VEGF RECEPTOR-2 (RS2071559) GENE POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO SMALL-VEssel VASCULAR DEMENTIA.

Raquel Manso-Calderón¹,², Purificación Cacabelos¹, María Dolores Sevillano¹, María Elisa Herrero²,³, Rogelio González-Sarmiento⁴,⁵

¹Department of Neurology, Hospital Universitario de Salamanca, Spain  
²Department of Neurology, Hospital Nuestra Señora de Sonsoles, Spain  
³Department of Neurology, Hospital del Bierzo, Spain  
⁴Department of Medicine, University of Salamanca, Unidad de Medicina Molecular, Spain  
⁵University of Salamanca, Instituto de investigación biomédica de Salamanca (IBSAL), Spain

Introduction—There is increasing evidence for the involvement of endothelial dysfunction in ischemic brain injury.

Objective—We evaluated whether single nucleotide polymorphisms (SNPs) of vascular endothelial growth factor (VEGF), kinase insert domain-containing receptor (KDR) -a type 2 VEGF receptor- and endothelial nitric oxide synthase (eNOS) are associated with increased risk of Vascular Dementia (VaD) in the Spanish population.

Patients and Methods—150 patients with probable VaD (NINDS-AIREN criteria) and 150 controls were screened for the VEGF (C(-2578)A/rs699947 and T(-460)C/rs833061), KDR (A(-604)G/rs2071559) and eNOS (G(+894)T/rs1799983) SNPs. Subgroup analysis was performed to determine whether the effect of these polymorphisms is specific to certain etiological subtypes of VaD.

Results—Subjects carrying -604AA genotype in KDR were less susceptible to VaD (OR=0.48, p=0.012) after correction for age and gender. Further analysis for VaD subtype revealed a significant difference between small-vessel VaD patients and controls (GG vs. AA: adjusted OR=2.91, 95%CI=1.28-6.63, p=0.011; AG-AA vs. GG: AOR=0.38, 95%CI=0.20-0.70, p=0.002), but not for large-vessel VaD patients. There was no association between C-2578A and T-460C VEGF and G+894T eNOS SNPs and VaD risk.

Conclusion—KDR rs2071559 polymorphism is a possible genetic determinant for the risk of small-vessel VaD. This finding supports previous stroke studies with a negative effect of SNP-604 on small-vessel disease by causing defective endothelial cell development and abnormal blood vessel growth, as well as increasing endothelial damage and endothelial dysfunction; in contrast with a positive effect of SNP-604 on large-artery atherosclerosis by downregulating VEGF-KDR signaling, reducing neovascularization and retarding the plaque growth.