J Neurol (2010) 257:459–460
DOI 10.1007/s00415-009-5363-4

LETTER TO THE EDITORS

Glucocerebrosidase mutations p.L444P and p.N370S are not associated with multisystem atrophy, progressive supranuclear palsy and corticobasal degeneration in Polish patients

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Received: 25 April 2009 / Revised: 30 September 2009 / Accepted: 15 October 2009 / Published online: 1 November 2009

Recently, mutations in the *GBA* gene coding for lysosomal beta-glucocerebrosidase have been found as a risk factor for Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB) [1–3]. These mutations seem to participate in the formation of Lewy bodies. PD and DLB have been classified as synucleinopathies; the third most common synucleinopathy are multisystem atrophies (MSA), which may share with PD and DLB at least part of the molecular pathogenesis. The incidence of mutations in the *GBA* gene in PD patients is variable and related to different populations studied, methods of DNA testing (sequencing versus looking for the most common mutations only), and different control groups. Lewy bodies were also found in some patients with tauopathies like Progressive Supranuclear Palsy (PSP) and corticobasal degeneration (CBD) [4–6]. Thus lysosomal dysfunction caused by GBA mutations may alter or disrupt the processing of the alpha- or beta-synuclein [4]. To identify mutations in the *GBA* gene, genomic DNA was extracted from the white blood cells by standard techniques. A screening for mutations, p.L444P and p.N370S was performed in a group of 66 MSA patients (MSA-P = 34) and (MSA-C = 31), 34 PSP patients and in five cases of CBD. The patients were diagnosed at two movement disordered centers according to clinical criteria and the level of diagnosis (possible and probable) is shown in Table 1. PCR-RFLP methods were used as described earlier. Our results were compared to incidence of GBA mutations in other European populations and in PD/DLB patients [1–3].

None of the examined mutations in the *GBA* gene has been found in our cohort of patients with MSA, PSP and CBD.

Although a limited number of our patients, and a less sensitive technique than direct sequencing [7], cannot completely rule out the possibility of increased frequency of p.L444P and p.N370S mutations in the beta-glucocerebrosidase gene (*GBA*), it seems rather unlikely that the incidence of these particular *GBA* mutations in MSA and PSP are compatible to their frequency in PD (about 4%) and DLB (from 4 to 23%), as reported in the literature [2, 8]. As yet, a total number of the published patients with MSA tested for *GBA* mutations are below the level of sensitivity because the incidence of the heterozygote state for the above mutations in European populations, excluding Scandinavia, is about 0.3%. Our results are also in agreement with those of neuropathologically confirmed MSA patients, published recently [9]. These results may indicate that PD and (DLB) have another pathway in formation of Lewy bodies than has MSA [10]. We also didn't see differences between parkinsonian and cerebellar type of MSA. Moreover, we didn't identify any *GBA* mutations in PSP and CBD patients.

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Table 1 Diagnoses of patients tested for the presence of the glucocerebrosidase (GBA) mutations: p.L444P and p.N370S

Diagnosis	Possible	Probable	Total
MSA-P	4	30	34
MSA-C	3	28	31
PSP	3	31	34
CBD	1	4	5
Total			104

Acknowledgments This work was supported by the Polish Ministry of Science and Higher Education, Grant # N N402 4404 33.

Conflict of interest statement None.

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