Hereditary spastic paraplegias (HSP) are neurodegenerative diseases mainly characterized by lower limb spasticity associated, in complicated forms, with additional neurological signs. We have analysed a large series of index patients (n = 76) with this condition, either from families with an autosomal recessive inheritance (n = 43) or isolated patients (n = 33), for mutations in the recently identified SPG11 gene. We found 22 truncating mutations, including the first four splice-site mutations, segregating in seven isolated cases and 13 families. Nineteen mutations were novel. Two recurrent mutations were found in Portuguese and North-African patients indicating founder effects in these populations. The mutation frequency varied according to the phenotype, from 41%, in HSP patients presenting with a thin corpus callosum (TCC) visualized by MRI, to 4.5%, in patients with mental impairment without a TCC. Disease onset occurred during the first to the third decade mainly by problems with gait and/or mental retardation. After a mean disease duration of 14.9 +/- 6.6 years, the phenotype of 38 SPG11 patients was severe with 53% of patients wheelchair bound or bedridden. In addition to mental retardation, 80% of the patients showed cognitive decline with executive dysfunction. Interestingly, the phenotype also frequently included lower motor neuron degeneration (81%) with wasting (53%). Slight ocular cerebellar signs were also noted in patients with long disease durations. In addition to a TCC (95%), brain MRI revealed white matter alterations (69%) and cortical atrophy (81%), which worsened with disease duration. In conclusion, our study reveals the high frequency of SPG11 mutations in patients with HSP, a TCC and cognitive impairment, including in isolated patients, and extends the associated phenotype [1)].

Pallidal Deep Brain Stimulation for the Treatment of Levodopa-Responsive Juvenile Dystonia and Parkinsonism Secondary to SPG11 Mutation [2)].

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2)
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