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Cognitive reserve and patient-reported outcomes in multiple sclerosis

Carolyn E Schwartz[1,2], Erin Snook[3], Brian Quaranto[1], Ralph HB Benedict[4] and Timothy Vollmer[5,6]

Abstract

Background: Adaptation and compensation in the face of changing pathology may be better understood by considering the concept of cognitive reserve, which may protect against disability in multiple sclerosis (MS).

Objectives: The present work investigates the relationship between cognitive reserve and demographic characteristics, health behaviors, and patient-reported outcomes (PROs).

Methods: Cross-sectional data (n=1142) were drawn from the North American Research Committee on MS (NARCOMS) Registry, from whom additional survey data were collected. Cognitive reserve was measured using the Stern and Sole-Padulles measures, the O*NET occupational classification system, and the Godin Leisure-Time Exercise Questionnaire. PROs were assessed using generic (SF -12v2, Perceived Deficits Questionnaire, Ryff Psychological Well-Being, Diener Satisfaction with Life Scale) and disease-specific (Patient-Determined Disease Steps, Performance Scales) measures. Psychometric analysis created unidimensional cognitive reserve subscales. Regression models examined relationships between cognitive reserve, demographic characteristics, and PROs.

Results: The cognitive reserve measures assessed distinct but related constructs. Individuals with high cognitive reserve were more likely to report lower levels of perceived disability and perceived cognitive deficits, and higher levels of physical health, mental health, and well-being. Both active and passive reserve are associated with better outcomes, independent of demographic factors, and these associations apply to both generic and disease-specific outcomes.

Conclusions: This expanded measurement of cognitive reserve captures both the passive and active aspects of the construct, and there is a consistent and substantial relationship with PROs. Individuals with high passive and/or active reserve are healthier and experience higher levels of well-being.

Keywords

Cognitive reserve, multiple sclerosis, patient-reported outcomes, quality of life, health

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Introduction

Cognitive reserve theory posits passive and active aspects of reserve.[1] *Passive reserve* focuses on factors that are antecedent to disease onset,[2] such as premorbid intelligence[3] and brain reserve capacity (i.e. brain size, neuronal count).[4] Here we are interested in how much brain damage can be sustained before reaching a threshold for clinical expression.[5–7] This aspect of cognitive reserve is generally measured with proxy measures of premorbid 'intellectual enrichment' (e.g. education, occupation, childhood enrichment activities).[2] In contrast, *active reserve* is conceptualized as behaviors and activities that an individual currently engages in, that keep the brain active and fit. Active processes allow the brain to cope with damage by enlisting compensatory mechanisms. Leisure activities (e.g. going to an art museum, exercise) and cognitively demanding tasks (e.g. playing a musical instrument) are examples.[5]

[1]DeltaQuest Foundation, Inc., Concord, USA.
[2]Departments of Medicine and Orthopaedic Surgery, Tufts University Medical School, Boston, USA.
[3]Department of Kinesiology, University of Massachusetts Amherst, USA.
[4]Department of Neurology, The Jacobs Neurological Institute, School of Medicine and Biomedical Sciences, University of Buffalo, USA.
[5]Department of Neurology, University of Colorado Denver, USA.
[6]Rocky Mountain Multiple Sclerosis Center, Aurora, USA.

Corresponding author:
Carolyn Schwartz, 31 Mitchell Road, Concord, MA 01742, USA.
Email: carolyn.schwartz@deltaquest.org.

It is important to bear in mind that there are many components or measures of cognitive reserve that may act additively or synergistically with other markers.[8] For example, educational achievement is thought to influence cognitive reserve by its effect on brain processing efficiency. Crystallized or verbal intelligence is not only resistant to age-related decline, but may also be augmented over the adult life course.[9,10] Research on older adults has confirmed that past cognitive activity contributes to cognitive flexibility in old age primarily through its association with late life cognitive activity[11] and environmental complexity.[12] Thus, cognitive ability level is just as important as the activities pursued, supporting the importance of both passive and active reserve, respectively.[13]

Patient-reported outcomes (PROs) are commonly used to measure quality of life (QOL) because they are based entirely on patient self-perception. However, PROs are poorly related to some aspects of neurological disability, especially cognitive impairment.[14] To our knowledge, the relationship between cognitive reserve and PROs has not been addressed to date, and understanding this relationship may clarify some ambiguities concerning the validity of PROs. As a moderator of PROs, cognitive reserve may influence problematic health behaviors or coping styles. For example, cognitive reserve is likely to be related to the likelihood of smoking and obesity, perhaps in part because people with lower cognitive reserve may have less education, which may in turn negatively influence health behaviors. Both cognitive reserve and negative health behaviors have been found to affect the severity and course of disease.[15] In other words, it may be important to identify patients with multiple sclerosis (MS) with low cognitive reserve for preventive therapies or programs aimed at improving health and coping behaviors. The first steps, however, are to determine (a) what aspects of cognitive reserve are most relevant, and (b) what measures are most valid for this purpose.

The present work thus seeks to expand the assessment of cognitive reserve in a large cohort of patients with MS. We have acquired a sufficiently large sample to enable complex analyses of moderator relationships among components of an expanded measurement of cognitive reserve.

Methods

Sample and design

This secondary analysis involved cross-sectional data from 1142 people who report having MS recruited from the NARCOMS Registry. NARCOMS is a self-report registry of 36,000 individuals age 18 or over, who report having MS, with bi-annual surveys using paper or secure web-based forms capturing data on demographics, disease characteristics, disability, treatments and access to healthcare providers. Potential candidates for the study were selected from those NARCOMS registry participants who completed the latest two semi-annual update surveys online, and resided in the USA. These participants were sent an invitation to participate in this add-on survey after completing the Fall 2010 semi-annual update.

Procedure

An email notification describing the study was sent to the randomly selected cohort. This email included a unique identifier that was linkable to the NARCOMS database, and a link to a web-based set of questionnaires designed for this study. The survey engine is SurveyGizmo.com (www.surveygizmo.com), a user-friendly and HIPAA-compliant interface for collecting data in a secure environment. The SurveyGizmo questionnaire began with an online consent form and the measures described below. Data from the NARCOMS Fall Update and the SurveyGizmo data were then linked using the NARCOMS unique identifier, and data were de-identified prior to data analysis. The project was reviewed and approved by the institutional review boards associated with NARCOMS at the time of data collection (the Western IRB, Olympia, WA, USA) and DeltaQuest Foundation (the New England IRB, Newton, MA, USA).

Measures

Cognitive reserve was operationalized utilizing measures of both passive and active reserve. *Passive reserve* was measured using: (a) the Sole-Padulles measure of childhood cultural and educational enrichment[2] (Sole-Padulles Childhood Enrichment measure of passive reserve), which includes respondent's education level, parents' education levels, and childhood participation in music, the arts, and social activities; and (b) Occupational attainment, which was coded using the Occupational Information Network (O*NET)[16] database to identify job dimensions, including knowledge, cognitive and psychosocial skills required to perform the job. *Active reserve* was measured by: (a) the Stern measure of *current* hobbies and leisure activities[17] (Stern Leisure Activities measure of active reserve); and (b) the Godin Leisure Time Exercise Questionnaire.[18] (Note: Items from both the Sole-Padulles and Stern measures are shown in Table 2.)

In addition, demographic characteristics, health behaviors, and PROs were collected. PROs collected comprised disease-specific and generic measures. Disease-specific measures included: (1) *the Performance Scales*,[19] a measure of eight domains of perceived neurological disability (mobility, hand function, vision, fatigue, cognition, bladder/bowel, sensory, and spasticity) aggregated for an overall index of neurological disability; (2) *the Patient-Determined Disease Steps*,[20] a self-report measure of perceived disability that was modeled after and correlates

highly with the Expanded Disability Status Scale (EDSS). Generic measures included: (3) the *Perceived Deficits Questionnaire*,[21] a five-item Likert-scaled measure of perceived neurocognitive deficits; (4) the *Short-Form-12 v2* (SF-12v2),[22] a generic measure of functional health that yields physical and mental health component scores (PCS and MCS); (4) subscales from the *Ryff Psychological Well-Being Measure*[23] to assess purpose in life, personal growth, self-acceptance, and social relatedness; and (5) the *Diener Satisfaction with Life Scale*,[24] a five-item Likert scaled measure of subjective well-being.

Statistical analyses

Because the Stern and Sole-Padulles cognitive reserve measures had not been developed using standard psychometric methods, their factor structure was unknown and there were no interpretation guidelines. We thus began by creating summary scores for each of the cognitive reserve measures separately using factor analysis, keeping items within a subscale if they had a factor loading of 0.30 or greater. The eigenvalue criterion value was determined using the Watkins'[25] Monte Carlo PCA, specifying the number of variables, observations, and 1000 replications. These operationalizations of cognitive reserve are thus relatively uncharacterized measures, so clinically important cut-points (e.g. minimally important difference) are not known. In this first study using these measures, we created arbitrary cut-points of the top and bottom quartiles on the measures. Although it is possible that other studies using these measures in different MS samples would derive different arbitrary cut-points, we believe that the relatively large sample size of this study and the relatively simple analytic approaches used buffer this work from Type I error. Further, the clear differences between top and bottom quartiles on these measures have intuitive meaning, and are thus relatively interpretable.

Univariate regressions were computed to examine relationships between cognitive reserve and continuous demographic variables or PRO scores. Chi-square or *t*-tests were computed for categorical and continuous outcomes, respectively. Pearson correlations were computed to examine associations between cognitive reserve scores, using Cohen's criteria[26] for thresholds for small (i.e. r=0.10–0.29), medium (i.e. r=0.30–0.49), and large (i.e. $r \geq 0.50$) effect sizes. Hierarchical regression modeling evaluated the relationship between cognitive reserve indicators and PROs after adjusting for demographic characteristics that were selected in the 'baseline' model that included all of the demographic characteristics. To reduce the number of comparisons, we created a well-being composite score that included the Ryff Psychological Well-Being subscales and the Satisfaction With Life Scale (Eigenvalue=2.89, α=0.86). Because over half of the sample listed their current occupation as retired, disabled or unemployed, we were unable to code them for occupational attainment. We used logistic regression to characterize the resulting selection bias, and did not include the Occupational Information Network (O*NET) scores in the hierarchical modeling to avoid the potential bias resulting from such informative censoring.

Results

Sample

Table 1 shows the sample demographic characteristics for the full sample and the sub-sample, which were used in the univariate and multivariable regression analyses, respectively. The full study sample had a mean age of 54 years, and 75% of the participants were female, which is consistent with the gender distribution in MS.[27] Less than half of the sample was employed, with a median annual income between $50,000 and $100,000 in both the employed sub-sample and in the entire sample. Most participants lived in a private home, endorsed drinking alcohol monthly or less, and were non-smokers. The median body mass index characterized the sample as overweight (body mass index of 25–29.9), with a mean body mass index of 27.4 (SD 6.5).

The sub-sample we were able to score for occupational attainment was somewhat different from the full sample (Table 1). In addition to being more likely to be employed and reporting a higher income, the group was slightly younger, more likely to be divorced, less likely to refuse answering the question about income change, less likely to be of normal body mass index, and more likely to report less alcohol use. These sample differences may introduce bias in the multivariable analyses, despite adjusting for these covariates in the analyses.

Factor structure of cognitive reserve measures

Table 2 shows the items, frequency distribution of responses, and the factor loadings for the Stern Leisure Activities measure of active reserve, and Sole-Padulles Childhood Enrichment measure of passive reserve. Both measures were unidimensional with one factor for each measure (Eigenvalue=2.51 and 1.55, respectively). We used a cut-off factor loading of 0.30 to retain items, and both measures showed reasonable-to-good internal consistency reliability (α reliability = 0.72 and 0.58, respectively). Table 3 shows the descriptive statistics of these measures as well as the Godin Leisure-Time Exercise Questionnaire and the O*NET occupational education level coding, for the full sample and subsample. Despite the above-noted differences in some sociodemographic characteristics, the two samples did not differ on their mean cognitive reserve indicator scores.

Table 1. Sample demographic characteristics.

Variable	*N*=1142	*N*=624	β coefficient	
Gender: % female	75.1	75.6	0.07	
Mean Age (sd)	54.4 (9.2)	53.7 (8.96)	–0.1	
Mean Body Mass Index (sd)	27.4 (6.5)	27.7 (6.5)	0.01	
% underweight (BMI<18.5)	3.0%	2.8%	–0.14	
% normal weight (BMI 18.5–25)	37.1%	34.8%	–0.25	*
% overweight (25.1–30)	31.1%	32.2%	0.13	
% obese (>30)	28.7%	30.1%	0.17	
Marital				
Never married	8.6%	9.7%	0.15	
Married	71.4%	68.5%	–0.20	+
Divorced	10.9%	13.5%	0.44	**
Widowed	3.6%	3.2%	–0.10	
Separated	1.3%	0.8%	–0.83	
Cohabitation/Domestic Partner	4.2%	4.1%	–0.02	
Employment Status				
Full-time	25.6%	28.0%	0.22	+
Part-time	13.2%	13.4%	0.11	
Not Employed	61.1%	58.5%	–0.23	*
Annual Income				
Less than $15,000	5.4%	6.1%	0.02	
$15,001–30,000	12.3%	14.9%	0.56	***
$30,001–50,000	15.0%	18.9%	0.48	**
$50,001–100,000	30.0%	36.7%	0.57	***
Over $100,000	19.8%	23.4%	0.50	***
Do not wish to answer	17.4%	0.0%	–	
Income change in past six months				
Yes	20.9%	22.6%	0.36	**
No	73.7%	76.1%	0.07	
Do not wish to answer	5.3%	1.2%	–1.92	***
If income changed, how?				
Increased	29.2%	31.2%	0.02	
Decreased	64.8%	63.8%	0.01	
Lost all income	5.9%	4.9%	–0.15	
Residence status				
Private home	97.1%	96.8%	–0.01	
Private home with home health aid	2.3%	2.7%	0.11	
Assisted living	0.2%	0.0%	–	
Nursing home	0.4%	0.5%	0.68	
Alcohol Use				
Never	30.5%	33.6%	0.21	+
Monthly or less	27.2%	28.2%	0.12	
2–4 times per month	19.0%	17.6%	–0.21	
2–3 times per week	11.2%	9.0%	–0.38	*
4 or more times a week	12.0%	11.5%	–0.02	
Smoking				
No, not at all.	88.5%	87.9%	–0.12	
Yes, some days.	3.6%	4.0%	0.33	
Yes, every day	7.9%	8.0	0.01	
Cigarettes per day (among smokers only, *n*=163) mean (sd)	12.9 (8.2)	12.6 (8.0)	–0.01	
Secondhand smoke exposure: % yes	9.9%	8.9%	–0.21	

Table 2. Items and factor structure for cognitive reserve measures.

Scale	Item	% Respondents			Factor Loading
Stern Leisure Activities	How often have you … in the past month?	*Often*	*Sometimes*	*Never*	
	Gone to lectures or concerts?	6	32	62	0.46
	Gone to the theatre or movies?	6	34	60	0.31
	Traveled or gone on tours?	10	35	55	0.42
	Gone for walks or rides?	30	48	22	0.46
	Done arts and crafts or hobbies?	20	38	42	0.37
	Sang or played a musical instrument?	14	28	58	0.31
	Visited with relatives, friends, or neighbors in your home or theirs?	37	56	7	0.36
	Taken part in sports, dancing, or exercise?	27	34	39	0.46
	Cooked or prepared food as a hobby?	27	37	36	0.32
	Participated as a member of a group or organization?	28	37	34	0.65
	Participated in church or religious activities?	26	20	54	0.36
	Done volunteer work?	19	28	33	0.59
Scale	Item	Response Option (% endorsed)			Factor Loading
Sole-Padulles Childhood Enrichment	Self-reported education	(1)	High school/GED or less (9%)		0.33
		(2)	College or technical school (65%)		
		(3)	Graduate school training (26%)		
	Father's level of education	(1)	High school/GED or less (48%)		0.48
		(2)	College or technical school (37%)		
		(3)	Graduate school training (15%)		
	Mother's level of education	(1)	High school/GED or less (55%)		0.44
		(2)	College or technical school (37%)		
		(3)	Graduate school training (7%)		
	Family interest in the Arts (literature, music, art)	(1)	Not at all (19%)		0.50
		(2)	A little bit (25%)		
		(3)	Somewhat (20%)		
		(4)	Quite a bit (18%)		
		(5)	A great deal (19%)		
	Learned a foreign language	(1)	None (30%)		0.45
		(2)	Basic knowledge (56%)		
		(3)	Good ability in one foreign language (11%)		
		(4)	Good ability in two or more foreign languages (4%)		
	Learned music in private lessons	(0)	No (53%)		0.36
		(1)	Yes (47%)		
	Did you form many friendships?	(1)	Few (23%)		0.39
		(2)	Medium (44%)		
		(3)	Many (33%)		
	Past participation in social activities?	(1)	Rarely (8%)		0.41
		(2)	Occasionally (37%)		
		(3)	Frequently (55%)		

Table 3. Summary statistics for cognitive reserve measures.

	n=1142		*n*=624		*p*-value
	Mean	SD	Mean	SD	
Stern Leisure Activities	8.987	1.916	8.967	1.922	0.83
Sole-Padulles Childhood Enrichment	8.220	2.401	8.260	2.457	0.74
Godin Leisure-Time Exercise Questionnaire	19.216	21.197	19.485	21.000	0.80
O*NET education score‡	3.602	0.931	3.583	0.919	0.75

‡O*NET sample size: *n*=658 and 374, in the larger and smaller groups, respectively.

Table 4. Cognitive reserve outcome correlation matrix.

	O*Net Education	Stern Leisure Activities	Godin Leisure-Time Exercise Questionnaire	Sole-Padulles Childhood Enrichment	Education Category
O*Net Education					
Stern Leisure Activities	0.1402***				
Godin Leisure-Time Exercise Questionnaire	0.1067**	0.4147****			
Sole-Padulles Childhood Enrichment	0.2176****	0.1952****	0.1194***		
Education Category	0.4544****	0.1777****	0.1346****	0.3489****	

*p<0.05 Cohen's Effect Size (ES) for Correlations
**p<0.01 Small ES 0.1–0.29
***p<0.001 Moderate ES 0.30–0.49
****p<0.0001 Large ES> 0.5

Inter-correlations of cognitive reserve measures

Table 4 shows the inter-correlations among the operationalizations of cognitive reserve, and provides Cohen's[26] interpretation guidelines for correlation coefficients. Three of the four operationalizations were moderately inter-correlated: the Stern Leisure Activities measure, the Sole-Padulles Childhood Enrichment measure, and the Godin Leisure-Time Exercise Questionnaire. In contrast, the O*NET index of training required for one's occupational attainment was minimally correlated with all of these measures, although it was moderately correlated with self-reported education. These inter-correlations suggest that the indicators of cognitive reserve measure distinct constructs (i.e. the correlations are relatively small), and thus should all be included in subsequent multivariable models investigating the relationship between cognitive reserve and PROs. For sample size and bias considerations noted above, O*NET was not included in subsequent multivariable analyses.

Cognitive reserve, demographics, and health behaviors

We found relatively consistent and significant relationships between both passive and active reserve indicators and demographics (see Tables 5a and 5b, respectively). High cognitive-reserve individuals were more likely to be female, younger, married, living without aid in a private home, and have a body mass index that was lower and in the normal range. They were more likely to be working part- or full-time; they were also less likely to report lower annual incomes and more likely to report incomes over $100,000. High cognitive-reserve individuals were less likely to report never consuming alcohol in the past month, more likely to be report drinking alcohol four or more times per week; and less likely to be current smokers.

Cognitive reserve and PROs: univariate results

Individuals with high cognitive reserve were also more likely to report lower levels of perceived disability on the Patient-Determined Disease Steps[20] and Performance Scales,[19] lower levels of perceived cognitive deficits on the Perceived Deficits Questionnaire,[21] and higher levels of perceived physical and mental health on the SF-12v2 (see Tables 5a and 5b, respectively). Their self-reported eudaemonic well-being (i.e. purpose in life, self-acceptance, positive relations with others, and life satisfaction) were also higher (p<0.0001 in all comparisons). These findings were highly consistent across the Stern, Godin, and Sole-Padulles, and somewhat similar in the comparisons with the O*NET measure. Since the latter comparisons had a

Table 5a. Demographic and outcome comparison by top/bottom quartile for active cognitive reserve measures.

Variable	Stern Leisure Activities			Godin Leisure-Time Exercise Questionnaire		
	Bottom (*n*=286)	Top (*n*=285)	χ^2 or t	Bottom (*n*=292)	Top (*n*=271)	χ^2 or t
Demographics						
Gender (% female)	67.8	80.4	12.0***	70.6	77.9	3.9*
Current Age, Fall 2010 (mean)	54.6	54.5	0.01	56.7	52.6	5.2****
(SD)	9.4	8.8		8.6	9.7	
Body Mass Index (BMI) (mean)	27.2	27.6	0.6	28.5	26.6	3.5***
(SD)	6.1	6.9		7.4	5.7	
% underweight (BMI<18.5)	4.3	2.1	2.1	4.2	2.2	1.7
% normal weight (BMI 18.5–25)	34.8	40.6	2.1	28.8	43.9	13.7****
% overweight (25.1–30)	29.4	29.3	0	31.9	31.2	0
% obese (>30)	31.6	27.9	0.9	35.1	22.9	10.3***
Marital Status						
% Never married	9.9	7.4	1.1	8.1	9.3	0.3
% Married	65.3	75.3	6.8**	67.4	73.2	2.3
% Divorced	17.4	8.1	10.9***	14	8.9	3.5
% Widowed	2.8	4.6	1.2	4.2	3	0.6
% Separated	0	1.1	3	1.4	1.5	0
% Cohabitation/Domestic Partner	4.6	3.5	0.4	4.9	4.1	0.2
Employment Status						
% Full-time	22.3	24.7	0.5	17.8	33	17.1****
% Part-time	8.1	18.4	12.9****	8	16.7	9.7**
% Not Employed	69.6	56.9	9.9*	74.2	50.4	33.8****
Annual Income						
% Less than $15,000	8.9	2.8	9.4*	7	2.2	7.1**
% $15,001–30,000	15.6	10.3	3.6	15.8	8.2	7.6**
% $30,001–50,000	18.4	15.6	0.8	16.8	13	1.6
% $50,001–100,000	30.5	25.8	1.5	30.2	28.9	0.1
% Over $100,000	12.8	25.8	15.4****	12.6	29.2	23.3****
% Do not wish to answer	13.8	19.8	3.6	17.5	18.5	0.1
Income change in past six months						
% Yes	21.6	19.4	0.4	19.9	20.7	0.1
% No	72.4	76.3	1.1	73.9	74.4	0
% Do not wish to answer	6	4.2	0.9	6.3	4.8	0.5
If income changed, how?						
% Increased	23	43.6	5.6*	15.8	39.3	7.9**
% Decreased	70.5	56.4	2.5	77.2	57.1	5.2*
% Lost all income	6.6	0	3.7*	7	3.6	0.6
Residence status						
% Private home	94	98.2	6.85**	93	98.9	12.1***
% Private home with home health aid	5.3	1.8	5.2*	5.6	1.1	8.5*
% Assisted living	0	0	–	0.35	0	0.9
% Nursing home	0	0	–	1.1	0	2.8
Alcohol Use						
% Never	41.5	23.3	21.3****	41.1	24.5	17.1****
% Monthly or less	28.4	26.9	0.2	24.2	25.7	0.2
% 2–4 times per month	14.5	22.3	5.6*	20.7	19.7	0.1

(Continued)

Table 5a. (Continued)

Variable	Stern Leisure Activities			Godin Leisure-Time Exercise Questionnaire		
	Bottom (*n*=286)	Top (*n*=285)	χ^2 or t	Bottom (*n*=292)	Top (*n*=271)	χ^2 or t
% 2–3 times per week	6.4	13.8	8.5**	6.3	13.4	7.9**
% 4 or more times a week	9.2	13.8	2.9	7.7	16.7	10.6***
Smoking						
% No, not at all.	79.8	93.6	23.5****	84.2	94.1	13.7****
% Yes, some days.	6.4	2.5	5.1*	3.5	1.9	1.4
% Yes, every day	13.8	3.9	17.3****	12.3	4.1	12.2****
Quality of Life Measures						
Patient-Determined Disease Steps (mean)	4.3	2.74	8.16****	4.66	2.29	12.90*****
(SD)	2.2	2.35		2.17	2.18	
Performance Scales Sum (mean)	20.22	13.95	8.81****	20.28	13.35	9.53****
(SD)	8.75	8.24		8.72	8.52	
Perceived Deficits Questionnaire (mean)	7.11	5.33	4.69****	6.74	5.73	2.49*
(SD)	4.81	4.26		4.85	4.8	
SF-12v2 PCS (mean)	33.81	42.31	–8.75****	32.66	44.03	–11.93****
(SD)	10.67	11.67		10.44	11.38	
SF-12v2 MCS (mean)	46.31	51.42	–5.60****	47.41	50.49	–3.22**
(SD)	11.23	9.63		11.67	10.02	
Ryff Psychological Well-Being Subscales						
Personal Growth (mean)	36.03	42.42	–13.34****	37.75	41.00	–6.38****
(SD)	6.5	4.82		6.44	5.63	
Positive Relations with Others (mean)	37.63	45.74	–12.58****	40.29	43.49	–4.51****
(SD)	8.54	6.77		8.92	7.84	
Purpose in Life (mean)	31.55	36.81	–11.87****	32.8	35.7	–5.97****
(SD)	5.79	4.75		5.92	5.62	
Self-Acceptance (mean)	34.43	43.3	–12.37****	36.05	41.66	–7.05****
(SD)	9.73	7.21		9.94	8.91	
Diener Satisfaction with Life Scale (mean)	15.99	24.02	–13.60****	16.67	23.44	–10.90****
(SD)	6.97	7.15		7.31	7.48	

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$.

much smaller sample size, direct comparison of *p*-values and effect sizes is somewhat problematic. Nonetheless, the fundamental finding is similar across active and passive indicators of cognitive reserve.

Cognitive reserve and PROs: results of hierarchical models

Table 6 shows the final models resulting from this model-building and Appendix A (Tables 6a–6f) shows the full output from the series of hierarchical models tested.

Disease-specific PROs. Our analyses revealed that the Patient-Determined Disease Steps measure of perceived disability was associated with lower scores on the Stern and Godin measures of active reserve, after adjusting for demographic and health behaviors. Passive reserve was not associated with this outcome. The model explained approximately one-third of the variance in this perceived disability measure.

The Performance Scales score was similarly associated with lower scores on the two measures of active reserve, and there was also a trend suggesting that the Sole-Padulles passive reserve measure was related to this outcome. The model explained slightly less variance, and included fewer demographic and health behavior covariates.

Generic PROs. We found that the SF-12v2 Physical Component Score was associated with higher scores on the Stern and Godin active reserve indicators, but not with the

Table 5b. Demographic and outcome comparison by top/bottom quartile for passive cognitive reserve measures.

Variable	Sole-Padulles Childhood Enrichment			O*NET Work Zone Required Training Code		
	Bottom (*n*=278)	Top (*n*=274)	χ^2 or t	Bottom (*n*=67)	Top (*n*=124)	χ^2 or t
Demographics						
Gender (% female)	67.3	82.8	–4.3***	77.6	75.8	0.08
Current Age, Fall 2010 (mean)	56.2	53.1	4.0***	52.4	54.1	–1.3
(SD)	8.5	9.5		9.3	8.7	
Body Mass Index (mean)	28.5	26.7	3.2***	27.6	27.1	0.5
(SD)	6.7	6.3		5.8	7.2	
% underweight (BMI<18.5)	2.6	3.0	0.1	0	2.4	1.6
% normal weight (BMI 18.5–25)	31.7	40.0	4.0*	31.7	43.9	2.6
% overweight (25.1–30)	28.4	33.3	1.5	41.3	30.1	
% obese (>30)	37.3	23.7	11.7***	27	23.6	0.3
Marital Status						
% Never married	7.4	10.7	1.9	14.3	8.1	1.7
% Married	74.5	68.9	2.1	68.2	77.2	1.8
% Divorced	10.3	10.7	0.0	12.7	8.9	0.6
% Widowed	4.1	4.1	0.0	0	1.6	1
% Separated	1.1	1.1	0.0	1.6	2.4	0.1
% Cohabitation/Domestic Partner	2.58	4.44	1.4	3.2	1.6	0.5
Employment Status						
% Full-time	22.1	30.6	5.0*	39.7	39.5	0
% Part-time	8.9	15.5	5.6*	31.7	23.4	1.5
% Not Employed	69.0	53.9	13.1***	28.6	37.1	1.3
Annual Income						
% Less than $15,000	4.4	4.4	0.0	7.9	0.8	6.8**
% $15,001–30,000	18.8	10.4	7.7**	7.9	6.5	0.1
% $30,001–50,000	21.8	13.0	7.3**	23.8	6.5	11.5***
% $50,001–100,000	23.3	32.2	5.4*	33.3	34.1	0.1
% Over $100,000	12.9	24.1	11.2***	12.7	36.6	11.7***
% Do not wish to answer	18.8	15.9	0.8	14.3	15.4	0.1
Income change in past six months						
% Yes	18.5	25.1	3.5	14.3	26.6	3.6
% No	75.3	71.2	1.1	81	73.4	1.3
% Do not wish to answer	6.3	3.7	1.9	4.8	0	6.0**
If income changed, how?						
% Increased	24.0	29.4	0.4	33.4	45.4	0.4
% Decreased	76.0	61.8	2.7	55.6	48.4	0.1
% Lost all income	0.0	8.8	4.6*	11.1	6.1	0.3
Residence status						
% Private home	97.4	95.9	0.9	96.8	98.4	0.5
% Private home with home health aid	2.2	3.3	0.6	1.6	1.6	0
% Assisted living	0.0	0.0	0.0	1.6	0	2
% Nursing home	0.4	0.7	0.3	0	0	–
Alcohol Use						
% Never	34.7	29.3	1.8	36.5	18.7	7.1**
% Monthly or less	31.4	22.6	5.3*	19	26	1.1

(Continued)

Table 5b. (Continued)

Variable	Sole-Padulles Childhood Enrichment			O*NET Work Zone Required Training Code		
	Bottom (*n*=278)	Top (*n*=274)	χ^2 or t	Bottom (*n*=67)	Top (*n*=124)	χ^2 or t
% 2–4 times per month	15.9	20.4	1.8	19	24.4	0.7
% 2–3 times per week	10.3	14.1	1.8	17.5	13.8	0.4
% 4 or more times a week	7.8	13.7	5.0*	7.9	17.1	2.9
Smoking						
% No, not at all.	87.8	90.0	0.6	81	95.1	9.6**
% Yes, some days.	3.0	4.4	0.8	4.8	1.6	1.6
% Yes, every day	9.2	5.6	2.7	14.3	3.2	7.8**
Quality of Life Measures						
Patient-Determined Disease Steps (mean)	3.75	3.13	3.09**	3.08	2.78	0.85
(SD)	2.25	2.44		2.15	2.31	
Performance Scales Sum (mean)	18.32	15.36	3.92***	14.65	14.57	0.06
(SD)	8.61	9.01		7.58	8.46	
Perceived Deficits Questionnaire (mean)	7.40	6.12	3.21**	6.58	4.98	2.5*
(SD)	4.73	4.67		4.05	4.23	
SF-12v2 PCS (mean)	36.36	40.09	–3.65***	40.43	40.85	–0.23
(SD)	11.23	11.86		10.84	11.97	
SF-12v2 MCS (mean)	47.67	49.91	–2.33*	49.39	51.57	–1.38
(SD)	11.37	10.30		10.5	9.52	
Ryff Psychological Well-Being Subscales						
Personal Growth (mean)	37.71	41.25	–6.79****	38.61	41.84	–3.83***
(SD)	6.43	5.78		6.21	5.19	
Positive Relations with Others (mean)	39.59	43.09	–4.99****	41.27	43.52	–1.95*
(SD)	8.46	7.98		7.99	7.42	
Purpose in Life (mean)	33.16	34.70	–3.18**	33.63	35.76	–2.87**
(SD)	5.94	5.38		5.01	4.83	
Self-Acceptance (mean)	37.38	40.05	–3.36***	38.91	40.79	–1.46
(SD)	9.64	9.01		8.85	8.36	
Diener Satisfaction with Life Scale (mean)	18.59	21.03	–3.83****	20.55	21.52	–0.84
(SD)	7.24	7.71		7.77	7.59	

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$.

Sole-Padulles passive reserve measure, after adjusting for covariates. This model explained about one-third of the variance in the dependent variable. In contrast, the SF-12v2 Mental Component Score was associated only with the Stern active reserve measure, after adjusting for covariates, and the model explained only 7% of the variance. The Perceived Deficits Questionnaire was also associated with only the Stern active reserve measure, after adjusting for covariates; and the model explained only 13% of the variance in the dependent variable. The Well-Being composite was, however, associated with the Stern and Godin (trend) active reserve measures, and with the Sole-Padulles passive reserve measure, after adjusting for covariates.

Discussion

Our findings suggest that higher active and passive reserve scores are associated with better generic and disease-specific outcomes. Even after adjusting for significant demographic and health-behavior covariates, higher levels of reserve were associated with lower levels of perceived disability, higher levels of functional health, and higher levels of eudaemonic well-being.

Further examination of our findings suggests that active and passive reserve may play different roles in PROs. Figure 1 displays our results superimposed on a pyramid reflecting Maslow's hierarchy of needs[28] to illustrate that

Table 6. Hierarchical linear regression modeling of predictors of PROs.

Predictors	β	std err	*t*	*p*
Outcome: Patient-Determined Disease Steps				
Gender	–0.06	0.19	–1.80	0.07
Age	0.12	0.01	3.36	0.00
Not Employed	0.31	0.17	8.41	0.00
Annual Income	–0.08	0.07	–2.29	0.02
Alcohol Usage	–0.06	0.06	–1.60	0.11
Stern Leisure Activities	–0.13	0.05	–3.61	0.00
Godin Leisure-Time Exercise Questionnaire	–0.22	0.00	–5.84	0.00
Model Adjusted R^2	0.31			
N	624			
Outcome: Performance Scales				
Not Employed	0.38	0.64	10.57	0.00
Annual Income	–0.08	0.28	–2.13	0.03
Alcohol Usage	–0.05	0.24	–1.39	0.16
Stern Leisure Activities	–0.16	0.18	–4.21	0.00
Godin Leisure-Time Exercise Questionnaire	–0.14	0.02	–3.71	0.00
Sole-Padulles Childhood Enrichment	–0.05	0.13	–1.43	0.15
Model Adjusted R^2	0.29			
N	624			
Outcome: SF-12v2 Physical Component Score				
Gender	0.05	0.98	1.52	0.13
Age	–0.13	0.05	–3.46	0.00
BMI	–0.08	0.06	–2.16	0.03
Not Employed	–0.31	0.89	–8.16	0.00
Stern Leisure Activities	0.16	0.24	4.09	0.00
Godin Leisure-Time Exercise Questionnaire	0.21	0.02	5.32	0.00
Sole-Padulles Childhood Enrichment	0.04	0.17	1.16	0.25
Model Adjusted R^2	0.30			
N	564			
Outcome: SF-12v2 Mental Component Score				
Age	0.10	0.05	2.39	0.02
Not Employed	–0.19	0.93	–4.48	0.00
Stern Leisure Activities	0.18	0.23	4.38	0.00
Model Adjusted R^2	0.07			
N	564			
Outcome: Perceived Deficits Questionnaire				
Age	–0.12	0.02	–3.17	0.00
BMI	0.08	0.03	2.05	0.04
Married	0.13	0.43	2.98	0.00
Not Employed	0.20	0.40	4.94	0.00
Annual Income	–0.23	0.18	–5.20	0.00
Stern Leisure Activities	–0.12	0.09	–3.04	0.00
Model Adjusted R^2	0.13			
N	624			
Outcome: Well-Being Composite				
Gender	0.09	1.90	2.64	0.01
Not Employed	–0.08	1.72	–2.10	0.04
Annual Income	0.13	0.73	3.68	0.00
Smoking	0.00	1.47	–0.03	0.98
Stern Leisure Activities	0.39	0.48	10.12	0.00
Godin Leisure-Time Exercise Questionnaire	0.07	0.04	1.79	0.07
Sole-Padulles Childhood Enrichment	0.10	0.34	2.94	0.00
Model Adjusted R^2	0.29			
N	624			

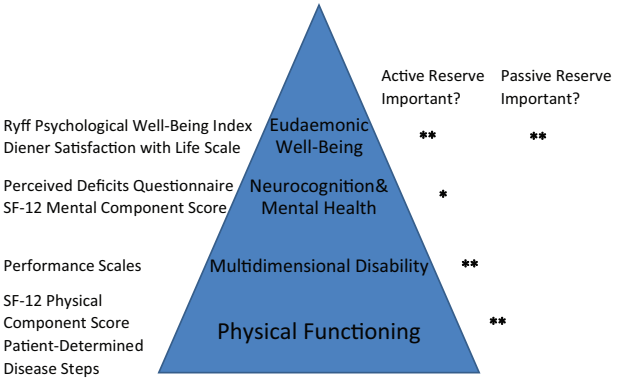

Figure 1. Importance of cognitive reserve.
Maslow's hierarchy of needs is a useful framework for conceptualizing the impact of cognitive reserve indicators and PROs. The active reserve indicators were associated with all examined PROs, but the passive reserve indicators were associated with only the Performance Scales (trend), and the Well-Being Composite score (highly significantly). These results suggest that active reserve is relevant for aspects of PROs that tap multiple life and existential domains, whereas passive reserve has an independent effect only for existential well-being..

that active reserve indicators (particularly the Stern Leisure Activities measure) were associated with all examined PROs, but the passive reserve indicator was associated with only the Well-Being Composite score. These results suggest that active reserve is relevant for aspects of PROs that tap multiple life and existential domains, whereas passive reserve has an independent effect only for existential well-being.

This work expands cognitive reserve research by extending the measurement of passive reserve to include not only proxies of premorbid abilities and achievement but also of childhood enrichment activities. This approach is consistent with other investigators in the field (e.g. Sole-Padulles et al.[2]). This work is distinct because it involves a relatively large sample that allows for the examination of extreme subgroups (i.e. top and bottom quartiles) with sufficient power to detect small-to-moderate effects.[26] Thus by expanding the operationalization of passive reserve to include past enrichment activities as well as proxies of brain structure, this study was able to investigate the impact of a broader range of past or premorbid factors that may influence present function. In combination with the measures of active reserve, the study allows a comprehensive evaluation of how cognitive reserve influences health outcomes.

The limitations of the present work should be acknowledged. First, the NARCOMS data provide an opportunity to look at the interrelationships between clinically relevant constructs in a large MS sample, but there are drawbacks. The data are entirely self-reported, so triangulating patient- and clinician-reported indicators of disease progression is not possible. Second, our not finding a relationship between reserve and mental health may reflect a non-linear or synergistic relationship with other unmeasured characteristics. Further, this study is cross-sectional and correlational, so any conclusions about causal relationships between cognitive reserve and patient-reported outcomes are not justified on the basis of this study. Finally, this study adapted existing measures of cognitive reserve which were not psychometrically developed, and thus may have underestimated the magnitude of the relationships among the constructs. Future research should hone these measures to improve their reliability, perhaps by modifying item response options.

In summary, this study supports the importance of cognitive reserve, and its possible role in explaining PROs in MS. By measuring cognitive reserve multi-dimensionally, our findings suggest that this construct extends beyond the native intelligence indicators that have been used in prior foundational research in this field.[1] Although there is a body of evidence supporting that general intelligence may be a fundamental cause of differences in morbidity and mortality,[29] our results suggest that current activities that enhance brain and body health also contribute unique variance in explaining health outcomes in MS. This distinction is important because it provides a possible handle for implementing change. We believe, for example, that this line of investigation could have important implications for designing behavioral and rehabilitation interventions to enhance active reserve with an aim of keeping patients actively participating in social and occupational pursuits. It is also possible such an approach to the long-term management of MS may delay the onset of the progressive phase of disability progression.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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Appendix A

Table 6a. Full output of the hierarchical linear regression modeling of predictors of PROs: Patient-Determined Disease Steps.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	–0.423	0.196399	–2.16	0.031	–0.07737										
age	0.0325	0.00988	3.29	0.001	0.124113										
BMI	0.0047	0.012894	0.37	0.713	0.013189										
married	0.0194	0.204162	0.09	0.924	0.003827										
not employed	1.6483	0.186183	8.85	0.000	0.345755										
annual income	–0.226	0.086642	–2.61	0.009	–0.11287										
alcohol usage	–0.18	0.064996	–2.78	0.006	–0.1024										
smoking	–0.111	0.148927	–0.75	0.455	–0.02685										
Model Adjusted R^2	0.2263														
N	624														
Cognitive Reserve Indicators															
Stern Leisure Activities						–0.22783	0.050319	–4.53	0	–0.18624					
Godin Leisure-Time Exercise Questionnaire						–0.03043	0.00453	–6.72	0	–0.2718					
Sole-Padulles Cognitive Reserve Index						–0.01959	0.036097	–0.54	0.588	–0.02047					
Model Adjusted R^2	0.1485														
N	624														
Final Model															
gender											–0.33554	0.186367	–1.8	0.072	–0.06132
age											0.031293	0.009313	3.36	0.001	0.119343
not employed											1.469844	0.174728	8.41	0.000	0.308327
annual income											–0.16347	0.071527	–2.29	0.023	–0.08167
alcohol usage											–0.09838	0.061589	–1.6	0.111	–0.05583
Stern Leisure Activities											–0.16425	0.045441	–3.61	0.000	–0.13427
Godin Leisure-Time Exercise Questionnaire											–0.02413	0.004131	–5.84	0.000	–0.21556
Model Adjusted R^2	0.3090														
N	624														

Table 6b. Full output of the hierarchical linear regression modeling of predictors of PROs: Performance Scales.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	−1.361	0.743021	−1.83	0.0670	−0.06554										
age	0.0368	0.03738	0.98	0.3250	0.036962										
BMI	0.0871	0.048779	1.79	0.0750	0.063899										
married	1.2506	0.772387	1.62	0.1060	0.065109										
not employed	6.9685	0.704369	9.89	0.0000	0.385117										
annual income	−0.976	0.327783	−2.98	0.0030	−0.12851										
alcohol usage	−0.57	0.245895	−2.32	0.0210	−0.08518										
smoking	0.5314	0.563421	0.94	0.3460	0.033739										
Model Adjusted R^2	0.2313														
N	624														
Cognitive Reserve Indicators															
Stern Leisure Activities						−0.96522	0.193641	−4.98	0.000	−0.20787					
Godin Leisure-Time Exercise Questionnaire						−0.08215	0.017433	−4.71	0.000	−0.19335					
Sole-Padulles Cognitive Reserve Index						−0.29017	0.13891	−2.09	0.037	−0.07989					
Model Adjusted R^2	0.1248														
N	624														
Final Model															
not employed											6.807573	0.644029	10.57	0.000	0.376224
annual income											−0.58888	0.277069	−2.13	0.034	−0.07751
alcohol usage											−0.33245	0.23842	−1.39	0.164	−0.0497
Stern Leisure Activities											−0.7435	0.176732	−4.21	0.000	−0.16012
Godin Leisure-Time Exercise Questionnaire											−0.05911	0.015923	−3.71	0.000	−0.13912
Sole-Padulles Cognitive Reserve Index											−0.1817	0.126722	−1.43	0.152	−0.05003
Model Adjusted R^2	0.2851														
N	624														

Table 6c. Full output of the hierarchical linear regression modeling of predictors of PROs: SF-12v2 Physical Component Score.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	2.0513	1.029837	1.99	0.047	0.076008										
age	–0.206	0.054303	–3.79	0.000	–0.1515										
BMI	–0.174	0.068744	–2.52	0.012	–0.09603										
married	–0.677	1.076865	–0.63	0.530	–0.0267										
not employed	–7.717	0.987521	–7.81	0.000	–0.32417										
annual income	0.7949	0.465546	1.71	0.088	0.077708										
alcohol usage	0.5229	0.342873	1.52	0.128	0.05968										
smoking	–1.058	0.80367	–1.32	0.189	–0.05005										
Model Adjusted R^2	0.2077														
N	564														
Cognitive Reserve Indicators															
Stern Leisure Activities						1.156486	0.2635	4.39	0.000	0.189124					
Godin Leisure-Time Exercise Questionnaire						0.148215	0.023484	6.31	0.000	0.266944					
Sole-Padulles Cognitive Reserve Index						0.366496	0.187292	1.96	0.051	0.077297					
Model Adjusted R^2	0.1587														
N	564														
Final Model															
gender											1.481837	0.976191	1.52	0.130	0.054907
age											–0.17717	0.05125	–3.46	0.001	–0.13052
BMI											–0.13956	0.06472	–2.16	0.031	–0.07724
not employed											–7.29828	0.894409	–8.16	0.000	–0.30659
Stern Leisure Activities											0.995066	0.243097	4.09	0.000	0.162726
Godin Leisure-Time Exercise Questionnaire											0.116268	0.021849	5.32	0.000	0.209406
Sole-Padulles Cognitive Reserve Index											0.201066	0.172957	1.16	0.246	0.042406
Model Adjusted R^2	0.2959														
N	564														

Table 6d. Full output of the hierarchical linear regression modeling of predictors of PROs: SF-12v2 Mental Component Score.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	0.5766	1.032419	0.56	0.5770	0.023395										
age	0.1232	0.054439	2.26	0.0240	0.09943										
BMI	0.087	0.068916	1.26	0.2080	0.052697										
married	–0.142	1.079565	–0.13	0.8950	–0.00613										
not employed	–4.034	0.989997	–4.07	0.0000	–0.18555										
annual income	0.7618	0.466713	1.63	0.1030	0.081561										
alcohol usage	0.2393	0.343732	0.7	0.4870	0.029914										
smoking	–1.18	0.805685	–1.47	0.1430	–0.06117										
Model Adjusted R^2	0.0451														
N	564														
Cognitive Reserve Indicators															
Stern Leisure Activities						0.938989	0.257044	3.65	0.000	0.168157					
Godin Leisure-Time Exercise Questionnaire						0.030375	0.022909	1.33	0.185	0.05991					
Sole-Padulles Cognitive Reserve Index						0.180291	0.182704	0.99	0.324	0.041641					
Model Adjusted R^2	0.0399														
N	564														
Final Model															
age											0.126365	0.052864	2.39	0.0170	0.101948
not employed											–4.18924	0.934738	–4.48	0.0000	–0.19272
Stern Leisure Activities											1.004638	0.229126	4.38	0.0000	0.179914
Model Adjusted R^2	0.0706														
N	564														

Table 6e. Full output of the hierarchical linear regression modeling of predictors of PROs: Perceived Deficits Questionnaire.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	0.7479	0.420296	1.78	0.076	0.067849										
age	–0.057	0.021144	–2.68	0.007	–0.10743										
BMI	0.0564	0.027592	2.05	0.041	0.077988										
married	1.3063	0.436907	2.99	0.003	0.128137										
not employed	2.1011	0.398432	5.27	0	0.218796										
annual income	–0.928	0.185413	–5.01	0	–0.23023										
alcohol usage	–0.012	0.139092	–0.09	0.93	–0.00345										
smoking	0.6039	0.318704	1.89	0.059	0.072246										
Model Adjusted R^2	0.1268														
N	624														
Cognitive Reserve Indicators															
Stern Leisure Activities						–0.35906	0.108336	–3.31	0.001	–0.1457					
Godin Leisure-Time Exercise Questionnaire						–0.00712	0.009753	–0.73	0.466	–0.03156					
Sole-Padulles Cognitive Reserve Index						–0.10157	0.077715	–1.31	0.192	–0.05269					
Model Adjusted R^2	0.0274														
N	624														
Final Model															
age											–0.06573	0.020731	–3.17	0.002	–0.12444
BMI											0.055671	0.027197	2.05	0.041	0.076919
married											1.291479	0.433831	2.98	0.003	0.126685
not employed											1.966342	0.398292	4.94	0	0.20476
annual income											–0.93469	0.179715	–5.2	0	–0.23182
Stern Leisure Activities											–0.28402	0.09343	–3.04	0.002	–0.11525
Model Adjusted R^2	0.1333														
N	624														

Table 6f. Full output of the hierarchical linear regression modeling of predictors of PROs: Well-Being factor score.

Predictors	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β	coeff	std err	*t*	*p*	β
Demographic Variables															
gender	8.0842	2.140523	3.78	0.000	0.146449										
age	0.1472	0.107685	1.37	0.172	0.05564										
BMI	–0.18	0.140525	–1.28	0.201	–0.0496										
married	0.9107	2.225123	0.41	0.682	0.01784										
not employed	–7.052	2.029174	–3.48	0.001	–0.14665										
annual income	3.0769	0.94429	3.26	0.001	0.152397										
alcohol usage	1.0966	0.708382	1.55	0.122	0.061687										
smoking	–3.439	1.623124	–2.12	0.035	–0.08216										
Model Adjusted R^2	0.0968														
N	624														
Cognitive Reserve Indicators															
Stern Leisure Activities						5.168333	0.476773	10.84	0.000	0.418809					
Godin Leisure-Time Exercise Questionnaire						0.098728	0.042923	2.3	0.022	0.087428					
Sole-Padulles Cognitive Reserve Index						1.234144	0.342015	3.61	0.000	0.127857					
Model Adjusted R^2	0.2488														
N	624														
<u>Final Model</u>															
gender											5.006395	1.899293	2.64	0.009	0.090693
not employed											–3.6118	1.723388	–2.1	0.037	–0.07511
annual income											2.689858	0.730328	3.68	0	0.133225
smoking											–0.03913	1.47303	–0.03	0.979	–0.00093
Stern Leisure Activities											4.849702	0.479181	10.12	0	0.392989
Godin Leisure-Time Exercise Questionnaire											0.076038	0.042362	1.79	0.073	0.067335
Sole-Padulles Cognitive Reserve Index											0.994118	0.337949	2.94	0.003	0.10299
Model Adjusted R^2	0.2803														
N	624														