Putting HD patient data to work

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Presenter Disclosures

Amrita Mohan

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose
Key takeaways

1. HD research participant data is absolutely critical to clinical research

2. A cool example of how HD individuals’ data is being used

3. YOU are important to the success of clinical research
Background: HD observational studies
HD observational studies are VERY important

Guide clinical development

• Understand course of disease
• Design better drug trials
• Improve patient care

Credit: Rob Sinclair
Thank You
Data gathered in HD observational studies

• ~15 studies known so far
  – Variety of data
    • clinical assessments (e.g. UHDRS)
    • neuro-imaging
    • molecular (through biosamples)
  – Visit-based
    • each visit spanning a few hours, by participants
Recent example: Use of biosamples from different HD observational studies
Huntingtin gene is important in HD but other genes are involved as well

- CAG length good predictor of age of motor onset
- However a wide range exists!

Other genes that affect age of motor onset?

Plot credit: GeM consortium
Other genes that affect motor onset in HD

Using DNA from ~7000 HD research participants spanning Enroll-HD, Registry, Predict-HD and COHORT

More genes identified

- Common good variant +1.4 years
- Common bad variant -1.6 years
- Rare bad variant -6 years

Genetic Modifiers of HD (GeM-HD) Consortium Cell 2015
Modifier of HD onset at MLH1 locus HMG 2017
1. Not only is the *huntingtin* gene critical

2. Other genes are also involved that affect age of motor onset

3. Such findings are now possible due to new technologies and data collected through HD observational studies
Pooling biosamples from multiple HD studies is powerful.

What about clinical measurements in HD observational studies?
Clinical measurement types gathered

- Motor Function Cognitive
- Psychiatric
- Quality of Life Medical History
- CAG Family Physical Treatment
- Health & Disability Health Economics
- Q-motor/TMS Nutrition
- Medication & Co-morbidity
A lot of HD clinical measurement data now available

<table>
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<th>Cohort study</th>
<th># Participants</th>
<th>CAG</th>
<th>Max visits</th>
<th>Mean visits</th>
<th>Motor</th>
<th>Functional</th>
<th>Psychiatric</th>
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<th>Q-motor Oculomotor/TMS</th>
<th>Health and Disability</th>
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</table>
A lot of HD clinical measurement data now available

200 million data points

A lot of data!!
CHDI-IBM partnership
2015 -
A 3-step data crunching cartoon

1. Collect data
2. Clean up
3. Identify patterns & predict
Data crunching process at IBM

1. Enroll-HD, Registry, Predict-HD, TRACK-HD/ON

2. Missing value analysis
2. Match variables
2. QC/Outlier check
2. Merge de-identified patient records
2. Unify category coding

Combined HD observational study dataset

Largest HD observation study dataset
Current clinical understanding of HD

- Practical understanding of course of disease after motor onset
- HD staging begins after clinical diagnosis
- No clear understanding of preceding decades: Difficult to bring therapies earlier
Can we improve our understanding of the course of HD using combined observational study data?
Using the combined HD observational study dataset

A 9-state HD progression/staging model

A measure of HD severity
Distinct changes tracked over the course of HD

- Motor, cognition, GCI + occupation
- Function, SF & Caregiver survey
- Cognition, motor & function
- Motor, cognition + MMSE
- Function, cognition, motor, physio & MMSE
- Cognition, motor + moderate activities (walking, climbing)

Distance between states proportional to expected durations in years
Why is this research exciting?
1. More detailed picture of the course of HD

Two states

Premanifest

Nine states

Manifest

HD severity
2. Will enable targeted clinical decision making

What’s next?
How long?
Better trials
3. A way to bring therapies earlier

- No clear understanding of preceding decades: Difficult to bring therapies earlier
To wrap up

HD patient data is absolutely essential to gain fast, new insights
A number of other projects currently supported by CHDI that are striving to learn new insights.

- IBM: Neuroimaging & speech analysis
- Neuroimaging HD staging
- GNS Healthcare: Progression changes
- The University of Iowa: Enroll-HD data analysis
- AIDFM: Environmental factors affecting HD

Other collaborative efforts that are using HD patient data.
Thank You

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