Digital, high-frequency, long-term monitoring of motor and non-motor symptoms in Huntington’s disease (HD)

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Summary
A study is underway to determine if smartphones and wrist-worn wearable technology can be used to monitor HD symptoms in daily life using at-home tests and continuous movement tracking. The first results from the study show that most patients consistently completed the tests and that this may be a useful way of monitoring patients’ symptoms, supplementing clinical visits.

Methods
Study Design
- Patients with HD in the ongoing ISIS 443139-CS2 clinical study (n=46) receive a smartphone (Galaxy S7; Samsung, Seoul, South Korea) and smartwatch (Moto G 360 2nd Gen Sport; Motorola, Chicago, USA) during screening.
- Patients first complete active tests using these tools in a teaching session in the clinic. The active tests are then done remotely at home and at follow-up clinical visits. For passive monitoring, patients are asked to carry the devices with them as they go about their daily activities (Figure 1).
- The sensor data is securely transferred via WiFi to Roche, where it is processed and analysed.
- Adherence data examines the average number of active tests done per week and average hours/day per week of sensor data collected.
- Sensor data will be compared to clinical data.
- The relationship between UHDRS item Maximal Chorea and respective sensor-derived features is assessed using Spearman’s rank-order correlation.
- Sensor data is compared to data collected from similar tests completed by independent HCs (N=35, age = 56.23 ± 8.33, 27 male/8 female).1
- Wilcoxon tests were used for comparisons between HD patients and healthy controls.

Table 1: ISIS 443139-CS2 patient sub-population analyzed for this poster*

<table>
<thead>
<tr>
<th>N</th>
<th>Age (years)</th>
<th>Gender (male/female)</th>
<th>Independence scale</th>
<th>TFC</th>
<th>TMS</th>
<th>Montreal Cognitve Assessment (total)</th>
<th>SWR</th>
<th>SDMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>41</td>
<td>48.66 ± 9.95</td>
<td>25/16</td>
<td>86.95 ± 8.13</td>
<td>11.10 ± 1.61</td>
<td>25.34 ± 12.56</td>
<td>24.86 ± 3.24</td>
<td>74.39 ± 22.58</td>
<td>34.24 ± 12.59</td>
</tr>
</tbody>
</table>

*Preliminary non-randomized data from patients with UHDRS and sensor data within the first 16 days of the study, Mean (±SD).


Fig 1: Smartphone test activities and schedule

Methods
- Analysis of the normalized Acc path from study participants (Figure 3a) reveals:
  - correlation with associated chorea items from UHDRS (left hand: r = 0.65 [P=0.0001] right hand: r=0.49 [P=0.0003])
  - the HD group shows increases in normalized Acc Path compared to the independent HC group (left P=0.0001, right P=0.0001).

Fig 2: Study participants display good adherence to remote digital monitoring assessments

- Average number of active tests done per study week, not including the walk test. 3173 active tests have been performed as of data cut off.
- Each participant completed an average of 23 walk tests per week during the first 16 weeks.

Fig 3: The chorea test illustrates the benefits of digital high-frequency monitoring
- This was a proof-of-concept pilot study of a single symptomatic domain of HD.
- The chorea test is designed to detect choreatic movements in the upper limbs.
- Patients hold the smartphone in their outstretched hand for 30 seconds. They are asked to close their eyes and count down in intervals of 7s from a pre-specified number. The test is completed with the left and the right hand.
- The normalized Acc path (as the sum of the euclidean distances between consecutive 3D acceleration signals normalized by test length) was computed using every chorea test performed by a patient from screening to Day 14 of the study.
- Choreatic movements from study participants and independent HCs can be visualized using acceleration data from the chorea test (Figure 3a).

Conclusions
- An app-based test suite has been developed to remotely monitor key HD symptoms. Smartphones and smartwatches equipped with this app have been successfully deployed in an ongoing clinical trial.
- Preliminary data suggests that patients adhere to smartphone and smartwatch based assessments, suggesting that these tools may provide an innovative way to learn more about patients’ daily symptoms in the clinical trial setting.
- Preliminary results from the chorea test show good agreement between clinical assessments of chorea severity and read-outs from a smartphone-based chorea test performed at home.
- Significant differences between an independent control group and patients showing no clinical chorea symptoms suggest a higher sensitivity of the digital test by using motion sensor and daily tests.
- The relationship of clinical to digital tests under the same clinical testing conditions is being further investigated.

This was a pilot analysis of a single domain of HD. Further studies will include other domains and also cover measurements from the daily life of a patient such as mobility, chorea events and severity over the day.

Abbreviations
- Acc, acceleration; HC, healthy control; HD, Huntington’s disease; PRO, patient reported outcomes; SDMT, Symbol Digit Modalities Test; SWR, Stroop Word Reading Test; TFC, Total Functional Capacity; TMS, Total Motor Score; UHDRS, Unified Huntington’s Disease Rating Scale.

References

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