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Short Communication

Association of brain-derived neurotrophic factor (*BDNF*) Val66Met polymorphism with Parkinson's disease in a Greek population

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ABSTRACT

Brain-derived neurotrophic factor (BDNF) enhances survival of dopaminergic neurons in the substantia nigra, whereas in patients with Parkinson's disease (PD), the expression of BDNF mRNA is decreased, thus making *BDNF* a candidate gene for PD susceptibility. The association between *BDNF* Val66Met polymorphism and PD has been evaluated in several studies with controversial results. Thus, we determined the distribution of *BDNF* Val66Met polymorphism in 184 Greek patients with sporadic PD and 113 control participants using polymerase chain reaction–restriction fragment length polymorphism, and explored the association of the polymorphism with certain clinical parameters of the disease. Our results do not support a major role for the *BDNF* Val66Met polymorphism in PD in the Greek population.

Brain derived neurotrophic factor (BDNF) is abundant in the brain and is important for neuronal growth, survival and differentiation of neuronal cells in the central nervous system.[1] It was the first neurotrophin described to promote the survival and dopamine uptake of embryonic midbrain dopaminergic neurons *in vitro*,[1] thus it was considered early on as a crucial protein for Parkinson's disease (PD).

BDNF encodes for a large promolecule (pro-BDNF) with a secretory signal peptide that presents BDNF as an extracellular factor. The Val66Met polymorphism in the 5′-pro-BDNF sequence alters the intracellular tracking and packaging of pro-BDNF, affecting the role of mature BDNF.[2] Interestingly, Val66Met (G196A) polymorphism has been linked to the clinical pathology of PD, as well as with cognitive impairment,[3] early onset of drug-induced dyskinesias[4] and planning ability.[5] Inconsistent results have been found regarding the Val66Met polymorphism as a risk factor for PD.[6] Moreover, in contrast to previous studies, a recent study[7] reported that the *BDNF* Val66Met polymorphism does not modify the clinical features of PD. The present study is the first to examine the genetic association of the Val66Met polymorphism with PD in the Greek population as well as its possible association with certain disease parameters, such as age of disease onset, presenting symptoms (akinetic or tremor type), side of symptom initiation, dyskinesias and dementia.

We examined 184 unrelated individuals diagnosed with PD according to the United Kingdom Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria[8] (mean [± standard deviation, SD] age: 63.9 ± 0.7 years), without positive family history and 113 control subjects (mean age ± SD: 71.6 ± 0.5 years). All participants gave informed consent for this study. Patients were assessed with the Unified Parkinson's Disease Rating Scale (UPDRS) score (Parts III and IV). Patients who scored a one grade higher tremor severity on the UPDRS than both rigidity and bradykinesia scores were classified as having the "tremor-dominant" type, whereas those patients who had either a bradykinesia or rigidity score one grade higher than the tremor score were classified as having the "akinetic" type. Patients who did not meet either of the two previous criteria were classified as having the "mixed type".[9] The Mini Mental State Examination (MMSE) was used for the evaluation of cognitive status. A MMSE score $\leqslant$ 24 was accepted as the cut-off score for dementia. A total of 135 patients had been taking L-Dopa for more than 3 years.

BDNF genotypes were determined using the polymerase chain reaction–restriction fragment length polymorphism method.[3] The distribution of *BDNF* genotypes in patients and controls are presented in Table 1, while the relationship of *BDNF* genotypes to clinical characteristics is shown in Table 2.

Our results show no difference in *BDNF* genotype frequencies between patients with PD and controls; thus, there does not seem to be a major role for this polymorphism in the pathogenesis of PD in Greek patients. Furthermore the *BDNF* Val66Met polymorphism was not related to clinical parameters such as the disease subtype, the side of symptom initiation, the age of disease onset or the presence of dyskinesias and dementia in Greek patients with PD. Further studies are needed to determine the role of *BDNF* polymorphism alone, or in interaction with, other genetic or environmental factors in PD pathogenesis.

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Table 1
Distribution of brain-derived neurotrophic factor (*BDNF*) genotypes in patients with Parkinson's disease (PD) and in the control participants in a Greek population

BDNF G196A	*BDNF* genotypes (*n*, %)			Significance
	G/G	G/A	A/A	
PD (*n* = 184)	62.5	33.7	3.8	$\chi^2 = 0.087$, $p = 0.977$
Controls (*n* = 113)	62.8	32.7	4.4	

Table 2
Distribution of *BDNF* genotypes and alleles in patients with Parkinson's disease (PD) in a Greek population in relation to clinical parameters

PD group		*BDNF* genotypes (*n*, %)			Significance
		G/G	G/A	A/A	
Age of onset (years)	PD > 50 (*n* = 51)	64.7	29.4	5.9	$\chi^2 = 1.240$,
	PD ⩽ 50 (*n* = 133)	61.7	35.3	3.0	$p = 0.545$
Predominant symptom type	Tremor (*n* = 93)	59.0	35.9	5.1	$\chi^2 = 1.742$,
	Mixed type (*n* = 13)	75.0	25.0	0.0	$p = 0.785$
	Bradykinesia and rigidity (*n* = 78)	63.4	33.3	3.2	
Side of symptom initiation	Right (*n* = 87)	66.7	29.9	3.4	$\chi^2 = 1.919$,
	Left (*n* = 90)	57.8	37.8	4.4	$p = 0.783$
	Bilateral (*n* = 7)	71.4	29.8	0.0	
Cognition	Demented (*n* = 18)	8.7	10.9	14.3	$\chi^2 = 0.413$,
	Non-demented (*n* = 166)	91.3	89.1	85.7	$p = 0.921$
Dyskinesia initiation (3 years after L-Dopa treatment)	Dyskinesias (*n* = 34)	61.8	29.4	8.8	$\chi^2 = 2.056$,
	No dyskinesias(*n* = 101)	66.3	30.7	3.0	$p = 0.465$

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