An update on the Genetics of Parkinson's disease

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Résumé

In the past twenty years there has been substantial progress in our understanding of the genetic factors involved in the etiopathogenesis of Parkinson's disease (PD).
Highly-penetrant mutations in each of different genes (e.g. *SNCA*, *LRRK2*, *VPS35*, *Parkin*, *PINK1*, and *DJ-1*) are established as rare causes of monogenic forms of the disease. Furthermore, variants with **incomplete penetrance** in the *LRRK2* and the *GBA* gene act as strong risk factors for PD, and are prevalent in some populations. Last, common variants of small effect size, modulating the risk for PD, have been identified by genome-wide association studies (GWAS) in several chromosomal loci.

In this lecture, I first outline the evolution of the research strategies to find new PD-related genes, and then focus on some clinically more relevant forms. Additional genetic determinants of PD likely remain to be identified, as the currently known mutations and variants only explain a minor fraction of the disease burden.

The current, powerful DNA sequencing technologies (whole-exome and whole-genome sequencing), nowadays widely used in both research and clinical practice, will hopefully accelerate the discovery of the remaining disease-related genetic factors.
Importantly, while additional genes for PD are being discovered, the first human clinical trials, based on some of the above-mentioned genetic discoveries, are being conducted in PD, with the hope to yield soon the first disease-modifying therapies.

Mots-Clés: Parkinson's disease, genetics

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