Huntington's disease

Huntington's disease (HD) is a fully penetrant neurodegenerative disease caused by a dominantly inherited CAG trinucleotide repeat expansion in the huntingtin gene on chromosome 4. In Western populations HD has a prevalence of 10.6-13.7 individuals per 100,000. It is characterised by cognitive, motor and psychiatric disturbance. At the cellular level mutant huntingtin results in neuronal dysfunction and death through a number of mechanisms, including disruption of proteostasis, transcription and mitochondrial function and direct toxicity of the mutant protein. Early macroscopic changes are seen in the striatum with involvement of the cortex as the disease progresses. There are currently no disease modifying treatments therefore supportive and symptomatic management is the mainstay of treatment. In recent years there have been significant advances in understanding both the cellular pathology and the macroscopic structural brain changes that occur as the disease progresses. In the last decade there has been a large growth in potential therapeutic targets and clinical trials. Perhaps the most promising of these are the emerging therapies aimed at lowering levels of mutant huntingtin. Antisense oligonucleotide therapy is one such approach with clinical trials currently underway. This may bring us one step closer to treating and potentially preventing this devastating condition [1)].

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McColgan P, Tabrizi SJ. Huntington's disease: a clinical review. Eur J Neurol. 2017 Aug 17. doi: 10.1111/ene.13413. [Epub ahead of print] PubMed PMID: 28817209.