"The presymptomatic phase of Huntington Disease"

Together with the rise in human life expectancy, cognitive impairment due to neurodegenerative disorders, such as in Alzheimer’s disease or Huntington’s disease (HD), has become one of the leading causes of disability in developed countries. Among genetic conditions, monogenic disorders with complete penetrance of the mutation give access to more homogeneous disease models and the phase before clinical onset of the disease, the presymptomatic phase. HD, an autosomal dominant disease affecting thousands of patients in Europe, can be regarded as a model for neurodegeneration and cognitive impairment. HD is a model disorder to study the presymptomatic phase of the disease because: i) the existence of a very long presymptomatic phase before the onset of disease symptoms, in which pathogenic events take place before prodromal (non specific) or evident clinical signs; ii) complete age-dependent penetrance of the mutation (expanded CAG repeat); iii) existence of a well established presymptomatic testing procedure which enables individuals at risk to access their genetic status and guarantee adapted follow up. Through the availability of a presymptomatic testing carriers and non-carriers after testing are available to be included in prospective follow up studies. One of these studies is TRACK HD, a prospective observational biomarker study in premanifest and early HD, evaluating a battery of potential outcome measures for therapeutic trials. In the search for non invasive biomarkers, we focussed our attention on energy metabolism since a systemic hypercatabolic profile is observed in carriers before onset of the disease and we showed evidence of chronic alteration in homeostasis of high energy phosphates in HD mouse models in the earliest stages of the disease (Mochel et al 2012). Related to this findings, preliminary data from our group indicate that a dietary anaplerotic approach, using triheptanoin, was able to correct markers of altered energy metabolism in HD patients.


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