Lack of Association Between *PRNP* 1368 Polymorphism and Alzheimer's Disease or Vascular Dementia

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Backgrounds

Polymorphisms of the prion protein gene (*PRNP*) at codons 129 and 219 play an important role in the susceptibility to Creutzfeldt-Jakob disease (CJD), and might be associated with other neurodegenerative disorders. Several recent reports indicate that polymorphisms outside the coding region of *PRNP* modulate the expression of prion protein and are associated with sporadic CJD, although other studies failed to show an association. These reports involved the polymorphism *PRNP* 1368 which is located upstream from *PRNP* exon 1. In a case-controlled protocol, we assessed the possible association between the *PRNP* 1368 polymorphism and either Alzheimer's disease (AD) or vascular dementia (VaD).

Methods

To investigate whether the *PRNP* 1368 polymorphism is associated with the occurrence of AD or VaD in the Korean population, we compared the genotype, allele, and haplotype frequencies of the *PRNP* 1368 polymorphism in 152 AD patients and 192 VaD patients with frequencies in 268 healthy Koreans

Results

No significant difference between Korean AD patients and controls was found in genotype or allele frequency of the *PRNP* 1368 polymorphism (Table 2). This result suggests that the *PRNP* 1368 polymorphism does not increase susceptibility to AD. We also investigated the genotype and allele frequencies of *PRNP* 1368 in 192 Korean VaD patients to determine whether this polymorphism correlated with VaD. There were no significant differences in genotype and allele frequencies between VaD patients and controls (Table 2). In addition, analysis of the haplotype frequency was performed in AD patients, VaD patients and controls. Six haplotypes of the 3 *PRNP* polymorphisms were constructed in Koreans. One (ht 5) of these six haplotypes was significantly over-represented in Korean VaD patients (Table 3).

Table 1: Characteristics of AD and VaD patients and controls

	Control	AD	P value[a]	VaD	P value[a]
Number of subjects	268	152		192	
Gender					
Male, n (%)	118 (44.0%)	51 (33.55%)	0.014	100 (52.1%)	0.090
Female, n (%)	150 (56.0%)	101 (66.45%)		92 (47.9%)	
Mean age at disease onset (years ± SD)	-	73.48 ± 8.00	0.006	71.95 ± 8.92	0.348
Mean age at blood collection (years ± SD)	71.17 ± 8.68	-		-	

[a]Based on the difference between controls and AD or VaD patients

Table 2: Genotype and allele frequencies of the PRNP 1368 polymorphism in the normal population, AD patients, and VaD patients

	Control (n = 268)	AD (n = 152)	VaD (n = 192)	AD *vs* Control OR[a]	95% CI[b]	P value	VaD *vs* control OR	95% CI	P value
Genotype frequency									
CC	103 (38.4)	56 (36.8)	84 (43.8)	-	-	-	-	-	-
CT	124 (46.3)	67 (44.1)	74 (38.5)	0.994	0.640 – 1.544	0.978	0.732	0.487 – 1.100	0.133
TT	41 (15.3)	29(20.1)	34 (17.7)	1.301	0.731 – 2.315	0.371	1.017	0.594 – 1.742	0.952
Allele frequency									
C	330 (61.6)	179 (58.9)	242 (63.0)	-	-	-	-	-	-
T	206 (38.4)	125 (41.1)	142 (37.0)	1.119	0.839 – 1.491	0.444	0.940	0.717 – 1.232	0.654

Figures in parentheses are percentage.

[a]Odds ratio

[b]Confidence interval

Table 3: Haplotype frequency of three PRNP polymorphisms in the normal population, AD patients, and VaD patients

Haplotypes	1368	Codon 129	Codon 219	Frequency			P value		
				AD	VaD	Control	AD *vs* Control	VaD *vs* Control	AD *vs* VaD
ht1	C	A	G	0.5592	0.5622	0.5951	-	-	-
ht2	T	A	G	0.3618	0.3623	0.3450	0.479	0.451	0.996
ht3	T	A	A	0.0263	0.0142	0.0292	0.990	0.167	0.215
ht4	T	G	G	0.0197	0.0037	0.0115	0.280	0.252	0.050
ht5	C	A	A	0.0164	0.0352	0.0109	0.333	0.013	0.226
ht6	C	G	G	0.0066	0.0224	0.0083	1.0	0.078	0.197

Conclusion

PRNP 1368 polymorphism was not significantly associated with incidence of sporadic AD and VaD in Koreans. However, in the haplotype analysis among 3 *PRNP* polymorphisms, we observed a significant association between haplotype ht5 and VaD. Our report is the first association study of a polymorphism outside the coding region of *PRNP* with AD and VaD.