

Pharmacogenetics of cerebrovascular metabolism modulators in dementia due to Alzheimer's disease

Farmacogenética dos moduladores do metabolismo cerebrovascular na síndrome demencial da doença de Alzheimer

Fabricio Ferreira de Oliveira

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Correspondence: Fabricio Ferreira de Oliveira; Universidade Federal de São Paulo, Escola Paulista de Medicina, Departamento de Neurologia e Neurocirurgia; Rua Botucatu, 740, Vila Clementino; 04023-900 São Paulo SP, Brasil; E-mail: fabricioferreiradeoliveira@hotmail.com

Supervisor: Paulo Henrique Ferreira Bertolucci (Departamento de Neurologia e Neurocirurgia).

Co-Supervisora: Marília de Arruda Cardoso Smith (Departamento de Morfologia e Genética).

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ABSTRACT

The aims of this study were to investigate risk factors for cognitive and functional decline among 193 patients with Alzheimer's disease dementia (AD), and to conduct pharmacogenetic analysis on cerebrovascular metabolism modulators, taking into account *APOE* haplotypes and the genotypes of *ACE*, *CETP*, *LDLR* and the *LXR-β* gene. For all patients, later age at AD onset was the most important risk factor for faster cognitive and functional decline, while the late-life coronary heart disease risk was inversely related to cognitive decline only for carriers of *APOE4+* haplotypes. Schooling was protective against cognitive decline only for women and carriers of *APOE4+* haplotypes, while higher body mass index in late life was protective against cognitive decline only for men. Carriers of the *APOE-ε4/ε4* haplotype had earlier AD onset, whereas genotypes of *CETP* and *LDLR* that had traditionally been associated with higher risk of AD were associated with later onset of dementia. Angiotensin-converting enzyme inhibitors caused a 50% reduction in Mini-Mental State Examination score changes, and had better disease-modifying properties than did centrally-acting angiotensin-converting enzyme inhibitors alone. Angiotensin receptor blockers had genetically mediated effects that led to faster cognitive and functional decline, while patients with genetic tendencies towards faster cognitive and functional decline had maximum benefits when they used lipophilic statins, and vice versa.

Keywords: Alzheimer disease, dementia, cerebrovascular disorders, neurodegenerative diseases, risk factors, pharmacogenetics, genetics.
