The effect of TOMM40 on spatial navigation in amnestic mild cognitive impairment.

doc. MUDr. Jan Laczó, Ph.D.,
Department of Neurology

Abstract

The very long (VL) poly-T variant at rs10524523 ("523") of the TOMM40 gene may hasten the onset of late-onset Alzheimer's disease (LOAD) and induce more profound cognitive impairment compared with the short (S) poly-T variant. We examined the influence of TOMM40 ‘523’ polymorphism on spatial navigation and its brain structural correlates. Participants were apolipoprotein E (APOE) ε3/ε3 homozygotes with amnestic mild cognitive impairment (aMCI). The homozygotes were chosen because APOE ε3/ε3 variant is considered ‘neutral’ with respect to LOAD risk. The participants were stratified according to poly-T length polymorphisms at ‘523’ into homozygous for S (S/S; n = 16), homozygous for VL (VL/VL; n = 15) TOMM40 poly-T variant, and heterozygous (S/VL; n = 28) groups. Neuropsychological examination and testing in real-space human analog of the Morris Water Maze were administered. Both self-centered (egocentric) and world-centered
(allocentric) spatial navigation was assessed. Brain magnetic resonance imaging scans were analyzed using FreeSurfer software. The S/S group, although similar to S/VL and VL/VL groups in demographic and neuropsychological profiles, performed better on allocentric navigation ($p \leq 0.004$) and allocentric delayed recall ($p \leq 0.014$), but not on egocentric navigation. Both S/VL and VL/VL groups had thinner right entorhinal cortex ($p \leq 0.043$) than the S/S group, whereas only the VL/VL group had thinner left entorhinal cortex ($p = 0.043$) and left posterior cingulate cortex ($p = 0.024$) than the S/S group. In conclusion, TOMM40 ‘523’ VL variants are related to impairment in allocentric spatial navigation and reduced cortical thickness of specific brain regions among aMCI individuals with (LOAD neutral) APOE ε3/ε3 genotype. This may reflect a specific role of TOMM40 ‘523’ in the pathogenesis of LOAD.


Published: 7. 6. 2016 / Responsible person: Mgr. Ing. Tereza Kůstková

Source URL (modified on 12. 4. 2019 - 9:17):