



Les comportements problématiques dans la maladie de Huntington

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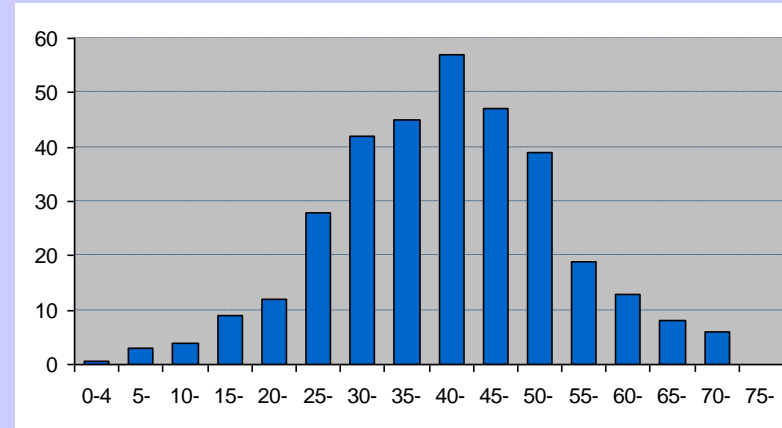
Introduction

- Maladie rare orpheline
- Neurodégénérative
- Maladie de l'adulte
- Chorée = terme plus utilisé
- Fréquence (prévalence 1/10 000)
- Maladie « modèle » en neurogénétique
 - Amplification triplets CAG (polyQ)

Généralités

- **Age de début** moyen = 35 ans
 - Extrêmes : 2 - 70 ans
 - Formes juvéniles = 10 %

- **Durée d'évolution** moyenne = 15-20 ans



- **Début insidieux**, signes initiaux discrets
- **Anosognosie** au début
- **Triade** classique :
 - Troubles moteurs
 - Signes psychiatriques
 - Démence

Histoire naturelle

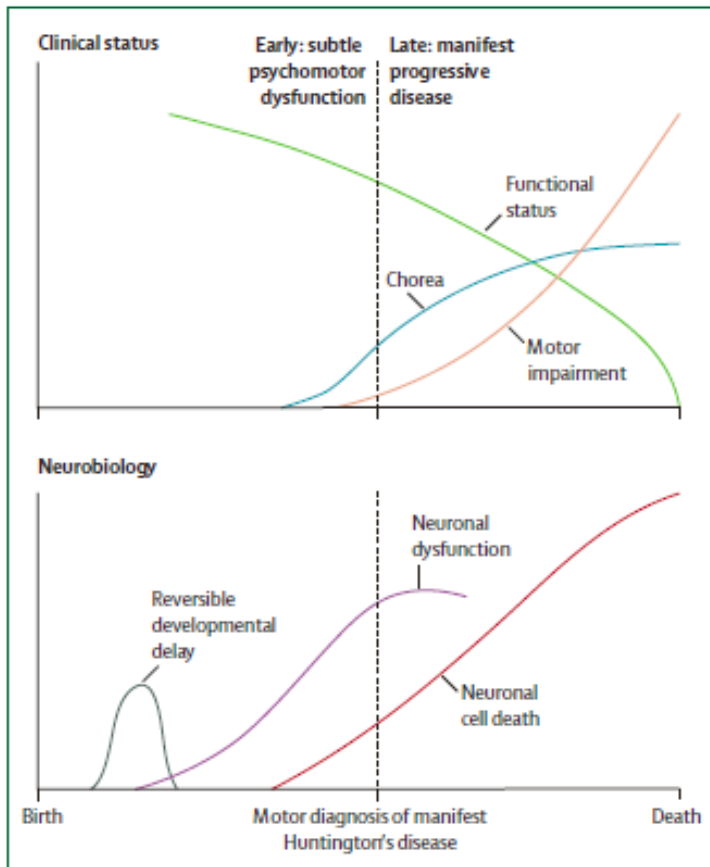
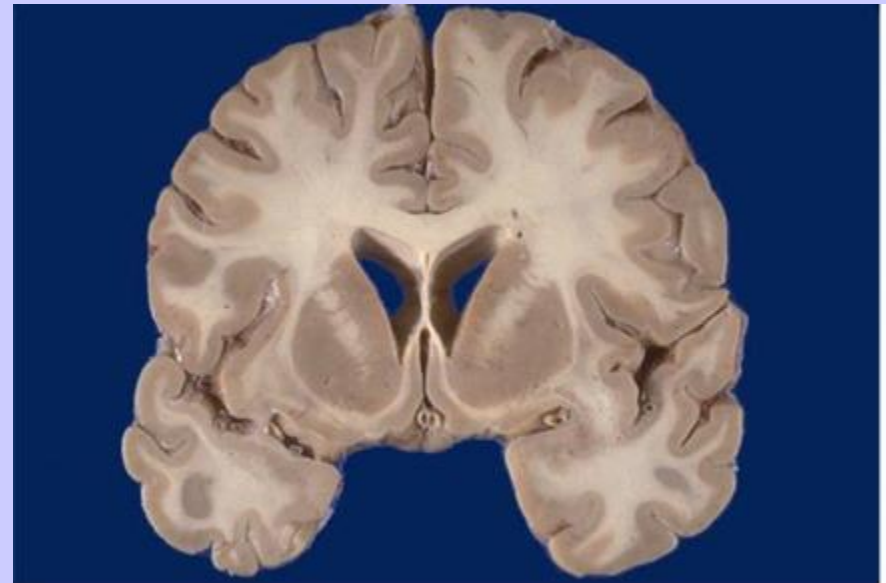


Figure 1: Progression of Huntington's disease over a patient's lifespan
Subtle signs and symptoms of Huntington's disease begin years before a motor diagnosis can be made, and correlate with neurobiological changes such as striatal atrophy, giving rise to the concept of a Huntington's disease prodrome. Chorea is often the earliest motor feature noted clinically, but motor impairment or bradykinesia and incoordination are more disabling. Early in the disease course, neuronal dysfunction is likely to be important, but later, neuronal cell death in vulnerable regions of the brain is predominant and correlates with motor impairment and functional disability.



WT



HD

Signes Cliniques

- **Signes moteurs**

- Chorée = le plus fréquent

Mouvements spontanés, involontaires, brusques, irréguliers, distribués au hasard, majorés par les émotions et la concentration

- Dystonie
- Mouvements oculaires anormaux
- Dysarthrie
- Apraxie bucolingale
- Troubles de la marche
- Bradykinésie / akinésie ; rigidité

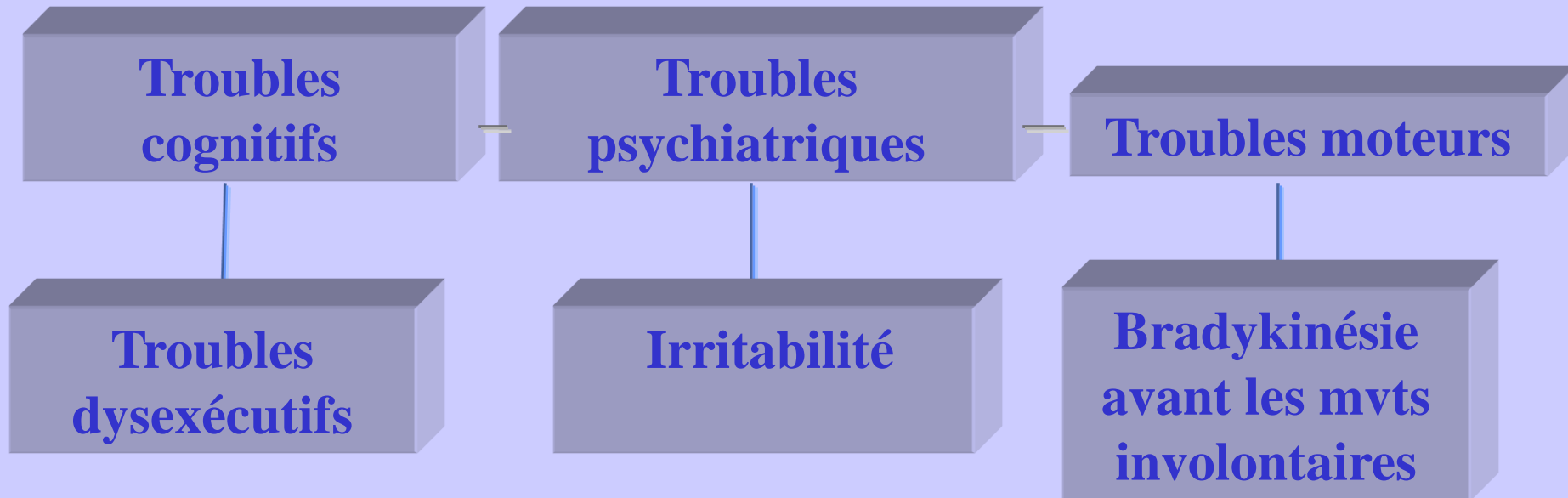
- **Troubles psychiatriques**

- Très fréquents au stade débutant (33 à 76 % des patients)
- Souvent avant le début des signes moteurs
- Impact négatif +++ sur la famille et le milieu sociopro
- **Comportement agressif, irritabilité, impulsivité**
- **Dépression +++ (9 - 44%)**
- Suicide (x 12)
- **Anxiété (60-80%),**
- **Apathie ++++**
- Obsessions/compulsions (30%)
- Psychose → schizophrénie ?
- Hyper/hypo-sexualité, addictions

- **Demence (altération cognitive)**
 - Frontale et sous-corticale
 - Déficits attention et concentration
 - Atteinte de la planification et des fonctions exécutives
 - Déficits visuospatiaux et de la construction
 - Déficit mnésique

La MH commence avant l'apparition des mouvements anormaux

Deux ans, en moyenne, avant l'apparition des symptômes moteurs il existe des troubles cognitifs (Rothlind et al, 1993; Paulsen et al, 2001)



- Hahn-Barma et al., 1998
- Paulsen et al. 2001
- Ho et al. 2003

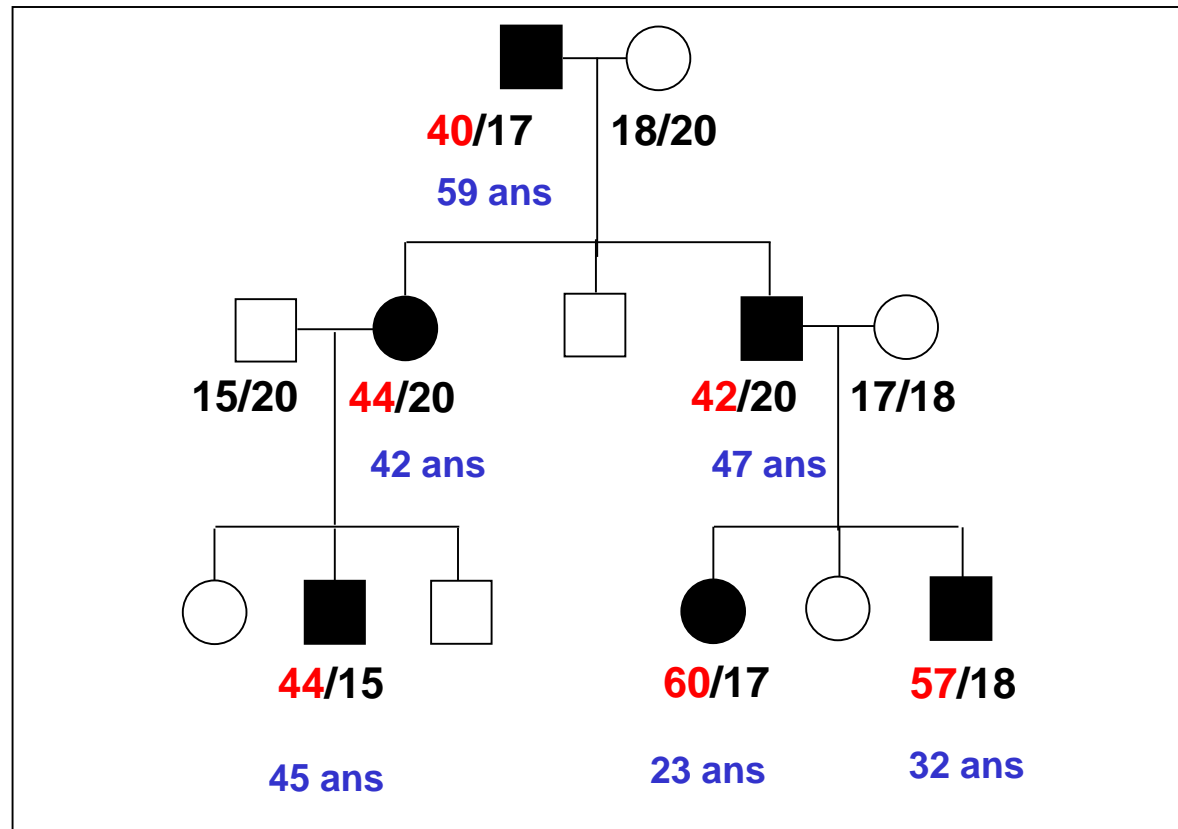
Kirkwood et al. 2002

- Sanchez-Pernaute et al., 2000
- Van Vugt et al., 2004

Génétique

- Transmission **dominante autosomique**
- Pénétrance complète à 70 ans
- Localisation sur le chromosome 4p16.3 (1984)
- Gène *IT15* codant pour la huntingtine (1993)
 - 67 exons (180kb)
 - Séquence codante = 10,3 kb
- Mutation par **amplification de triplets CAG**

L'anticipation dans la maladie de Huntington



- diminution de l'âge de début au cours des générations
- Liée à une augmentation du nombre de répétitions (instable)

Traitements symptomatiques

OPEN ACCESS Freely available online

PLOS ONE

Effectiveness of Anti-Psychotics and Related Drugs in the Huntington French-Speaking Group Cohort

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Abstract

Purpose: Huntington's disease is a rare condition. Patients are commonly treated with antipsychotics and tetrabenazine. The evidence of their effect on disease progression is limited and no comparative study between these drugs has been conducted. We therefore compared the effectiveness of antipsychotics on disease progression.

Methods: 956 patients from the Huntington French Speaking Group were followed for up to 8 years between 2002 and 2010. The effectiveness of treatments was assessed using Unified Huntington's Disease Rating Scale (UHDRS) scores and then compared using a mixed model adjusted on a multiple propensity score.

Results: 63% of patients were treated with antipsychotics during the survey period. The most commonly prescribed medications were dibenzodiazepines (38%), risperidone (13%), tetrabenazine (12%) and benzamides (12%). There was no difference between treatments on the motor and behavioural declines observed, after taking the patient profiles at the start of the drug prescription into account. In contrast, the functional decline was lower in the dibenzodiazepine group than the other antipsychotic groups (Total Functional Capacity: 0.41 ± 0.17 units per year vs. risperidone and 0.54 ± 0.19 vs. tetrabenazine, both $p < 0.05$). Benzamides were less effective than other antipsychotics on cognitive evolution (Stroop interference, Stroop color and Literal fluency: $p < 0.05$).

Conclusions: Antipsychotics are widely used to treat patients with Huntington's disease. Although differences in motor or behavioural profiles between patients according to the antipsychotics used were small, there were differences in drug effectiveness on the evolution of functional and cognitive scores.

Conclusion

- Handicap complexe rare
 - Très lourd
 - Plusieurs déficiences associées
 - Fardeau alourdi par contexte familial
- Prise en charge multidisciplinaire
 - Temps de coordination médicale et médico-sociale
 - N'existe pas dans les CHU hors CR MR...
 - Mission de l'ERHR ?