An Association Study of the Matrix Metalloproteinase-7, -26 Genetic Polymorphisms on the Risk of Ischemic Stroke

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Background: Previous studies indicated that matrix metalloproteinase-7 (MMP-7) and MMP-26 were associated with plaque stability. Therefore, we aimed to study the association of genetic polymorphisms of MMP-7, -26 with ischemic stroke.

Methods: A total of 1000 study subjects (500 ischemic stroke patients and 500 age-, sex- matched healthy controls) were recruited in our study. Information of demographic data, lifestyle, and disease history were collected from the study subjects using a structured questionnaire. The genotypes of selected SNPs from MMP-7 (rs10502001, rs11568818) and MMP-26 (rs2499953, rs2499966) were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Multivariate logistic regression models were used to analyze the relationship between genetic polymorphisms and risk of ischemic stroke.

Results: After adjusting age, gender, education, obesity, smoke, alcohol, hypertension, diabetes and heart diseases, a protective effect for ischemic stroke was found in study subjects with MMP-26 rs2499966 A allele (OR= 0.633, 95% C.I.= 0.461-0.868). There was a 23.7% decreased risk of developing ischemic stroke for each additional A allele (p for trend = 0.039). In study subjects with obesity, a 3.5-fold (95% C.I. = 1.840-6.596) increased odds for ischemic stroke were observed in MMP-7 rs10502001 T allele carriers. However, this was not seen in the subjects without obesity.

Conclusion: MMP-26 rs2499966 A allele was protective against ischemic stroke. However, a higher risk for ischemic stroke was seen in MMP-7 rs10502001 T allele carriers in obesity subgroup. Therefore, subjects who carry MMP-7 rs10502001 T allele have to avoid becoming obesity.

Table 1. The distribution of demographic information, disease history, and life style among ischemic stroke cases and controls

Variables	Cases N=500	Controls N=500	P value
Age (±SD)	61.33 ± 11.07	61.17 ± 10.99	0.8085
Feamls	167 (33.40%)	167 (33.40%)	1.0000
Education			
≤Elementary school	277 (56.76%)	105 (21.65%)	<0.0001
Junior/Senior high school	171 (35.04%)	184 (37.94%)	
University	40 (8.20%)	196 (40.41%)	
Smoking	241 (48.59%)	154 (30.86%)	<0.0001
Alcohol drinking	105 (21.13%)	67 (13.40 %)	0.0012
Hypertension	374 (74.80%)	263 (52.60%)	<0.0001
Diabetes	227 (45.40%)	83 (17.26%)	<0.0001
Heart disease	123 (24.65%)	78 (15.92%)	0.0006
Hyperlipidemia	414 (82.97%)	405 (81.00%)	0.4195
BMI (kg/m ²)	25.34 ± 3.63	24.6 ± 3.12	0.0006

Chi-square test for categorical variables and Student's t test for continuous variable

Table 3. Association between MMP 7 rs10502001 and risk of ischemic stroke after stratifying by smoking, alcohol drinking and obesity

Variables	Genotype	Cases (%) N=500	Controls (%) N=500	OR ^a (95% C.I.)
Smoking	No	CC	131 (51.57)	1.000
		CT+TT	123 (48.43)	1.040 (0.681-1.587)
	Yes	CC	127 (52.92)	1.000
		CT+TT	113 (47.08)	1.137 (0.701-1.845)
Alcohol drinking	No	CC	205 (52.43)	1.000
		CT+TT	186 (47.57)	1.152 (0.814-1.630)
	Yes	CC	54 (51.92)	1.000
		CT+TT	50 (48.08)	0.894 (0.418-1.915)
Obesity	No	CC	187 (55.33)	1.000
		CT+TT	151 (44.67)	0.761 (0.523-1.106)
	Yes	CC	64 (44.76)	1.000
		CT+TT	79 (55.24)	3.484 (1.840-6.596)***

a: adjusted by age, sex, education, obesity, smoking, alcohol drinking, hypertension, diabetes, heart disease **p< 0.005, ***p< 0.0001

Table 2. The distribution of genetic polymorphisms of MMP 7 and MMP 26 among patients with ischemic stroke and controls

SNPs	Cases (%) N=500	Controls (%) N=500	OR ^a (95% C.I.)
MMP 7			
rs10502001			
CC	262 (52.61)	261 (52.20)	1.000
CT	204 (40.96)	197 (39.40)	1.269 (0.911-1.769)
TT	32 (6.43)	42 (8.40)	0.643 (0.355-1.165)
Dominant model			1.126 (0.823-1.539)
Additive model			0.976 (0.765-1.245)
MMP 7			
rs11568818			
AA	422 (84.74)	428 (85.60)	1.000
AG	73 (14.66)	68 (13.60)	1.038 (0.659-1.635)
GG	3 (0.60)	4 (0.80)	0.576 (0.095-3.507)
Dominant model			1.007 (0.646-1.570)
Additive model			0.977 (0.647-1.475)
MMP 26			
rs2499953			
AA	240 (48.19)	253 (50.60)	1.000
AG	212 (42.57)	206 (41.20)	0.958 (0.691-1.328)
GG	46 (9.24)	41 (8.20)	0.955 (0.542-1.683)
Dominant model			0.957 (0.701-1.307)
Additive model			0.969 (0.762-1.233)
MMP 26			
rs2499966			
CC	291 (58.32)	273 (54.6)	1.000 reference
CA	173 (34.67)	201 (40.2)	0.590 (0.424-0.820)*
AA	35 (7.01)	26 (5.2)	0.992 (0.509-1.935)
Dominant model			0.633 (0.461-0.868)*
Additive model			0.763 (0.590-0.986)*

a: adjusted for age, sex, education, obesity, smoking, alcohol drinking, hypertension, diabetes, heart disease

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