

## **Education Modulates the Impact of White Matter Lesions on the Risk of Mild Cognitive Impairment and Dementia.**

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# Education modulates the impact of white matter lesions on the risk of mild cognitive impairment and dementia

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**Table 1, Supplemental Material.** Influence of education on the relationship between WML load and risk of MCI during the 7-year follow-up (Cox proportional hazard model), n=486, n. of events=121.

In order to examine the influence of education on relationship between WML and MCI, the MCI baseline cases and the dementia cases were excluded.

Variables	Education level			
	High*		Low†	
	HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>
<b>WML volume</b>				
1 <sup>st</sup> tertile (<0.3ml)	1.0 (Referent)		1.0 (Referent)	
2 <sup>nd</sup> tertile (0.3-1.5ml)	0.68(0.40-1.16)	0.16	0.75(0.19-2.89)	0.67
3 <sup>rd</sup> tertile (>1.5ml)	1.02(0.58-1.81)	0.93	3.61(1.20-10.88)	0.02
<b>Total brain volume (ml)</b>	1.00(0.99-1.01)	0.40	1.00(0.99-1.01)	0.64
<b>Brain atrophy(%)</b>	1.13(1.04-1.23)	<0.01	1.05(0.86-1.27)	0.65
<b>Hippocampal volume (ml)</b>	1.11(0.81-1.54)	0.52	0.76(0.40-1.46)	0.41
<b>Presence of silent brain infarcts</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	1.03(0.64-1.66)	0.90	1.74(0.77-3.91)	0.18
<b>Sex</b>				
Male	1.0 (Referent)		1.0 (Referent)	
Female	0.82(0.52-1.30)	0.41	1.12(0.40-3.10)	0.83
<b>APOE ε4 genotype</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	1.26(0.74-2.14)	0.40	1.11(0.42-2.97)	0.83
<b>Depressive symptomatology</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	1.76(1.06-2.93)	0.03	3.09(0.96-9.90)	0.06
<b>Previous history of vascular pathology</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	1.10(0.49-2.47)	0.82	0.76(0.17-3.45)	0.72
<b>Hypertension</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	0.94(0.60-1.46)	0.78	2.06(0.85-5.03)	0.11

\* n=362 , n. of events=92.

† n=122, n. of events=29.

Cox proportional hazard regression models with delayed entry were performed with age as the basic timescale and birth as the time origin.

**Table 2**, Supplemental Material. Influence of education on the relationship between WML load and risk of dementia during the 7-year follow-up (Cox proportional hazard model), n=637, n. of events=30.

In order to examine the influence of education on relationship between WML and dementia, the MCI baseline cases were included. The results should be interpreted with caution, because of the low number of events in each group.

Variables	Education level			
	High *		Low †	
	HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>
<b>WML volume (ml)</b>	1.02(0.99-1.05)	0.19	1.04(1.01-1.07)	0.02
<b>Total brain volume (ml)</b>	1.005(1.001-1.008)	0.01	1.00(0.99-1.01)	0.17
<b>Brain atrophy(%)</b>	1.21(0.97-1.51)	0.09	1.28(0.90-1.84)	0.76
<b>Hippocampal volume (ml)</b>	0.49(0.20-1.16)	0.10	0.18(0.06-0.54)	<0.01
<b>Presence of silent brain infarcts</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	1.50(0.39-5.79)	0.55	2.40(0.78-7.39)	0.13
<b>Sex</b>				
Male	1.0 (Referent)		1.0 (Referent)	
Female	1.82(0.54-6.08)	0.33	0.44(0.11-1.84)	0.26
<b>APOE ε4 genotype</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	2.39(0.71-8.06)	0.16	5.98(1.61-22.3)	<0.01
<b>Depressive symptomatology</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	0.59(0.11-3.31)	0.55	3.31(0.85-12.9)	0.08
<b>Previous history of vascular pathology</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	0.63(0.07-5.64)	0.68	3.54(0.67-18.7)	0.14
<b>Hypertension</b>				
No	1.0 (Referent)		1.0 (Referent)	
Yes	0.97(0.30-3.15)	0.96	0.24(0.06-0.98)	0.05

\* n=471 , n. of events=14.

† n=166, n. of events=16.

Cox proportional hazard regression models with delayed entry were performed with age as the basic timescale and birth as the time origin.