Hugh Rickards

Medication for Huntington’s disease
Contents

- From HC to HD...
- What are we treating and why?
- Different HD problems and their treatments.
The HD mutation and huntingtin protein

Glutamines QQQ......

NH₂ COOH

HD Protein (huntingtin)

Glutamines

CAG CAG CAG....

→ > ~70 juvenile onset HD
→ > 40 adult onset HD
→ 36-39 incomplete penetrance
→ 27-35 Intermediate allele
→ < 27 unaffected

180 kb DNA

1 2 3 66 67

HD brain cerebral cortex

Neuropil Aggregates

Nuclear Inclusions

Coronal section of normal (left) and HD (right) brains
TRACK-HD Premanifest A Subject

Baseline Scan
TRACK-HD Premanifest A Subject

12-month Scan
TRACK-HD Premanifest A Subject

24-month Scan
The “neuropsychiatric” striatum

A slice through monkey striatum after Haber et al. (2006)
From HC to HD

- “onset” is an artefact
- It’s a neuropsychiatric disorder
- It’s not a “movement disorder”
- Mental and behavioural change is often most disabling and bothersome
- It’s potentially modifiable.
HC is a movement disorder
Making the movements less disordered makes HC better
Some drugs make movement disorders less disordered
We should use these drugs on all people with HC who have disordered movements
HD is a brain disorder
Abnormal brains can lead to a variety of problems
Some of these problems can be treated effectively with drugs
We should treat people where appropriate.
Things that help diagnosis

Things that bother the patient

Things that bother other people

Things you can treat with meds

Social cognition deficit

Chorea
Factor analysis of psychiatric symptoms (N= 1000)

- Irritability/apathy/poor planning/perseveration
- Depression/Anxiety
- Psychosis (uncommon)

Rickards et al JNNP 2011
Mental symptoms that may respond to pharmacology

- Irritability
- Depression
- Anxiety disorders
- Perseveration
- Psychosis
Mental symptoms that won’t respond to pharmacotherapy

- Executive function deficit
- Apathy
- Social cognitive deficit.
Typical Clinic scenario

- Hugh: So how are things going?
- PWHD: Fine thanks....
- Relative/carer *facepalm*

FACEPALM
When words fail to describe the dismay, there is always Facepalm.

DOUBLE FACEPALM
When the Fail is so strong, one Facepalm is not enough.
Times when we need executive function

- Going anywhere.
- Having a party/wedding
- Having visitors/grandchildren etc.
- When anything doesn’t go to plan.
- Doing a lot of things at once

- Luckily the brain is very plastic and appears to compensate well in the earlier stages.
The results of Executive “system overload”

- Anxiety
  - Agoraphobia/social phobia
  - Generalised anxiety
  - Panic attacks
- Irritability/arguments
- Depression
- Social withdrawal
Managing executive dysfunction

- Everyone has to understand what it is!
- Keeping things simple
- Waiting
- Meaningful direction
- Pharmacological treatment after that.
Excessive angry response to minor stimulus
What are the causes??
- Cognitive overload
- Perseveration
- Hunger
- Depression
- Pain
- Additional illness (infection, subdural, constipation)
- Misunderstanding
- Frustration
- Premorbidly irritable
- Psychosis

Low cognitive capacity with disinhibition, mediated by anxiety.

Nimmaggadda 2011
Managing Irritability.

- Treat underlying cause.
- Manage relatives/carers
- Drugs for irritability
  - SSRI’s? mirtazepine
  - Neuroleptics (olanzapine)
  - Valproate/lamotrigine
  - Cannabinoids
Treating depression in HD.

- Do you need anti-chorea drugs??
- Antidepressants often work well.
- Social interventions
- Managing other symptoms (eg. Swallowing)
- Support.
• Seeing the other person’s point of view
  • Literally
  • Metaphorically
• Counterfactual reasoning
  • The ability to imagine a situation/viewpoint other than your own at this precise moment
  • This might explain the *facepalm* moments in clinic
  • Works alongside executive function to create strategic thinking
• THIS TYPE OF PROBLEM IS LIKE A “LATE ONSET ASPERGER SYNDROME”
The results of social cognition problems?

- Can’t negotiate solutions to conflicts
  - Relationship difficulties (according to the spouse)
- Apathy
- Irritability
- Avoidance of social situations
- Problems with strategising
- Not understanding that there IS a problem
- A problem for carer/spouse.
Managing social cognitive problems

- Family grief and acceptance.
- Managing interactions
  - Communicating more literally
  - Keeping routines
  - Carer support
- Pharmacological management of some consequences.
When to treat chorea

- When patient complains of it
- When it disturbs sleep/other routine
- When it causes mechanical damage

- Evidence base for tetrabenazine
- All neuroleptics (olanzapine helps weight maintenance)

- Anti-chorea drugs can impair cognition.
Dystonia

- Botox with rehab goal
- Clonazepam
- Appropriate aids/adaptations
- Reduce neuroleptics
Rigidity

- Reduce neuroleptics
- L-dopa in young onset HD
- Physiotherapy
Akathisia

- Check iron levels
- Reduce tetrabenazine/neuroleptics.
Myoclonus

- Clonazepam
- Valproate/levetiracetam
The evidence base is slim.

But there’s plenty of expert wisdom.

Try environmental approaches.

Think of the drugs you can stop.

Always consider the therapeutic goal of treating.

Don’t treat motor disorder just because it’s there.
Thank you!