 2018) and scores obtained in the WAIS III vocabulary and Peabody tests as a main variable related to crystallized intelligence (Tucker and Stern, 2011) and b) lifestyle, formed by the interrelated variables frequency of social activities and frequency of cultural activities, which have been shown to be the main proxies for engagement in active living (Lojo-Seoane, Facal, Guàrdia-Olmos *et al.*, 2014; Stern *et al.*, 2018; Verghese *et al.*, 2006; Wilson *et al.*, 2007). The structural model included the direct effect of CR on the cognitive constructs EM, WM, and GCP as an endogenous measurement model. This enables reflective analysis of the relationship between the CR construct and these three cognitive performance domains. In order to define these cognitive constructs, we proposed a formative system of indicators for each construct. For EM, the endogenous structure of the complete model included verbal short-term free recall, short-term cued recall, and long-term free recall from the CVLT. Working memory grouped the scores obtained in two different tasks —counting span and listening span—which measure simultaneous storage and processing: counting span correct series, listening span correct series, and listening span correct items (Case *et al.*, 1982). The GCP included the scores obtained in the following tests, which are especially sensitive in cognitive impairment research: MMSE and scores in the CAMCOG-R, i.e. the total score CAMCOG-R and the orientation subscore (Cullum *et al.*, 2000).

The LSEM includes the following effects: a) direct effects of CR on the three cognitive domains, EM1, WM1, and GCP1, corresponding to T1; b) direct effects of each cognitive domain at T1 on the corresponding cognitive domain at T2; and c) direct effects of each cognitive domain at T2 on the corresponding domain at T3. Thus, we studied the effects of CR on cognitive performance at T3 via each cognitive domain at T1 and T2. Moreover, we added the indirect effects of WM on EM and GCP at each time to obtain new information about the mediating role of WM on performance in other cognitive domains (Constantinidou *et al.*, 2014; Lojo-Seoane, Facal, Guàrdia-Olmos *et al.*, 2014; Lojo-Seoane *et al.*, 2018; Sandry *et al.*, 2015; Sandry and Sumowski, 2014).

The estimated SEM parameters and fit index were studied using used M Plus 5 for Windows. In order to evaluate the model fits to the equations, we used the most commonly accepted parameters (Hu and Bentler, 1999) in addition to the specific estimates for each parameter: the Comparative Fit Index (CFI), the Tucker-Lewis Index), and the root mean square error of approximation (RMSEA). Values equal to or higher than .95 are recommended for indicators of global fit (CFI), whereas for the RMSEA, a good fit is assumed when the value is below .08. We also used the Chi-square test for goodness of fit to analyze the structural fit between the matrix of initial correlations (R) between the observable values and the reproduced matrix Σ.

Results

Results for CR and cognitive performance measures

Mean values and standard deviations of demographic and CR measures at baseline are shown in Table 1. The participants included in the sample were more than 48 years old, of which 90 (42.5%) were middle-aged adults (less than 65 years old), 91 (42.9%) were young-old adults (less than 75 years old), and 31 (14.6%) older adults (more than 75 years old).

Information about mean values and standard deviations for neuropsychological measures and results from general linear model repeated measures (baseline and first and second follow-up assessments) are shown in Table 2. Significant differences were found for the three measures of EM (CVLT Short Delay Free Recall, CVLT Short Delay Cued Recall, and CVLT Long Delay Free Recall) and for one measure of GCP (CAMCOG-R total), with higher scores at T2 and T3 than at baseline. Only two measures of GCP (MMSE and CAMCOG-R Orientation) differed significantly between T2 and T3. No significant differences were found in any of the WM

Table 1. Mean values, standard deviations, and range of demographic and cognitive reserve measures (WAIS) at baseline ($N = 212$)

	MEAN	STANDARD DEVIATION	RANGE
Age	65.86	8.89	50-87
Years of education	9.82	4.5	1-20
Occupational attainment	3.12	1.07	1-6
Reading habits	3.16	1.08	1-4
Social activities	2.33	1.11	1-4
Cultural activities	1.81	1.15	1-4
WAIS vocabulary test	49.2	13.22	18-75
Peabody picture-vocabulary test	62.65	16.64	7-94

WAIS = Wechsler Adult Intelligence Scale.

measures. The effect size values (partial eta-squared) were so small that the observed differences are irrelevant to the purposes of this study. These results may indicate the existence of practice effects in the recalling variables (Campos-Magdaleno *et al.*, 2017).

Results of measurement model

The proposed LSEM (Figure 1) includes the direct effect of CR on performance in the three cognitive domains, EM, WM, and GCP, measured at three times. The effects of each observable indicator of CR are shown in Table 3 (all significant, $p < .001$), and the effects of each observable indicator (all significant, $p < .001$) of cognitive performance are shown in Table 4.

Results of longitudinal structural equation modeling

All relationships analyzed by longitudinal SEM were found to be significant (Figure 1). The proposed model shows at baseline (T1) direct negative effect of CR on EM1 ($\gamma = -.255$; $p = .024$), direct positive effects of CR on WM1 ($\gamma = .723$; $p < .001$) and GCP1 ($\gamma = .272$; $p = .001$), and indirect positive effect of CR through WM1 on EM1 ($\beta = .845$; $p = .001$) and GCP1 ($\beta = .716$; $p < .001$). The model also showed positive effects of EM and WM at baseline on their corresponding factors at T2 assessment (EM1-EM2, $\beta = .214$, $p < .001$; WM1-WM2, $\beta = .473$, $p < .001$), and of EM and WM at T2 on EM and WM at T3 (EM2-EM3, $\beta = .252$, $p < .001$; WM2-WM3, $\beta = .636$, $p < .001$). The relationship between GCP1 and GCP2 was negative ($\beta = -.189$, $p < .001$), but that between GCP2 and GCP3 was positive ($\beta = .217$, $p < .001$). Working memory had positive effects on the other cognitive domains at each assessment time, at baseline (EM, $\beta = .848$, $p = .001$; GCP, $\beta = .726$, $p = .001$), at T2 (EM2, $\beta = .822$, $p = .001$; GCP2 $\beta = .985$, $p < .001$), and at T3 (EM3, $\beta = .735$; $p < .001$; GCP3, $\beta = .743$; $p < .001$).

Cognitive reserve had an indirect effect on the cognitive performance in T2 and T3 through WM at each assessment. The indirect effect is the result of the multiplication of the corresponding direct effects. Thus, the indirect effect of CR mediated through WM at baseline on EM was .718 x .848 = .608 and on GCP was .718 x .726 = .521. The indirect effect of CR mediated through WM at T2 on EM was .718 x .473 x .822 = .279 and on GCP was .718 x .473 x .985 = .335. The indirect effect of CR mediated through WM at T3 on EM was .718 x .473 x .636 x .735 = .159 and on GCP was .718 x .473 x .636 x .743 = .160.

The goodness-of-fit measures obtained for the model were reasonably satisfactory (Table 5). The value of ratio between Chi square and degrees of freedom was adequate as indicating an excellent fit. In addition, CFI (.94), TLI (.95), and RMSEA (.022) values showed an adequate fit.

Discussion

The objective of this study was to examine the longitudinal influence of CR on the cognitive performance of individuals with SCCs. The proposed structural model showed a significant effect of CR over time (36 months). In addition, CR was found to have effect through WM on other cognitive domains at baseline and at follow-up assessments.

In relation to the first specific objective, we examined the evolution of cognitive performance in three assessments (over 36 months), considering the mediating effect of CR. The proposed model showed that cognitive performance for each factor at each evaluation time had a positive direct effect on cognitive performance of the corresponding factor at the next follow-up assessment. Nevertheless, we found only one negative effect, for GCP at T1 on T2. This effect could be explained by the higher direct effect of WM at T2 on GCP at T2. Thus, CR has significant positive effect on all studied cognitive domains at each assessment time through direct effect or indirect effect via WM. Other studies have reflected the longitudinal protective effect of CR on cognitive performance (Lojo-Seoane *et al.*, 2018; Mazzeo *et al.*, 2019; Sumowski *et al.*, 2014). Vaughan *et al.* (2014) found that CR influenced cognitive performance at baseline but not over 2 to 3 years. However, our results indicated that, considering the indirect effect of CR through WM at each assessment time, the protective effect of CR on cognitive performance occurs at baseline and also after 3 years. The differences between the methodology used by the authors and that used in the current

Table 2. Results of general linear model repeated measures (mean values, standard deviations in parentheses, and range) for neuropsychological measures at each assessment (T1: baseline; T2: first follow-up; T3: second follow-up)

	MEAN (SD) T1	MEAN (SD) T2	MEAN (SD) T3	F	DIFFERENCES BETWEEN ASSESSMENTS	EFFECT SIZE (ηp^2)
CVLT Short Delay Free Recall	9.34 (3.69)	10 (3.93)	10.18 (4.2)	9.96*	T1 < T2, T3	.045
CVLT Short Delay Cued Recall	10.54 (3.43)	11.22 (3.38)	11.4 (3.75)	10.99*	T1 < T2, T3	.050
CVLT Long Delay Free Recall	10.19 (3.77)	10.78 (4)	10.9 (4.48)	7.09*	T1 < T2, T3	.033
Counting span correct series	2.65 (1.14)	2.79 (1.3)	2.72 (1.25)	.97		.005
Listening span correct series	1.39 (1.15)	1.51 (1.18)	1.4 (1.17)	1.21		.006
Listening span correct items	14.91 (7.79)	15.63 (8.95)	15.87 (8.08)	1.77		.009
MMSE	27.63 (2.07)	27.41 (2.53)	27.19 (2.62)	4.55*	T3 < T2, T1	.021
CAMCOG-R orientation	9.53 (0.79)	9.62 (0.89)	9.37 (1.17)	6.8*	T3 < T2	.031
CAMCOG-R total	86.47 (9.11)	87.94 (9.67)	88.01 (10.44)	8.89*	T1 < T2, T3	.040

CVLT = California Verbal Learning Test; MMSE = Mini-Mental State Examination; CAMCOG-R = Cambridge Cognitive Examination-Revised; SD = standard deviation.
* significant differences.

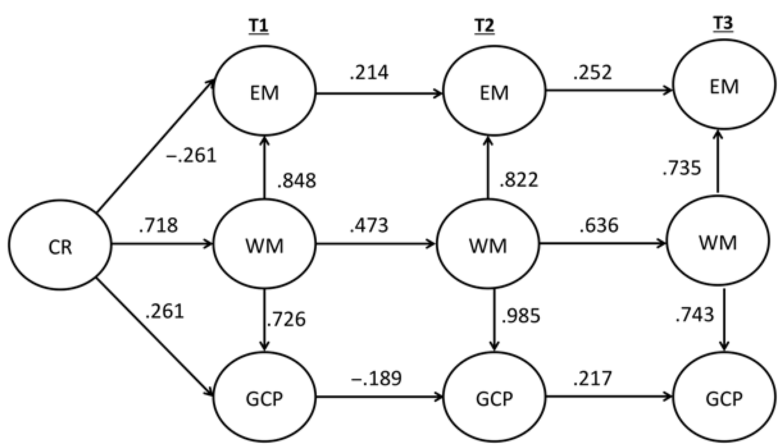

Figure 1. Standardized estimates of each free parameter in the proposed structural equation model of the relationship between measures of cognitive performance assessed at baseline (T1), first follow-up (T2) and second follow-up (T3), mediated by CR.

study could explain the differences in the results. Vaughan *et al.* (2014) analyzed the influence of CR using a change score model, while we used a longitudinal model with direct scores measured three times, in which the influence of CR over time was observed through direct and indirect effects.

With respect to the mediating effect of WM and thus the second specific objective of this work, we can confirm the indirect effect of CR on other cognitive domains via WM over time observed in the previous studies (Lojo-Seoane, Facal, Guàrdia-Olmos *et al.*, 2014; Lojo-Seoane *et al.*, 2018). Working memory performance had a transverse effect on other cognitive domains such as EM and on the GCP at each assessment. The transverse effect of the WM was greater than the longitudinal effect of the cognitive domains on themselves and greater than the indirect effect of the CR. The mediating role of WM in the CR relationship has received support in different clinical populations such as traumatic brain injury (Sandry *et al.*, 2015) and multiple sclerosis (Sandry and Sumowski, 2014) and amnestic MCI (Constantinidou *et al.*, 2014). Our findings may contribute to a better understanding of

Table 3. Standardized estimates of the effects for each observable variable of cognitive reserve

COGNITIVE RESERVE	λ
Years of education	.706
Occupational attainment	.571
Reading habits	.406
Social activities	.482
Cultural activities	.358
Peabody picture-vocabulary test	.848
WAIS vocabulary test	.865

WAIS = Wechsler Adult Intelligence Scale.

Table 4. Standardized estimates of the effects for each observable variable of cognitive performance at each time (T1, T2, and T3)

COGNITIVE PERFORMANCE		λ T1	λ T2	λ T3
EM	CVLT short-term free recall	.946	.981	.984
	CVLT short-term cued recall	.942	.980	.989
	CVLT long-term free recall	.944	.988	.992
WM	Counting span correct series	.525	.991	.919
	Listening span correct series	.510	.99	.788
	Listening span correct items	.625	.990	.931
GCP	MMSE total	.789	.919	.991
	CAMCOG-R Orientation	.535	.788	.993
	CAMCOG-R total	.897	.931	.996

EM = episodic memory; WM = working memory; GCP = general cognitive performance; CVLT = California Verbal Learning Test; MMSE = Mini-Mental State Examination; CAMCOG-R = Cambridge Cognitive Examination-Revised.

the relationship between CR and cognitive performance, considering WM as an important mechanism through which CR may exert its protective effect on other cognitive domains. We suggest that the protection may be due to an increase in the processing resources that contribute to maintaining or even improving performance in tasks related to other cognitive domains. This is an interesting issue regarding research and clinical practice on cognitive decline and cognitive impairment because, according to the CR hypothesis, an individual with cognitive impairment and who has a high CR would have more processing resources to deal with GCP tasks, specifically those related to EM performance. In this case, that individual would be more able to mask the symptoms of impairment. Likewise, a high CR could mask symptoms of objective cognitive deterioration in people with SCCs. At the same time, our findings are relevant with respect to the role of the intervention to preserve and enhance cognitive capacity of older adults; training-specific strategies that promote using WM, such as dual tasking, executive coordination, and complex decisions, produce enrichment effects on adult cognitive development (Hertzog *et al.*, 2008) and could influence a better GCP in the future.

Table 5. Fitting indices derived from robust maximum likelihood estimation applied to the structural model

INDICATOR	ESTIMATE
χ^2 with df = 363	435.346
Ratio χ^2/df	1.199
Comparative Fit Index	.94
Tucker-Lewis index	.95
Root mean square error of approximation	.022

This study has some limitations: a) In this work, only one specific model of the many possible models has been tested, taking into account the standard statistical assumptions. b) We only had information of two of the five proxies of CR, reading and participation in social and cultural activities, from the last 3 years. As a measure of CR, it would be interesting to have the frequency of these activities throughout life. c) Our sample was constituted by the totality of individuals with SCCs, without distinguishing between individuals with MCI, individuals with subjective cognitive decline (SCD), and cognitively healthy individuals; further research is needed to explore the effect of CR on the progress of different subtypes of people with SCCs, such as those diagnosed with MCI and subjective cognitive decline and those confirmed as healthy controls, taking into account the possible transition between diagnostic states and possible progression to dementia (Facal *et al.*, 2015). d) Other limitation of this study is the percentage of attrition (47%) over time; longitudinal research is required to study attrition and to enable general conclusions about the effects of CR to be reached.

In conclusion, the results of this study show that CR has a longitudinal effect on cognitive performance, confirming the importance of engaging in cognitive activities throughout life. The participation of these activities provides resources that can compensate for any possible impairment. Furthermore, we confirmed that the protective effect of CR is generally exerted through WM, thus highlighting the clinical importance of this cognitive domain in detecting cognitive impairment as well as cognitive intervention. In future studies, we will examine how CR impacts the shape of change in EM, WM, and GCP. In addition, we will explore the effect of CR on the progress of participants with SCCs and those diagnosed with MCI, taking into account the possible transition between diagnostic states and possible progression to dementia.

Conflict of interest

None.

Description of authors' roles

Cristina Lojo-Seoane wrote the paper, collected data, and collaborated in statistical analysis. David Facal collaborated in writing the paper and in the design of the study and revised the final version of the paper. Joan Guàrdia-Olmos was responsible for statistical analysis and revised the final version of the paper. Arturo X. Pereiro collaborated in the design of study, supervised the data collection, and made a critical revision of the manuscript. María Campos-Magdaleno and Sabela C. Mallo collaborated in the data collection and performed a critical review of the manuscript. Onésimo Juncos-Rabadán designed the study, supervised the data collection, and collaborated in writing the paper.

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