Impact of Huntington's disease on working and driving

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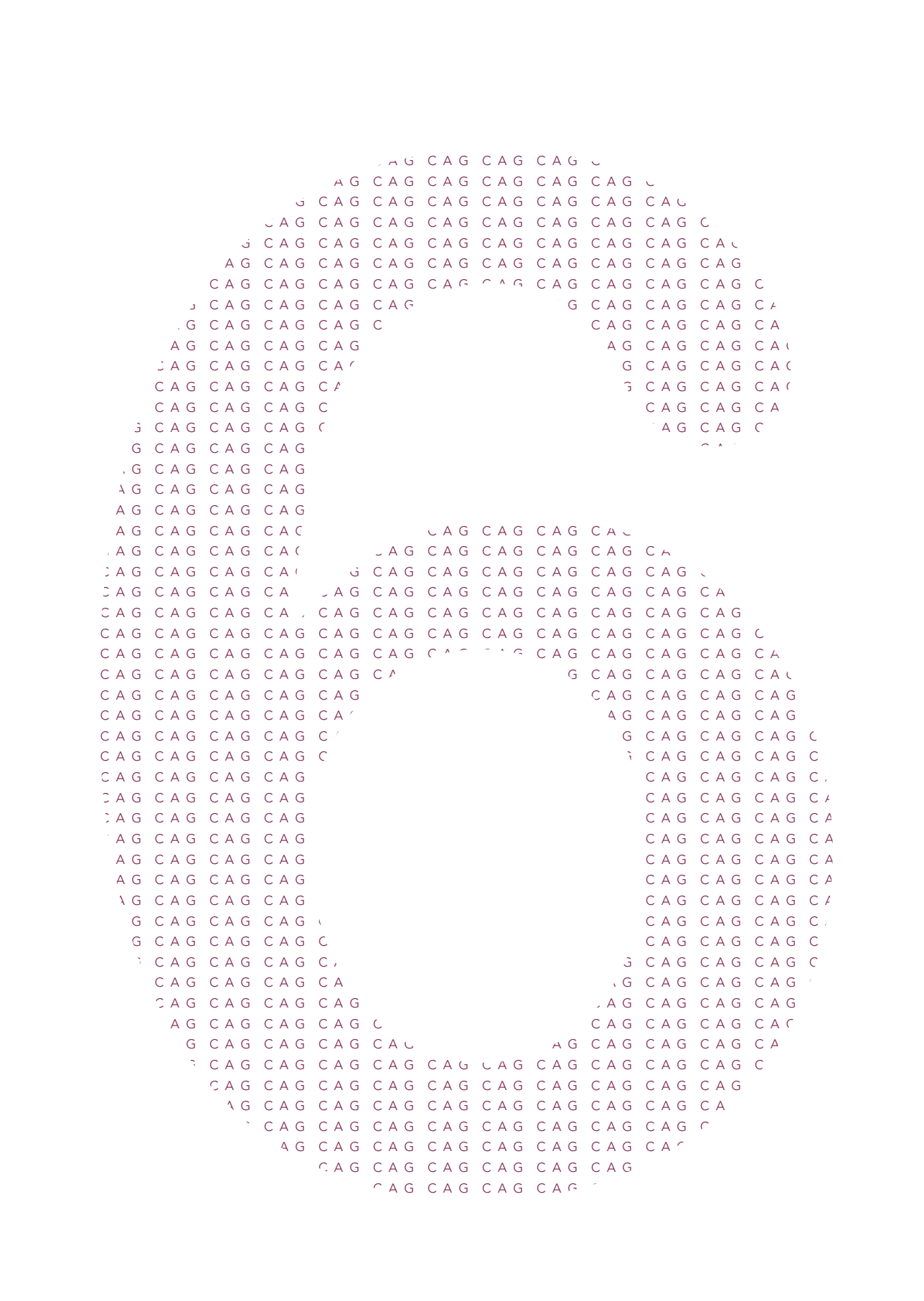
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Predictors of simulated driving performance in Huntington's disease

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Published as: Jacobs M, Hart EP, Mejia Miranda Y, Groeneveld G, van Gerven JMA, Roos RAC. Predictors of simulated driving performance in Huntington's disease.
Parkinsonism and Related Disorders. 2018 [e-pub ahead of print]

ABSTRACT

Background

As the disease progresses, patients with Huntington's disease (HD), an inherited neurodegenerative disorder, become less independent in their daily life activities and have to consider if they can still drive a car. For most patients, the decision to quit driving is difficult and affects their independence and social activities.

Objective

To investigate if cognitive, motor, or psychiatric symptoms can predict driving performance in HD gene carriers using a simulator situation.

Methods

Twenty-nine controls, 28 premanifest HD, and 30 manifest HD participated in this observational, cross-sectional study and underwent neuropsychological, motor, and psychiatric evaluations. All participants drove a motorway scenario in a driving simulator to evaluate driving performance. Group differences were analyzed using Analysis of Covariance and stepwise forward linear regression analysis was used to investigate which clinical assessments were predictors of driving simulator outcomes.

Results

Manifest HD drove slower and had less vehicle control in the driving simulator compared to controls and premanifest HD. They also performed worse on all clinical assessments compared to controls. Postural sway and slower speed of information processing were predictors of the driving simulator outcome measures. Psychiatric symptoms were unrelated to simulated driving. There were no significant differences between premanifest HD and controls.

Conclusions

ncreased postural sway and slower speed of processing are predictive of driving simulator performance in manifest HD. Worse performance on these clinical tasks might be useful as a first screening and could assist clinicians in their referral for an official on-road driving test.

INTRODUCTION

Although on-road driving tests remain the gold standard to evaluate driving ability, simulators are increasingly being used to investigate fitness to drive. Driving simulators have the advantage that challenging situations can be presented in a standardized setting, with a high reproducibility and without any risks for other traffic participants.[1] Further, driving simulator performances correlate with on-road driving assessments.[2–4] Currently, only two studies used a driving simulator to investigate driving competence in Huntington's disease (HD).[5,6] HD is an autosomal dominant neurodegenerative disorder caused by a gene mutation located on chromosome 4.[7] The disease is clinically characterized by motor impairments, cognitive decline, and behavioral changes.[8] The symptoms gradually progress, resulting in increased functional disabilities and less independence.[8] These two simulator studies showed that patients with HD had slower reaction times and committed more overall errors compared to healthy controls.[5,6] HD patients who failed an on-road driving test also performed worse on a driving simulator assessment.[6]
In addition, worse performances on neuropsychological assessments have been related to unsafe road performances in HD and might assist when deciding to cease driving.[9] Cognitive impairments were also more sensitive to discriminate between on-road pass/fail scores than motor disturbances.[6] However, it is not known if these neuropsychological tests are also able to predict driving simulator performances in HD using continuous simulator outcome measures. In addition, possible alterations in driving performance have not been studied in asymptomatic HD gene carriers. The aim of this current study was to determine motor, cognitive and behavioral predictors of simulated driving performances in HD gene carriers compared to healthy individuals.

METHODS

Participants

Fifty-eight HD gene carriers (28 premanifest HD, 30 manifest HD) and 29 controls participated in this cross-sectional observational study. All participants were at least 18 years of age, had a valid Dutch driver's license, and drove at least 300 kilometers in the previous 12 months. All HD participants had a confirmed CAG expansion of ≥36 in the *HTT* gene. Based on the Total Motor Score of the Unified Huntington's Disease Rating Scale (UHDRS-TMS), HD gene carriers were divided in manifest

(TMS>5) and premanifest HD (TMS ≤5).[10] Exclusion criteria were major comorbidities unrelated to HD (e.g., other neurological disorders or ophthalmic disorders), drug use in the four weeks prior to the study visit, alcohol abuse, and current participation in intervention trials. Alcohol was not allowed 24 hours before the study visit. The study was approved by the local ethics committee of the Leiden University Medical Center and all participants signed written informed consent.

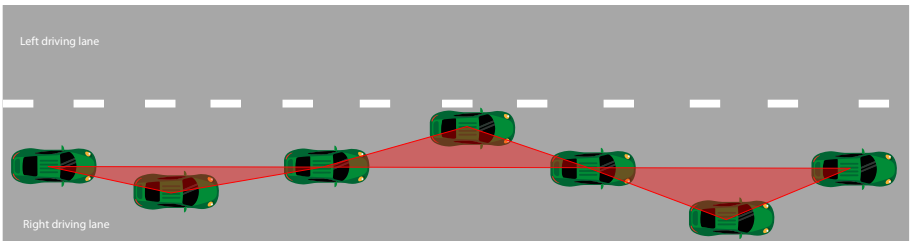
Demographic and clinical characteristics

Participants were asked if they restricted themselves in their driving behavior (e.g., not driving long distances), to gather information about self-reported adaptations or concerns about driving ability. The UHDRS was administered to assess the degree of motor disturbances (TMS) and functional capacity (TFC).[10] The UHDRS-TMS (range 0 – 124) reflects motor impairments that are common in HD, including oculomotor function, chorea, dystonia, tongue protrusion, gait, and bradykinesia. Higher scores indicate increased motor dysfunction. The UHDRS-TFC (range 0 – 13) includes items on the capacity to work, manage finances, and the ability to carry out domestic chores. Lower scores indicate more functional disability.

Driving simulator

The driving simulator (DriveMaster LT, GreenDino B.V., Wageningen, the Netherlands) consisted of three 24-inch flat panel monitors, a steering wheel, gas-, brake-, and clutch pedals, and gearshifts. The dashboard, side mirrors and rear-view mirror were displayed on the screens. Instructions were provided both verbally and on the simulator screen. For the current study, a selection of measures was used from a comprehensive study that included both urban and motorway driving scenarios. A motorway scenario was selected for this study since this type of scenario has been proven sensitive to detect driving impairments.[11] Participants started with a practice trial to get familiarized with operating the simulator, after which the simulator assessment started. The motorway scenario had a duration of 30 minutes with a maximum allowed speed of 100 km/h. Participants were allowed to overtake other vehicles. In the final ten minutes of the motorway session, lane closings were marked by a red cross above the road, indicating that the participant needed to switch lanes. The time in seconds that the participant switched lanes before the lane closure was recorded as reaction time. The primary outcome variable was the standard deviation of the lateral position in centimeters (SDLP), which is a validated outcome measure in driving simulator studies.[11] It is a measure of vehicle control, with more weaving of the car resulting in higher SDLP values (Figure 1). Secondary outcome measures were.

FIGURE 1 Standard Deviation of the Lateral Position



Note: Example of the Standard Deviation of the Lateral Position. More deviation from the center of the driving lane results in higher deviation scores.

Quantitative motor assessments

Saccadic eye movements and smooth pursuit were measured by following a horizontal moving light on a computer screen. Three electrodes were placed (one on the forehead and one on either side of the lateral canthi of both eyes) for the registration of electro-oculographic signals. Saccadic inaccuracy (%) and average percentage of time that the eyes were in smooth pursuit of the target light (%) were used as outcome variables.[12]

Postural sway was assessed with a string potentiometer, which assesses body movements in a single plane. A string was attached to the waist (e.g., on the belt or pants), and participants were requested to stand still with their feet 20 centimeters apart and their eyes closed for 2 minutes. The total anterior-posterior body sway path in millimeters was the outcome measure.[12]

Motor activation and fluency was measured with a finger tapping task.[12] Participants were instructed to tap the space bar of a keyboard as quickly as possible with the index finger of their dominant hand. The task consisted of five trials of 10 seconds each. The mean tapping rate was used as outcome variable.

Cognitive assessments

The cognitive battery comprised of both paper-pencil and computerized assessments. The paper-pencil cognitive scores included the total number of correct responses on the written Symbol Digit Modalities Test (SDMT),[13] which measures psychomotor speed and visual attention, the correct responses on the Stroop test (color, word, and interference),[14] measuring speed of processing and executive functions, and the completion time in seconds of the Trail Making Test part B

(TMT-B),[15] which was used to assess cognitive flexibility and executive functions. Lower total scores on the SDMT and Stroop test indicated worse performances. Lower completion times on the TMT-B indicated better performances.
The computerized cognitive assessments consisted of the Sustained Attention to Response Task (SART)[16] and an adaptive tracking task.[12] The SART was used to measure attentional control and vigilance. Participants needed to press the spacebar of a keyboard as quickly and accurately as possible when the digits 1 – 9 randomly appeared on the computer screen, except when the number three (3) appeared. The digits were presented for 250 milliseconds and followed by a screen with a cross inside a circle that appeared for 900 milliseconds (i.e., mask stimulus). Each SART contained of 225 trials (200 go and 25 no-go digits). The total number of commission errors (i.e., participant pressed the spacebar when the number three appeared) was the outcome measure.
During the adaptive tracking task,[12] measuring visuo-motor control and vigilance, participants were instructed to keep a dot inside a moving circle using a joystick for 3.5 minutes. The joystick was operated with the dominant hand. This task was adaptive to the participants' performance, meaning that the speed of the moving circle increased when a participants' effort was successful. The speed of the moving circle reduced if the participant was not able to keep the dot inside the circle. The outcome variable was the average percentage of time (%) that the dot was inside the circle.

Neuropsychiatric assessments

The short version of the Problem Behavior Assessment-short (PBA-s)[17] is a semi-structured interview that was used to assess the following symptoms: depression, suicidal ideation, anxiety, irritability, aggressive behavior, apathy, perseveration, obsessive-compulsive behavior, paranoid thinking, hallucinations, and disorientation. Severity and frequency scores are rated for each item on a 5-point scale (range 0 – 4), with a score of zero meaning that the symptom is absent and a score of four indicates that the symptom is causing severe problems in daily life. The total score is obtained by adding all sub-scores (range 0 – 176), with higher scores indicating more psychiatric and behavioral problems.
Two self-report questionnaires were administered that focus on self-evaluation of neuropsychiatric symptoms. The Frontal System Behavior Scale (FrSBe) is a 46-item questionnaire that assesses behavior that is associated with damage to frontal regions of the brain.[18,19] Each item is rated on a 5-point scale (1 – 5). The total score ranges from 46 – 230, and this score was used in this study as outcome measure. The

Hospital Anxiety Depression Scale – Snaith Irritability Scale (HADS-SIS)[20–22] was used to measure self-reported symptoms of anxiety, depression, and irritability. It contains 22 items, each scored on a 4-point scale (0 – 3), with a total score that ranges from 0 – 66.

Statistical analyses

Group differences on motor, cognitive, and neuropsychiatric assessments were analyzed using Analysis of Covariance (ANCOVA), corrected for age. The analyses on neuropsychiatric assessments were also corrected for gender. Analyses on cognitive assessments were additionally corrected for years of education. Simple contrasts (controls as reference group) were used to detect differences between premanifest and manifest HD versus controls. Contrasts were only interpreted if the ANCOVA revealed a significant main effect of group. Group differences on driving outcome measures were analyzed using Analysis of Variance or Kruskal-Wallis test when applicable.

Bivariate correlations were calculated between driving simulator parameters and clinical assessments that were significantly different between HD gene carriers and controls. Subsequently, stepwise forward linear regression analyses were performed to determine the prediction model of these simulator parameters. Only significant correlations were entered into the regression model.

All analyses were performed with the Statistical Package for Social Sciences (SPSS) for Windows version 23.0.

RESULTS

Three participants could not perform any of the driving simulator assessments due to symptoms of simulator sickness during the practice session. Twelve participants (14.3%) experienced symptoms of simulator sickness during the driving assessment, resulting in missing data on certain simulator outcome measures. Six manifest HD participants were unable to complete all computerized cognitive assessments due to disease severity. One control participant could not complete the computerized assessments due to time constraints. All available data for all assessments were included in the analyses, following an intention-to-treat approach. An overview of missing data per outcome measure is provided in Table S1. Demographics of all participants are reported in Table 1.

TABLE 1 Demographics

	Controls	Premanifest HD	Manifest HD
N	29	28	30
Age (years)	48.7 ± 11.0	38.4 ± 8.3	52.8 ± 10.5
Gender m/f (%m)	11/18 (38%)	15/13 (54%)	16/14 (53%)
CAG repeat length	*NA*	41.6 ± 2.4	42.5 ± 2.5
Years of education	15.6 ± 3.4	17.4 ± 3.0	16.4 ± 3.2
UHDRS-TFC	13.0 (11 – 13)	13.0 (8 – 13)	10 (5 – 13)
Simulator sickness yes/no (%yes)	3/26 (10%)	3/25 (11%)	9/21 (30%)

Data are mean ± SD, except for gender (total number)
CAG = Cytosine-Adenine-Guanine; NA = not applicable; UHDRS-TFC = Unified Huntington's Disease Rating Scale-Total Functional Capacity

Manifest HD performed worse on all motor, cognitive, and neuropsychiatric assessments compared to controls, except for the smooth pursuit variable (Table 2). In addition, manifest HD had higher scores on the SDLP and drove slower in the driving simulator compared to controls (Table 2). There were no significant differences between premanifest HD and controls on the clinical assessments and driving simulator outcomes. Bivariate correlations, using Pearson *r*, were calculated between SDLP, mean speed, and clinical assessments. Correlations between these parameters were only calculated for the manifest HD group since we did not observe any differences between premanifest HD and controls. Thus, we were only interested in correlations between driving simulator outcomes and clinical assessments in the manifest HD group.

TABLE 2 Group comparisons on clinical measures and driving simulator

	Controls (*N*=29)	Premanifest HD (*N*=28)	Manifest HD (*N*=30)	Premanifest HD vs Controls	Manifest HD vs Controls
Motor function					
UHDRS-TMS[b]	1.8 ± 1.4	2.5 ± 1.3	22.1 ± 12.6	$p = 0.848$	**$p < 0.001$**
Finger tapping[a]	61.0 ± 8.5	62.7 ± 6.9	51.3 ± 12.3	$p = 0.812$	**$p < 0.001$**
Saccadic inaccuracy (%)[b]	5.4 ± 1.5	5.6 ± 2.3	7.4 ± 2.1	$p = 0.430$	**$p = 0.001$**
Smooth pursuit (%)[a]	39.7 ± 8.1	40.6 ± 9.6	37.7 ± 6.7	NS	NS
Body sway (mm)[a]	293.0 ± 133.9	310.8 ± 223.8	1013.3 ± 1411.3	$p = 0.933$	**$p = 0.002$**
Cognition					
SDMT[a]	56.2 ± 11.1	56.7 ± 10.8	40.9 ± 11.7	$p = 0.233$	**$p < 0.001$**
Stroop – color[a]	81.1 ± 13.8	80.6 ± 12.9	58.9 ± 15.2	$p = 0.501$	**$p < 0.001$**
Stroop – word[a]	106.6 ± 17.3	102.9 ± 14.3	75.0 ± 16.2	$p = 0.103$	**$p < 0.001$**
Stroop – interference[a]	48.5 ± 9.8	49.8 ± 10.6	37.0 ± 12.7	$p = 0.610$	**$p < 0.001$**
TMT – B[b]	42.2 ± 15.7	37.2 ± 12.0	78.7 ± 45.7	$p = 0.773$	**$p < 0.001$**
Adaptive Tracking[a]	28.8 ± 5.7	30.4 ± 5.4	20.3 ± 7.9	$p = 0.402$	**$p < 0.001$**
SART[b]	7.8 ± 4.9	8.6 ± 5.7	10.6 ± 5.3	$p = 0.673$	**$p = 0.014$**
Neuropsychiatry					
PBA-s (total score)[b]	4.9 ± 6.4	4.6 ± 5.0	15.9 ± 13.7	$p = 0.716$	**$p < 0.001$**
HADS-SIS (total score)[b]	11.3 ± 7.2	8.9 ± 5.8	16.4 ± 9.9	$p = 0.233$	**$p = 0.016$**
FrSBe (total score)[b]	75.2 ± 17.7	74.5 ± 12.4	97.8 ± 25.3	$p = 0.848$	**$p < 0.001$**
Driving simulator					
SDLP[b]	35.9 ± 7.3	32.1 ± 6.8	42.6 ± 17.9	$p = 0.238$	**$p = 0.041$**
Mean speed	99.2 ± 4.3	98.8 ± 2.7	96.3 ± 5.1	$p = 0.711$	**$p = 0.013$**
SD of mean speed[b]	4.5 (3.4 – 6.3)	3.7 (2.6 – 5.0)	4.7 (3.8 – 7.7)	NS	NS
Distance to preceding car	40.6 ± 7.4	44.0 ± 8.9	41.0 ± 10.5	NS	NS
Reaction Time[c]	-14.1 ± 11.1	-15.2 ± 10.9	-8.3 ± 12.3	NS	NS

Data are mean ± SD, except for SD of mean speed (median with IQR). Univariate ANCOVA with simple contrasts was used for motor, cognitive, and neuropsychiatric variables (controls as reference group). All these analyses were corrected for age. The analyses on neuropsychiatric assessments were also corrected for gender. Analyses on cognitive assessments were additionally corrected for years of education. ANOVA and Kruskal-Wallis test were performed for driving simulator outcome measures. Significant *p*-values ($p < 0.05$) are printed in bold. If no significant group effect was observed then this is indicated with NS.

FrSBe = Frontal Systems Behavior Scale; HADS-SIS = Hospital Anxiety and Depression Scale – Snaith Irritability Scale; NS = Not Significant; PBA-s = Problem Behavior Assessment short; SART = Sustained Attention to Response Task; SDLP = Standard Deviation of the Lateral Position; SDMT = Symbol Digit Modalities Test; TMT = Trail Making Test; UHDRS-TMS = Unified Huntington's Disease Rating Scale – Total Motor Score

[a] = higher scores represent better performances

[b] = higher scores represent worse performances

[c] = more negative values indicate earlier reaction to events

Significant correlations, in order of strength, were observed between the SDLP and body sway, finger tapping, UHDRS-TMS, adaptive tracker, Stroop interference, TMT-B, Stroop word, and Stroop color (Table 3). Scores on the SDMT and TMT-B were significantly correlated with mean speed (Table 3). Stepwise forward regression analyses, entering all significant correlations, showed that the body sway parameter was the only significant predictor for the SDLP, whereas the SDMT was the only significant predictor for mean speed. The prediction equation for the SDLP was: SDLP = 32.02 + (0.011061 * body sway (mm)). The prediction equation for mean speed was: Mean speed = 87.2 + (0.223093 * SDMT). Additional exploratory correlation analysis revealed a significant correlation in manifest HD between if the patient restricted him/herself in driving and the SDLP ($r = 0.52$, $p = 0.010$).

TABLE 3 Correlations between clinical assessments and driving simulator parameters in manifest HD

Task	SDLP	Mean Speed
UHDRS-TMS	0.57**	-0.02
Finger tapping	-0.58**	0.24
Saccadic inaccuracy	0.16	-0.26
Smooth pursuit	-0.20	-0.35
Body sway	0.64**	-0.11
SDMT	-0.38	0.52**
TMT – B	0.49*	-0.43*
Stroop – color	-0.44*	0.15
Stroop – word	-0.47*	0.16
Stroop – interference	-0.51*	0.17
SART	0.07	-0.05
Adaptive tracker	-0.55**	0.17
PBA-s – total score	0.04	-0.33
HADS-SIS – total score	0.06	-0.25
FrSBe – total score	0.05	-0.13

Pearson *r* with significant correlations printed in bold ** = $p < 0.01$; * = $p < 0.05$
FrSBe = Frontal Systems Behavior Scale; HADS-SIS = Hospital Anxiety Depression Scale – Snaith Irritability Scale; PBA-s = Problem Behavior Assessment short; SART = Sustained Attention to Response Test; SDMT = Symbol Digit Modalities Test; UHDRS-TMS = Unified Huntington's Disease Rating Scale Total Motor Score

DISCUSSION

The results of our study showed that manifest HD have less vehicle control compared to both controls and premanifest HD. Patients with HD also tended to drive slower compared to controls, indicating a certain level of cautiousness. Less vehicle control and slower driving speed can be considered errors on the operational and tactical level, which are the first two levels of the model by Michon (1989).[23] Our results are in line with previous findings showing that patients with HD commit most errors on these levels during on-road assessments.[9] This could indicate that patients with HD have difficulties with the operation of a car and adaptation to traffic situations. Adaptations on the third strategic level, such as no nighttime driving or no long-distance driving, can be managed before actual driving and might therefore be more difficult to detect with a simulator. Personal concerns and adaptations in driving behavior were, however, associated with decreased vehicle control.

We expected that manifest HD would have slower reaction times compared to controls and premanifest HD, since this was also reported in a previous simulator study.[5] In addition, slower speed of processing and inattention are one of the first cognitive deteriorations in HD.[24] In our study, manifest HD had the slowest reaction time to lane closures, but this was not significantly different from controls. This might be explained by the fact that patients with HD also drove slower compared to controls, which could indicate compensatory behavior and, therefore, they might have enough time to detect the lane closures. Another explanation could be that the reaction time to lane switching, as was used in our study, was not sensitive enough to detect possible slowing. More sudden and unexpected events are perhaps a more accurate measure of the reaction time and slower speed of processing.

Patients with HD performed worse on all clinical assessments compared to controls, except for smooth eye movements, which is in line with other studies reporting cognitive deterioration in manifest HD.[24,25] Previous studies have suggested that a cognitive evaluation is important in determining driving performance.[6,26] We observed that less vehicle control, measured with the SDLP, was highly correlated with almost all cognitive assessments. The amount of postural sway, was a predictor for the level of vehicle control and weaving of the car, indicating that specific motor disturbances such as balance and postural sway are associated with driving errors on the operational level. It is possible that, in case of HD, this assessment reflects the amount of truncal choreiform movements and not only balance or gait. This might also explain the association with the SDLP, since increased movement of the upper body could result in more swaying of the car. Previous studies only used the

total motor score of the UHDRS instead of specific motor evaluations, which could explain the discrepancy in results.[9] While the UHDRS-TMS was significantly correlated with vehicle control, it was not retained in the regression as a significant predictor. This result is in line with a previous finding where the TMS was also not predictive of driving performance.[9] Slower speed of processing, measured with the SDMT, was predictive of a slower driving speed in the driving simulator, suggesting that mental slowing also induces slower driving. Previous studies also included the SDMT, or a comparable task, in their prediction models which indicates that this test is a strong and robust predictor in multiple study designs.[6,27]

Worse performances on both the body sway test and SDMT could assist physicians in advising the patient about potential alterations in driving. The body sway test and SDMT can both be administered within five minutes, making these assessments relatively easy to use in the clinical practice. We feel that a clinical evaluation of driving ability should not only be based on the neurologists medical judgement, which is currently the national guideline in most European countries, but should also include a neuropsychological test battery.[28] HD is a heterogeneous disorder with deterioration on several domains and the onset of symptoms can vary per individual. Currently, there is no consensus on which neuropsychological assessments can predict driving ability in HD. We recommend to use clinical tests, such as the body sway and SDMT, as a first screening tool to determine the degree of deterioration due to HD. If the patient scores below a predefined cut-off score, then a formal driving assessment might be necessary. Some patients may already decide to quit driving by themselves when they acknowledge that the symptoms of HD are interfering with their functional capacity. Results on the screening battery could assist the treating clinicians in the discussion with the patient about potential driving cessation. At the moment, cut-off scores have not been determined, so it is important to establish these in future studies.

Neuropsychiatric behavior did not correlate with any of the driving simulator outcomes. In our study, only mild psychiatric disturbances were reported, so this might explain why we did not observe a significant correlation. However, it could also indicate that decreased driving performances already occur before the onset of severe psychiatric symptoms.

We did not observe any differences between premanifest HD and controls on the clinical and driving simulator assessments. This implies that alterations in driving performances are not yet present in this stage of HD and that they drive similar to healthy individuals when using the type of driving measures from our study. The distinction between HD stages is important in an attempt to examine when

alterations in driving first occur. It is known that cognitive symptoms can already be present years before the clinical motor diagnosis,[29] but it is still unclear when deteriorations in driving become overt. We are of the opinion that it is important to determine who is still able to drive safely instead of focusing on who is no longer fit to drive, since this might prolong the time a patient can be independent. A genetic confirmation of carrying the elongated CAG repeat alone should not be decisive for which individuals should cease driving. Clinical symptoms of the disease have to be present and individual evaluation is recommended. Our results showed that differences between HD patients and controls can be detected in a relatively easy and straightforward driving scenario. Using this type of motorway scenario has useful implications for future research, especially when investigating errors on the operational and tactical levels. Future studies are necessary to validate if the tests that emerged from our results are appropriate as a first screening tool and if they could be included in a clinical test battery. Although dropout due to simulator sickness occurred in our study, previous findings showed that symptoms of simulator sickness do not influence the outcome of simulator studies, and it are not necessarily the worst drivers who experience symptoms of sickness.[30,31] Another limitation of our study is that we cannot compare our findings to on-road evaluations, which is currently the gold standard. Still, our study revealed that increased postural sway and slower speed of processing are predictive of driving simulator performance in manifest HD. This highlights the importance of discussing driving and cognitive functioning for those treating patients with HD. Worse performances on clinical screening tasks might assist clinicians in their referral for an official on-road driving test.

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SUPPLEMENTARY TABLE 1 Missing data on all outcome measures

	Controls (*N*=29)	Premanifest HD (*N*=28)	Manifest HD (*N*=30)
Motor functioning			
UHDRS-TMS	0 (0%)	0 (0%)	0 (0%)
Finger tapping	1 (3%)	0 (0%)	0 (0%)
Saccadic inaccuracy (%)	1 (3%)	0 (0%)	4 (13%)
Smooth pursuit (%)	1 (3%)	0 (0%)	3 (10%)
Body sway	2 (7%)	0 (0%)	2 (7%)
Cognition			
SDMT	0 (0%)	0 (0%)	0 (0%)
Stroop – color	0 (0%)	0 (0%)	0 (0%)
Stroop – word	0 (0%)	0 (0%)	0 (0%)
Stroop – interference	0 (0%)	0 (0%)	0 (0%)
TMT – B	0 (0%)	0 (0%)	0 (0%)
Adaptive Tracker	1 (3%)	0 (0%)	2 (7%)
SART	1 (3%)	0 (0%)	1 (3%)
Neuropsychiatry			
PBA-s (total score)	0 (0%)	0 (0%)	0 (0%)
HADS-SIS (total score)	0 (0%)	1 (4%)	0 (0%)
FrSBe (total score)	0 (0%)	0 (0%)	0 (0%)
Driving simulator			
SDLP	1 (3%)	3 (11%)	5 (17%)
Mean speed (100 km/h)	1 (3%)	3 (11%)	5 (17%)
SD speed (100 km/h)	1 (3%)	3 (11%)	5 (17%)
Distance keeping	1 (3%)	3 (11%)	5 (17%)
Reaction time	6 (21%)	3 (11%)	11 (37%)

Reported are total number of missing data (%) per variable and per group

FrSBe = Frontal Systems Behavior Scale; HADS-SIS = Hospital Anxiety and Depression Scale – Snaith Irritability Scale; PBA = Problem Behavior Assessment short; SART = Sustained Attention to Response Task; SDLP = Standard Deviation of the Lateral Position; SDMT = Symbol Digit Modalities Test; TMT-B = Trail Making Test; UHDRS-TMS = Unified Huntington's Disease Rating Scale Total Motor Score

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