Acta Scientific Neurology (ISSN: 2582-1121)

Volume 7 Issue 2 February 2024

Letter to Editor

The APOE and MTHF Genes' Potential Role and Contribution to an Increased Risk of Vascular Dementia

Ivan Barbov[1-3] and Goce Kalcev[3]*

[1]*University Clinic of Neurology, Skopje, Republic of North Macedonia*

[2]*Faculty of Medicine, St. Cyril and Methodius-Skopje, Skopje, Republic of North Macedonia*

[3]*National Alliance for Neuromuscular Diseases and Neuroscience, GANGLION Skopje, Skopje, Republic of North Macedonia*

***Corresponding Author:** Goce Kalcev, National Alliance for Neuromuscular Diseases and Neuroscience, GANGLION Skopje, Skopje, Republic of North Macedonia

Received: October 06, 2023

Published: January 01, 2024

As life expectancy rises, the global number of dementia patients is expected to rise to 81.1 million by 2040. Vascular dementia (VaD) is traditionally regarded as the second most common cause of dementia after Alzheimer's disease (AD) [1]. It is essential to identify VaD risk factors in order to develop effective preventive and treatment strategies. Polygenetic influences may lead to a predisposition to developing VaD, according to epidemiological and animal studies [1].

The most extensively studied of these is apolipoprotein E (apoE). Given the inherent risk that hypertension, stroke, atherosclerosis, and other metabolic factors appear in the development of VaD, it is interesting to think about any possible role that apolipoprotein E (apoE) may play in this disease. Human apoE is polymorphic, with three major isoforms, apoE2, apoE3, and apoE4, that vary by single amino acid substitutions at positions 112 and 158, involving cysteine-arginine replacements [2]. In the central nervous system (CNS), apoE is produced by a variety of cells, including astrocytes, which transport cholesterol to neurons via apoE receptors that are members of the low-density lipoprotein (LDL) receptor family. Whether apoE4 presents a risk for the development of VaD has been the subject of numerous studies with inconsistent findings. It is engaging to think about whether environmental factors may have had an influence [3]. The relative distribution of APOE allele frequencies may differ across study populations, especially between ethnic and geographical groups. Diets, as an important environmental factor that contains saturated fat and cholesterol, may also confer an increased risk of VaD development, which would contribute even more to people carrying the APOE4 alleles [4]. Taken together, the evidence suggests that having one or both APOE4 alleles increases the risk and vulnerability of VaD, but not to the same extent as in AD.

The other gene, methylenetetrahydrofolate reductase (MTHFR), a key rate-limiting enzyme in the metabolism of homocysteine (Hcy), has captured the interest of researchers because plasma total homocysteine (tHcy) levels have been linked to vascular disease, poor cognitive function, and even VaD [5]. The MTHFR C677T polymorphism codes for a heat-sensitive variant characterized by decreased enzymatic activity and increased plasma tHcy levels [2], and it was also found to be associated with cognitive test performance independent of its influence on tHcy levels [6]. According to the outcomes of one meta-analysis, the T allele or TT genotype was associated with an increased risk of VaD in general populations [7]. The most significant link was found in the recessive model (OR = 1.95) in Asian populations, where the risk of developing VaD was 1.95 times higher in individuals with the MTHFR C677T TT genotype than in C allele carriers (CT plus CC genotype) [7]. Given the small number of inconsistent studies included in the current meta-analysis, the findings should be interpreted with prudence.

Additional work with larger sample sizes across diverse populations is needed to explore the potential link between VaD and the APOE and MTHFR polymorphisms. Further knowledge of and conformation of the existing genetic variants and polymorphisms would be of great importance for the identification of subjects with

an existing risk of developing an ischemic stroke and, thus, the creation and implementation of preventive strategies to prevent the development of vascular dementia.

Funding

This research received no external funding.

Acknowledgment

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.

Bibliography

1. Arvanitakis Zoe., *et al*. "Diagnosis and Management of Dementia: Review". *JAMA* 322.16 (2019): 1589-1599.

2. Rohn Troy T. "Is apolipoprotein E4 an important risk factor for vascular dementia?" *International Journal of Clinical and Experimental Pathology* 7.7 (2014): 3504-3511.

3. Pitas RE., *et al*. "Lipoproteins and their receptors in the central nervous system. Characterization of the lipoproteins in cerebrospinal fluid and identification of apolipoprotein B, E (LDL) receptors in the brain". *The Journal of Biological Chemistry* 262.29 (1987): 14352-14360.

4. Laitinen, M H et al. "Fat intake at midlife and risk of dementia and Alzheimer's disease: a population-based study". *Dementia and Geriatric Cognitive Disorders* 22.1 (2006): 99-107.

5. Nilsson Karin., *et al*. "Plasma homocysteine levels and different forms of vascular disease in patients with dementia and other psychogeriatric diseases". *Dementia and Geriatric Cognitive Disorders* 27.1 (2009): 88-95.

6. Elkins Jacob S., *et al*. "Methylenetetrahydrofolate reductase C677T polymorphism and cognitive function in older women". *American Journal of Epidemiology* 166.6 (2007): 672-678.

7. Peng Qiliu., *et al*. "The MTHFR C677T polymorphism contributes to increased risk of Alzheimer's disease: evidence based on 40 case-control studies". *Neuroscience Letters* 586 (2015): 36-42.