

Modifiable Risk Factors Associated With Neuropathologically Confirmed Alzheimer's Disease and Vascular Dementia Pathology

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Modifiable risk factor profiles may differ by dementia etiology, with depression and physical inactivity associated with AD pathology, while traumatic brain injury, hypertension, and diabetes were associated with VD pathology, suggesting a role for etiology-specific dementia prevention strategies.

INTRODUCTION	METHODS	RESULTS	REFERENCES																																																																																																												
• Dementia prevention increasingly targets modifiable risk factors. • Most evidence is based on clinical diagnoses, which have limited etiological specificity. • Neuropathology allows more accurate differentiation between Alzheimer's disease (AD) and vascular dementia (VD). • We examined associations between modifiable risk factors and neuropathologically confirmed AD and VD.	• Cross-sectional study using NACC (USA) and BAS (Brazil). • AD: 6,020 participants. • VD: 2,745 participants. • 2,068 controls shared between analyses. • Mixed AD–VD cases excluded. • 13 modifiable risk factors assessed. • Logistic regression adjusted for age, sex, and factor-specific confounders.	Sample characteristic: <table><tr><th colspan="4">AD PATHOLOGY</th><th colspan="4">VD PATHOLOGY</th></tr><tr><td>77.34</td><td>12.51</td><td>52.2 %</td><td>84.5 %</td><td>74.42</td><td>71.31</td><td>54.6 %</td><td>74.0 %</td></tr><tr><td>Mean age (y)</td><td>Education (y)</td><td>Male</td><td>White</td><td>Mean age (y)</td><td>Education (y)</td><td>Male</td><td>White</td></tr></table> Table 1. Modifiable risk factors associated with AD pathology (n=6,020) <table><tr><th>Risk factor</th><th>OR (95% CI)</th><th>p value</th></tr><tr><td>Less education</td><td>1.13 (0.87–1.48)</td><td>0.363</td></tr><tr><td>Hearing loss</td><td>0.84 (0.71–0.99)</td><td>0.048</td></tr><tr><td>High LDL cholesterol</td><td>1.19 (1.02–1.39)</td><td>0.031</td></tr><tr><td>Depression</td><td>1.52 (1.29–1.79)</td><td><0.001</td></tr><tr><td>Traumatic brain injury</td><td>1.44 (0.38–5.44)</td><td>0.593</td></tr><tr><td>Physical inactivity</td><td>1.49 (1.14–1.96)</td><td>0.004</td></tr><tr><td>Diabetes</td><td>0.91 (0.76–1.09)</td><td>0.321</td></tr><tr><td>Smoking</td><td>0.74 (0.64–0.85)</td><td><0.001</td></tr><tr><td>Hypertension</td><td>0.75 (0.65–0.87)</td><td><0.001</td></tr><tr><td>Obesity</td><td>0.57 (0.48–0.69)</td><td><0.001</td></tr><tr><td>Excessive alcohol</td><td>0.96 (0.78–1.18)</td><td>0.692</td></tr><tr><td>Social isolation</td><td>0.27 (0.21–0.34)</td><td><0.001</td></tr><tr><td>Visual loss</td><td>1.13 (0.98–1.31)</td><td>0.092</td></tr></table> Statistically significant at α = 0.05. Table 2. Modifiable risk factors associated with VD pathology (n=2745) <table><tr><th>Risk factor</th><th>OR (95% CI)</th><th>p value</th></tr><tr><td>Less education</td><td>1.83 (1.14–2.94)</td><td>0.013</td></tr><tr><td>Hearing loss</td><td>0.98 (0.78–1.23)</td><td>0.856</td></tr><tr><td>High LDL cholesterol</td><td>1.01 (0.8–1.27)</td><td>0.956</td></tr><tr><td>Depression</td><td>1.30 (1.03–1.64)</td><td>0.027</td></tr><tr><td>Traumatic brain injury</td><td>3.19 (1.02–9.99)</td><td>0.045</td></tr><tr><td>Physical inactivity</td><td>2.17 (1.45–3.27)</td><td><0.001</td></tr><tr><td>Diabetes</td><td>1.32 (1.02–1.70)</td><td>0.035</td></tr><tr><td>Smoking</td><td>0.98 (0.79–1.19)</td><td>0.815</td></tr><tr><td>Hypertension</td><td>1.42 (1.13–1.78)</td><td>0.003</td></tr><tr><td>Obesity</td><td>0.98 (0.75–1.27)</td><td>0.859</td></tr><tr><td>Excessive alcohol</td><td>1.22 (0.89–1.68)</td><td>0.214</td></tr><tr><td>Social isolation</td><td>0.91 (0.69–1.18)</td><td>0.459</td></tr><tr><td>Visual loss</td><td>0.96 (0.77–1.19)</td><td>0.729</td></tr></table> Statistically significant at α = 0.05. CONCLUSION • AD and VD showed distinct risk factor profiles. • Findings highlight the importance of considering dementia etiology when targeting prevention strategies.	AD PATHOLOGY				VD PATHOLOGY				77.34	12.51	52.2 %	84.5 %	74.42	71.31	54.6 %	74.0 %	Mean age (y)	Education (y)	Male	White	Mean age (y)	Education (y)	Male	White	Risk factor	OR (95% CI)	p value	Less education	1.13 (0.87–1.48)	0.363	Hearing loss	0.84 (0.71–0.99)	0.048	High LDL cholesterol	1.19 (1.02–1.39)	0.031	Depression	1.52 (1.29–1.79)	<0.001	Traumatic brain injury	1.44 (0.38–5.44)	0.593	Physical inactivity	1.49 (1.14–1.96)	0.004	Diabetes	0.91 (0.76–1.09)	0.321	Smoking	0.74 (0.64–0.85)	<0.001	Hypertension	0.75 (0.65–0.87)	<0.001	Obesity	0.57 (0.48–0.69)	<0.001	Excessive alcohol	0.96 (0.78–1.18)	0.692	Social isolation	0.27 (0.21–0.34)	<0.001	Visual loss	1.13 (0.98–1.31)	0.092	Risk factor	OR (95% CI)	p value	Less education	1.83 (1.14–2.94)	0.013	Hearing loss	0.98 (0.78–1.23)	0.856	High LDL cholesterol	1.01 (0.8–1.27)	0.956	Depression	1.30 (1.03–1.64)	0.027	Traumatic brain injury	3.19 (1.02–9.99)	0.045	Physical inactivity	2.17 (1.45–3.27)	<0.001	Diabetes	1.32 (1.02–1.70)	0.035	Smoking	0.98 (0.79–1.19)	0.815	Hypertension	1.42 (1.13–1.78)	0.003	Obesity	0.98 (0.75–1.27)	0.859	Excessive alcohol	1.22 (0.89–1.68)	0.214	Social isolation	0.91 (0.69–1.18)	0.459	Visual loss	0.96 (0.77–1.19)	0.729	Livingston, G., et al. (2024). Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. The Lancet, 404(10452), 572–628. Suemoto, C. K., et al. (2023). Risk factors for dementia in Brazil: Differences by region and race. Alzheimer's & Dementia, 19(5), 1849–1857. ACKNOWLEDGMENTS  The present study was supported by the São Paulo Research Foundation (FAPESP), Brazil (Grant No. 2025/11695-7). CONTACT Cintia Monteiro Carvalho, PhD carvalhocm.to@gmail.com 
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