

McFall, G. P., Wiebe, S. A., Vergote, D., Westaway, D., Jhamandas, J., & Dixon, R. A. (2013).

IDE (rs6583817) polymorphism and type 2 diabetes differentially modify executive function in older adults. *Neurobiology of Aging*, *34*, 2208-2216.

We tested independent and interactive contributions of a recently noted and promising insulin degrading enzyme polymorphism (*IDE*; rs6583817) and type 2 diabetes (T2D) to executive function performance, concurrently and longitudinally. Regarding normal neurocognitive decline and Alzheimer's disease, T2D is a known risk factor and this *IDE* variant might contribute risk or risk reduction via the minor (A) or major (G) allele. We compared normal aging and T2D groups (baseline $n = 574$; ages 53–95 years) over 2 longitudinal waves (mean interval = 4.4 years). We used confirmatory factor analysis, latent growth curve modeling, and path analysis. A confirmed single-factor model of 4 executive function tasks established the cognitive phenotype. This *IDE* variant predicted concurrent group differences and differential change in cognitive performance. Furthermore, the *IDE* major allele reduced risk of cognitive decline. T2D predicted performance only concurrently. Both *IDE* and T2D are associated with executive function levels in older adults, but only *IDE* moderated 2-wave change. Previously linked to Alzheimer's disease, this *IDE* variant should be further explored for its potential influence on cognitive phenotypes of normal aging.