

Supplementary Material

Vascular Brain Lesions, Cognitive Reserve, and Their Association with Cognitive Profile in Persons with Early-Stage Cognitive Decline

Supplementary Table 1. Association of Predictors, Not Dichotomized, with Cognition

	MoCA		Memory		Executive Function		Processing Speed	
	β	95% CL	β	95% CL	β	95% CL	β	95% CL
Education ^a								
High school or less	--	--	--		--	--	--	--
Technical college	0.02	-1.46, 1.43	0.12	-0.27, 0.51	0.15	-0.22, 0.52	0.24	-0.12, 0.62
University: Undergraduate	0.48	-0.91, 1.89	0.06	-0.32, 0.43	0.24	-0.12, 0.60	0.11	-0.24, 0.46
University: Graduate	0.85	-0.54, 2.24	0.08	-0.29, 0.46	0.27	-0.09, 0.62	0.04	-0.30, 0.40
Occupation	2.41	1.05, 3.77	0.23	-0.13, 0.60	0.47	0.12, 0.82	0.50	0.15, 0.85
Household Income ^b								
Less than \$40k	--	--	--		--	--	--	--
\$40k to <\$60k	-0.57	-1.98	-0.08	-0.46, 0.30	-0.06	-0.42, 0.31	0.15	-0.21, 0.51
\$60k to <\$80k	0.53	-0.87, 1.93	-0.03	-0.40, 0.35	0.44	0.08, 0.80	0.27	-0.09, 0.63
>\$80k	0.47	-0.89, 1.84	-0.03	-0.39, 0.34	0.25	-0.10, 0.60	0.23	-0.12, 0.57
Multilingual	-1.01	-1.92, -0.09	-0.15	-0.39, 0.09	-0.06	-0.27, 0.19	0.06	-0.17, 0.28
Married	-1.59	-2.66, -0.52	-0.31	-0.60, -0.05*	-0.33	-0.61, -0.05	-0.17	-0.43, 0.10
Social Activities ^c								
Low	--	--	--		--	--	--	--
Medium	-0.43	-1.39, 0.53	0.02	-0.24, 0.28	0.11	-0.14, 0.36	0.16	-0.08, 0.41
High	-0.12	-1.47, 1.23	0.14	-0.22, 0.50	0.08	-0.26, 0.43	0.09	-0.25, 0.43
High Physical Activity	0.78	-0.23, 1.78	0.08	-0.19, 0.36	0.08	-0.06, 0.21	0.11	-0.02, 0.24

For this analysis, cognitive reserve proxy variables were entered in their original form, without dichotomizing them. Beta coefficient for MoCA is the estimated different in points, otherwise it represents the estimated difference in z score. Adjusted for age and education. MoCA, Montreal Cognitive Assessment.

^a p for trend. MoCA: p=0.11; memory: p=0.78, executive function: p=0.16; processing speed: p=0.70.

^b p for trend. MoCA: p=0.20; memory: p=0.99, executive function: p=0.03; processing speed: p=0.18.

^c p for trend. MoCA: p=0.67; memory: p=0.46, executive function: p=0.37; processing speed: p=0.29.

Supplementary Table 2. Sensitivity Analysis including SCI versus MCI Status as a Covariate
Interaction Between Cognitive Reserve and Vascular Lesion Burden

Predictors of Executive Function	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.15 (0.09, 0.21)	<0.0001	0.14 (0.06, 0.22)	0.0005
Vascular Lesion Burden	-0.30 (-0.57, -0.03)	0.04	-0.41 (-1.05, 0.22)	0.20
Interaction	---	---	0.03 (-0.09, 0.15)	0.90

Predictors of Processing Speed	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.12 (0.06, 0.18)	<0.0001	0.07 (-0.01, 0.15)	0.07
Vascular Lesion Burden	-0.16 (-0.41, 0.09)	0.21	-0.43 (-1.06, 0.20)	0.17
Interaction	---	---	0.06 (-0.06, 0.18)	0.71

Predictors of Memory	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.02 (-0.05, 0.08)	0.59	0.02 (-0.06, 0.10)	0.10
Vascular Lesion Burden	0.00 (-0.25, 0.26)	0.97	0.02 (-0.627, 0.67)	0.94
Interaction	---	---	-0.00 (-0.13, 0.12)	0.94

Predictors of MoCA	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.42 (0.19, 0.65)	0.004	0.42 (0.12, 0.71)	0.007
Vascular Lesion Burden	-0.67 (-1.61, 0.27)	0.16	-0.71 (-3.12, 1.70)	0.56
Interaction:	---	---	0.01 (-0.45, 0.47)	0.97

Three-way interactions between SCI versus MCI status, cognitive reserve, and vascular lesion burden were tested but were non-significant: executive function p=0.85, processing speed p=0.52, memory p=0.68, MoCA p=0.40. Therefore, SCI versus MCI was entered into the model as an independent variable and results were not stratified by SCI and MCI. Beta coefficient for MoCA is the estimated difference in points, otherwise it represents the estimated difference in z score.

Adjusted for age, sex, and SCI versus MCI status. MoCA, Montreal Cognitive Assessment.

*p≤0.05, †p≤0.01.

Supplementary Table 3. Sensitivity analysis using Education as the Only Proxy for Cognitive Reserve

Interaction Between Cognitive Reserve and Vascular Lesion Burden				
Predictors of Executive Function	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
High Education	0.16 (-0.07, 0.39)	0.17	0.10 (-0.18, 0.38)	0.51
Vascular Lesion Burden	-0.36 (-0.63, -0.09)	0.01	-0.44 (-0.80, -0.09)	0.02
Interaction	---	---	0.18 (-0.30, 0.65)	0.47
Predictors of Processing Speed	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
High Education	0.13 (-0.09, 0.35)	0.23	0.07 (-0.21, 0.34)	0.64
Vascular Lesion Burden	-0.23 (-0.49, 0.02)	0.08	-0.33 (-0.67, 0.02)	0.06
Interaction	---	---	0.19 (-0.27, 0.65)	0.41
Predictors of Memory	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
High Education	0.05 (-0.18, 0.28)	0.65	0.02 (-0.26, 0.31)	0.87
Vascular Lesion Burden	-0.03 (-0.30, 0.24)	0.81	-0.07 (-0.43, 0.28)	0.69
Interaction	---	---	0.08 (-0.40, 0.56)	0.75
Predictors of MoCA	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
High education	1.14 (0.25, 2.03)	0.01	1.02 (-0.09, 2.13)	0.07
Vascular Lesion Burden	-0.99 (-2.04, 0.06)	0.06	-1.15 (-2.54, 0.23)	0.10
Interaction:	---	---	0.34 (-1.52, 2.20)	0.72

High education was defined as some university or a university degree. Beta coefficient for MoCA is the estimated different in points, otherwise it represents the estimated difference in z score. Adjusted for age, sex, and SCI versus MCI status. MoCA, Montreal Cognitive Assessment.

Supplementary Table 4. Sensitivity Analysis Using a Cognitive Reserve Score Without Marital Status

Interaction Between Cognitive Reserve and Vascular Lesion Burden				
Predictors of Executive Function	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.17 (0.10, 0.23)	<0.0001	0.15 (0.07, 0.23)	0.0002
Vascular Lesion Burden	-0.31 (-0.56, -0.06)	0.02	-0.49 (-1.10, 0.13)	0.12
Interaction	---	---	0.04 (-0.09, 0.17)	0.54
Predictors of Processing Speed	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.13 (0.06, 0.19)	<0.0001	0.10 (0.02, 0.18)	0.01
Vascular Lesion Burden	-0.19 (-0.45, 0.06)	0.13	-0.44 (-1.06, 0.17)	0.16
Interaction	---	---	0.06 (-0.07, 0.19)	0.38
Predictors of Memory	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.04 (-0.03, 0.10)	0.28	0.03 (-0.05, 0.12)	0.43
Vascular Lesion Burden	-0.02 (-0.29, 0.25)	0.86	-0.06 (-0.71, 0.60)	0.87
Interaction	---	---	0.01 (-0.13, 0.15)	0.92
Predictors of MoCA	Without Interaction		With Interaction	
	beta (95% CI)	p	beta (95% CI)	p
Cognitive Reserve	0.51 (0.26, 0.77)	<0.0001	0.56 (0.24, 0.88)	0.0006
Vascular Lesion Burden	-0.88 (-1.91, 0.15)	0.09	-0.30 (-2.79, 2.20)	0.82
Interaction:	---	---	-0.14 (-0.66, 0.39)	0.61

For this sensitivity analysis, the cognitive reserve score was calculated by allocating 3 points for professional/managerial/qualified non-manual occupations, and 2 points each for annual household income \geq \$60,000 per year, and high physical activity (total potential points 7). Beta coefficient for MoCA is the estimated different in points, otherwise it represents the estimated difference in z score. Adjusted for age, sex, and SCI versus MCI status. MoCA, Montreal Cognitive Assessment.