CO147

Impact of Huntington's Disease on Driving: A Review of Driving Simulator Measures and Association With Clinical Outcomes Assessments

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Background

- Huntington's disease (HD) is a genetic, neurodegenerative disease characterized by motor, behavioral, and cognitive symptoms.[1]
- Cognitive decline can begin many years prior to motor manifestation, first noticed in executive functions involving multitasking, organizing thoughts, planning, and decision making.[2] As a result, patients may withdraw from more challenging activities during otherwise productive and independent phases of life.[3]
- One of the earliest concerns reported by patients with HD is the impact on driving abilities, particularly driving safety.[4,5]
- Driving is important for employment, general family responsibilities, social activities, and for the feeling of independence.[6]
- Measuring driving outcomes as a proxy for clinically relevant outcomes that require cognitive capabilities can be one way to closely track cognitive changes that occur in premanifest and early manifest HD.
- Understanding the relationship of meaningful driving outcomes and clinical outcomes assessments (COAs) frequently used in HD to comprehend cognitive impairment changes can be a useful way to build the clinical meaningfulness of COAs.

Objective

- To summarize literature on the impact of HD on driving (as measured by simulator measures) and the relationship between clinical outcomes assessments (COAs) and driving simulator measures in an HD population (Figure 1).

Methods

Design

Targeted literature review in PubMed from 2011-2021; English language only; search terms for driving, simulators, and cognitive assessments

Population

Patients with HD

Driving outcomes

Accidents, attention/reaction, distance control, general errors, infractions, lane position, and speed

Analyses

- Driving outcomes in HD vs. control: standardized mean differences (Hedge's g method)
- Driving outcomes and COAs in HD: correlation coefficients with confidence intervals calculated with R metacor using reported or estimated sample size

Results

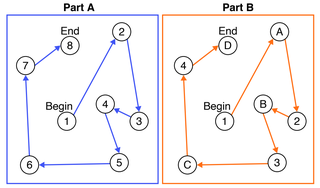
- 378 records were identified in PubMed, of which 4 (corresponding to 3 studies) were included in the review (Table 1).
- Studies were most commonly excluded due to population and outcomes of interest.
- Simulation measures included: number of accidents, response and reaction time (e.g., time to switch lanes prior to lane closure), distance to preceding cars, errors, number of traffic tickets, vehicle control measured by deviations in lane positioning, and driving speed measured by the mean speed and standard deviation in speed.
- Most consistently used COAs: Stroop test, Hopkins Verbal Learning Test, Wisconsin Card Sorting Test, Trail Making Test, Wechsler Adult Intelligence Scale–Revised (WAIS-R), and clinical rating scales.
- Compared with controls, patients with HD showed an increased frequency of accidents, tickets, and general errors (Figure 2).
- The strength of the correlations between COAs and driving measures in patients with HD ranged from low (0.04) to high (0.85) and varied across driving measure categories and COA measures (Figure 3).
- The Trail Making Test, commonly used in clinical evaluation of fitness to drive, was moderately correlated with speed (0.43) and lane position (0.49).

Table 1. Summary of Included Studies

Reference, Objective	Population (n)	Driving Outcomes	COAs
Devos et al. (2012)[7] **OBJECTIVE:** To identify the most accurate clinical predictors of fitness to drive in HD	• Manifest HD (30) • Healthy controls (30)	Fitness to drive (pass/fail): Binocular visual acuity, kinetic vision, contrast sensitivity, figure of Rey, UFOV, 4-choice reaction times, visual scanning, DA, Test for Attentional Performance; accident; traffic tickets; DA (responding to symbols presented in the periphery of the screen)	MMSE, TMT-A and TMT-B, Stroop Test, SDMT, UHDRS-TFC motor and behavioral scores, LVFT
Jacobs et al. (2018)[8] **OBJECTIVE:** to identify differences in drivinwg performance between HD gene carriers and healthy individuals in simulated urban and motorway environments	• Premanifest HD (28) • Manifest HD (30) • Healthy controls (29)	SDLP, mean speed, SD of mean speed, distance to preceding car in meters, reaction time to lane closures	UHDRS-TFC scores, finger tapping, saccadic inaccuracy, smooth pursuit, body sway, TMT-B, Stroop test, SDMT, adaptive tracking, SART, PBA-s, FrSBe, HADS-SIS
Jacobs et al. (2019)[9] **OBJECTIVE:** To investigate whether cognitive, motor, or psychiatric symptoms can predict driving performance in HD gene carriers using a simulator situation			
Rebok et al. (1995)[9] **OBJECTIVE:** To assess the influence of the neurological and cognitive impairments of HD on automobile driving	• HD: Driving (53) • HD: Not driving (20) • Healthy controls (22)	Errors (maintaining appropriate speed, use of turn signals, force applied to brake, use of accelerator, position of steering wheel); Evasive Action Skill task (situations in which appropriate action must be taken to avoid a collision); responding to cues presented on the screen (cue-recognition task)	• MMSE, TMT-A and TMT-B, Stroop test, HD-ADL, QNE, WAIS-R: Vocabulary and block design, WMS-R: logical memory and visual reproduction, VMI, FAS, BTA, HVLT, WCST, Motor-Free Visual Perception Test, Spatial Recognition Span Test, Reaction time tasks

BTA = brief test of attention; COA = clinical outcomes assessment; DA = divided attention; FAS = Controlled Oral Word Association Test; FrSBe = Frontal System Behavior Scale; HADS = Hospital Anxiety Depression Scale; HD-ADL = Huntington's disease activity of daily living; HVLT = Hopkins Verbal Learning Test; LVFT = Letter Verbal Fluency Test; MMSE = Mini-Mental State Examination; PBA-s = Problem Behavior Assessment–Short; QNE = quantitative neurological examination; SART = sustained attention to response task; SD = standard deviation; SDLP = standard deviation of the lateral position; SDMT = Symbol Digit Modalities Test; SIS = Snaith Irritability Scale; TFC = total functional capacity; TMT-A = Trail Making Test Part A; TMT-B = Trail Making Test Part B; UFOV = Useful Field of View; UHDRS = Unified Huntington's Disease Rating Scale; VMI = visual-motor integration; WAIS-R = Wechsler Adult Intelligence Scale-Revised; WCST = Wisconsin Card Sorting Test; WMS-R = Wechsler Memory Scale-Revised.
Note: Two publications regarding one study.[8,9]

Figure 1. Example of (A) Driving Simulator, (B) Scenario Displayed on Middle Screen, and (C) Sample COA: Trail Making Test

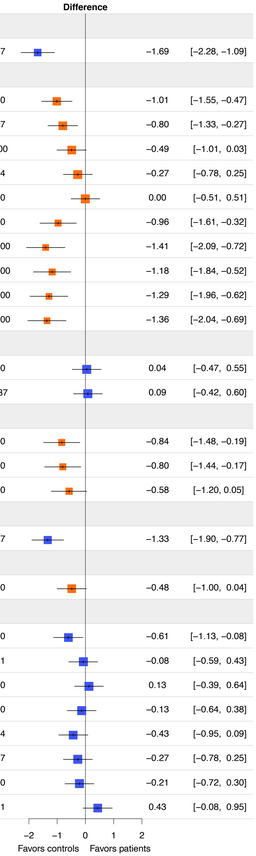


C. Trail Making Test, Part A and Part B

Note: Images are for representation purposes only. The actual tests used in the studies may look different.
Note: In the Trail Making Test, TMT requires the test-taker to connect numbers (Part A) or numbers and letters (Part B) in a sequential manner as indicated by arrows in the figure.
Source for A and B: Jacobs M, Hart EP, Miranda YM, Groeneveld GJ, van Gerven JMA, Roos RAC. Altered driving performance of symptomatic Huntington's disease gene carriers in simulated road conditions, Traffic Injury Prevention. 2018;19:7:708-14. doi: 10.1080/15389588.2018.1497796.
Source for C: Kim K, Jang JW, Baek MJ, Kim SY. A comparison of three types of trail making test in the Korean elderly: higher completion rate of trail making test-black and white for mild cognitive impairment. J Alzheimers Dis Parkinsonism. 2016;6(239):2161-460.

Figure 2. Descriptive Forest Plot of Differences in Simulated Driving Performance Between Patients With HD and Controls

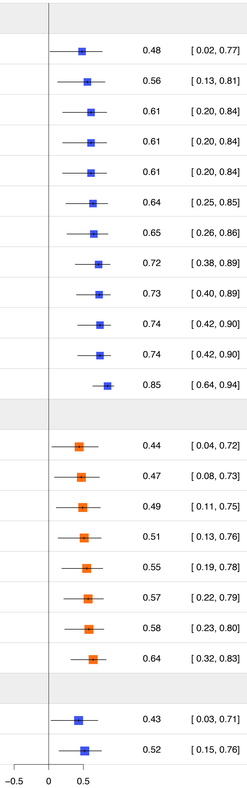
Study	Patients With HD N	Patients With HD Mean	Patients With HD SD	Healthy Controls N	Healthy Controls Mean	Healthy Controls SD	SMD	95% CI
Outcome Category = Accidents								
Devos (2012) – Accidents *	30	−2.00	1.4815	30	−0.00	0.7407	−1.69	[−2.28, −1.09]
Outcome Category = Attention/reaction								
Devos (2012) – Divided attention (response time) *	30	−3.37	2.4444	30	−1.58	0.3630	−1.01	[−1.55, −0.47]
Devos (2012) – Divided attention (correct answers)	30	16.00	5.1852	30	19.00	0.7407	−0.80	[−1.33, −0.27]
Jacobs (2018) – Reaction time (motorway scenario) *	30	8.30	12.3000	29	14.10	11.1000	−0.49	[−1.01, 0.03]
Jacobs (2018) – Reaction time (emergency stop) *	30	−1.70	0.3704	29	−1.60	0.3704	−0.27	[−0.78, 0.25]
Jacobs (2018) – Reaction time (pedestrian crossings) *	30	−1.70	0.8000	29	−1.70	0.8000	0.00	[−0.51, 0.51]
Rebok (1995) – Cue recognition – Number of valid responses	29	6.40	1.6155	16	7.70	0.4000	−0.96	[−1.61, −0.32]
Rebok (1995) – Cue recognition – Reaction time *	29	−1542.00	333.8802	16	−1105.00	244.0000	−1.41	[−2.09, −0.72]
Rebok (1995) – Cue recognition – Reaction time block 1 *	29	−1458.60	346.2661	16	−1068.20	282.8000	−1.18	[−1.84, −0.52]
Rebok (1995) – Cue recognition – Reaction time block 2 *	29	−1543.60	395.2711	16	−1084.50	240.4000	−1.29	[−1.96, −0.62]
Rebok (1995) – Cue recognition – Reaction time block 3 *	29	−1624.20	369.9608	16	−1163.60	246.0000	−1.36	[−2.04, −0.69]
Outcome Category = Distance control								
Jacobs (2018) – Distance to preceding car (motorway scenario)	30	41.00	10.5000	29	40.60	7.4000	0.04	[−0.47, 0.55]
Jacobs (2018) – Distance to preceding car (urban scenario)	30	57.00	35.7778	29	54.50	17.7037	0.09	[−0.42, 0.60]
Outcome Category = General errors								
Rebok (1995) – Drive to the city – percentage correct	28	75.00	11.1122	16	83.80	8.8000	−0.84	[−1.48, −0.19]
Rebok (1995) – Drive to the city – brake response errors *	28	−4.00	2.1166	16	−2.30	2.0000	−0.80	[−1.44, −0.17]
Rebok (1995) – Drive to the city – accelerator use errors *	28	−1.60	1.5875	16	−0.80	0.8000	−0.58	[−1.20, 0.05]
Outcome Category = Infractions								
Devos (2012) – Tickets *	30	−1.00	0.7407	30	−0.00	0.7407	−1.33	[−1.90, −0.77]
Outcome Category = Position								
Jacobs (2018) – SDLP *	30	−42.60	17.9000	29	−35.90	7.3000	−0.48	[−1.00, 0.04]
Outcome Category = Speed								
Jacobs (2018) – Mean speed (motorway scenario)	30	96.30	5.1000	29	99.20	4.3000	−0.61	[−1.13, −0.08]
Jacobs (2018) – SD of mean speed (motorway scenario) *	30	−4.70	2.8889	29	−4.50	2.1481	−0.08	[−0.59, 0.43]
Jacobs (2018) – Mean speed (30km zone)	30	29.70	3.3000	29	29.30	3.0000	0.13	[−0.39, 0.64]
Jacobs (2018) – Mean speed (50km zone)	30	47.10	5.1000	29	47.70	3.6000	−0.13	[−0.64, 0.38]
Jacobs (2018) – Mean speed (80km zone)	30	63.00	11.1111	29	66.70	4.4444	−0.43	[−0.95, 0.09]
Jacobs (2018) – SD of mean speed (30km zone) *	30	−3.70	1.4074	29	−3.40	0.6667	−0.27	[−0.78, 0.25]
Jacobs (2018) – SD of mean speed (50km zone) *	30	−5.80	1.7000	29	−5.50	1.0000	−0.21	[−0.72, 0.30]
Jacobs (2018) – SD of mean speed (80km zone) *	30	−7.90	4.6667	29	−9.50	2.0741	0.43	[−0.08, 0.95]



* Measures were converted where needed so that scales were in the same direction (i.e., so that higher scores reflected better performance) by multiplying the mean values by −1.

Figure 3. Descriptive Forest Plot of the Correlation Between Simulated Driving Outcomes and Clinical Outcomes Assessment in Patients With HD

Study	Total	COR	95% CI
Driving Measure Category = Attention/reaction			
Rebok (1995): QNE score total, Cue recognition task – accuracy on block 1 *	18	0.48	[0.02, 0.77]
Rebok (1995): QNE score total, Cue recognition task – Reaction time on block 1 **	18	0.56	[0.13, 0.81]
Rebok (1995): HVLT – third learning trial, Cue recognition task – Accuracy on block 1	18	0.61	[0.20, 0.84]
Rebok (1995): BTA – letter trial, Cue recognition task – reaction time block 3 ***	18	0.61	[0.20, 0.84]
Rebok (1995): WAIS–R Block design, Cue recognition task – reaction time block 1 ***	18	0.61	[0.20, 0.84]
Rebok (1995): HVLT – third learning trial, Cue recognition task – reaction time block 1 ***	18	0.64	[0.25, 0.85]
Rebok (1995): BTA – letter trial, Cue recognition task – Accuracy on block 3	18	0.65	[0.26, 0.86]
Rebok (1995): WAIS–R Block design, Cue recognition task – reaction time block 2 ***	18	0.72	[0.38, 0.89]
Rebok (1995): BTA – letter trial, Cue recognition task – reaction time block 2 ***	18	0.73	[0.40, 0.89]
Rebok (1995): WAIS–R Block design, Cue recognition task – Accuracy on block 3	18	0.74	[0.42, 0.90]
Rebok (1995): WAIS–R Vocabulary, Evasive Action task	18	0.74	[0.42, 0.90]
Rebok (1995): WAIS–R Block design, Cue recognition task – reaction time block 3 ***	18	0.85	[0.64, 0.94]
Driving Measure Category = Position			
Jacobs (2018): Stroop colour, SDLP ***	24	0.44	[0.04, 0.72]
Jacobs (2018): Stroop word, SDLP ***	24	0.47	[0.08, 0.73]
Jacobs (2018): TMT–B, SDLP **	24	0.49	[0.11, 0.75]
Jacobs (2018): Stroop interference, SDLP ***	24	0.51	[0.13, 0.76]
Jacobs (2018): Adaptive tracker, SDLP ***	24	0.55	[0.19, 0.78]
Jacobs (2018): UHDRS–TMS, SDLP **	24	0.57	[0.22, 0.79]
Jacobs (2018): Finger tapping, SDLP ***	24	0.58	[0.23, 0.80]
Jacobs (2018) :Body sway, SDLP **	24	0.64	[0.32, 0.83]
Driving Measure Category = Speed			
Jacobs (2018): TMT–B, Mean Speed *	24	0.43	[0.03, 0.71]
Jacobs (2018): SDMT, Mean Speed	24	0.52	[0.15, 0.76]



* Values for the cognitive assessment measure in the correlation have been multiplied by −1 to correct for the direction of scale.
** Values for each measure in the correlation have been multiplied by −1 to correct for the direction of scale.
*** Values for the driving outcome measure in the correlation have been multiplied by −1 to correct for the direction of scale.
BTA = brief test of attention; FrSBe = Frontal System Behavior Scale; HADS = Hospital Anxiety Depression Scale; HVLT = Hopkins Verbal Learning Test; PBA-s = Problem Behavior Assessment-short; QNE = quantitative neurological examination; SART = sustained attention to response task; SDLP = standard deviation of lateral position; SDMT = Symbol Digit Modalities Test; TMT-B = Trail Making Test Part B; UHDRS = Unified Huntington's Disease Rating Scale; WAIS-R = Wechsler Adult Intelligence Scale – Revised.
Note: Two publications regarding one study.[8,9]

Discussion

- Driving outcomes related to accidents, error, tickets, or reaction/attention better differentiated HD from healthy controls than outcomes related to speed, distance control, or lane positioning. This could indicate impairment in executive functioning domains like processing speed, working memory, and multitasking.
- Driving outcomes correlated with cognitive performance in domains relevant to HD pathology, such as visuospatial ability and psychomotor speed (WAIS-R), learning and memory (HVLT), and attention (BTA), suggesting that decline in these abilities may contribute to driving challenges.
- Key methodological challenges for this small study:
  - Most measures were only considered in single studies, and most studies reported on multiple measures.
  - Correlations considering the same driving outcome measure were not available across multiple studies.
- Further research is needed to adequately quantify the impact of HD on driving through various stages of the disease, as well as in identifying the functioning domains most significantly impacted.

Conclusions

Simulated driving performance shows promise as a potential outcome measure to assess the functional impact of HD on day-to-day activities. This can further help in establishing clinical meaningfulness of cognitive changes in HD and evaluate treatment effects for therapeutic development in HD.

References

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