Impact of Huntington's disease on working and driving

Essink-Jacobs, M.

CAG CAG CAG CAG

CAG CAG CAG CAG CAG CAG

CAG CAG CAG CAG CAG CAG CAG CAG

CAG CAG CAG CAG CAG CAG CAG CAG CAG CAG

CAG CAG CAG CAG CAG CAG CAG CAG CAG CAG CAG CAG

CAG CAG

General discussion

The primary aim of this thesis was to study employment and driving ability in gene carriers with Huntington's disease (HD). We aimed to investigate predictors of work cessation and examine the influence of different symptoms and signs of HD on driving performance.

Employment and Huntington's disease

Work stress and employment changes are frequently mentioned by premanifest HD gene carriers when asked if they experience difficulties in daily life.[1] Most patients reduce their amount of work and this reduction is often perceived as a negative change as a result of disease.[2] However, contrary results have shown that it remains unclear whether HD gene carriers attribute these employment changes to signs of HD.[3]

Our findings showed that problems with concentration and multi-tasking, and slower reactions influenced the decision to stop working (**chapter 2**). Working in a physically demanding job might not be a reason to stop working prematurely, since half of the gene carriers who were no longer working had jobs with non-physical work demands (**chapter 3**). The first cognitive changes in HD are characterized by problems in executive functions including planning, organization, cognitive flexibility and attention, which might be more crucial in nonphysical occupations that require higher levels of cognition. Further, we found that worse cognitive functioning, in particular slower speed of processing and cognitive inflexibility, and apathy are predictors of work cessation in HD gene carriers (**chapter 3**). Thus, cognitive and behavioral changes interfere more with the ability to work than the characteristic motor signs of HD. HD gene carriers retired more than a decade before the general retirement age, confirming that work cessation occurs during mid-adulthood and that signs of HD are associated with stopping work (**chapter 2** and **chapter 3**). This is similar in patients with Parkinson's disease, who generally also retire before the official retirement age because of the impact of the disease on their ability to work.[4] However, the number of studies focusing on work and HD is still very limited. No longer being able to work can result in psychological distress. In order to adjust to a new lifestyle, patients must develop active coping strategies. More than 50% of the HD gene carriers expressed concerns about genetic discrimination in the workplace.[5] Better mental health has been associated with less work-related disability in premanifest HD.[6] Counseling about possible career choices and evaluating the concerns of patients and families in the presymptomatic phase of the disease is, therefore, recommended. Patients in disease stages 1 and 2 experience the most changes in their health due to the progression of HD symptoms and show an increasing dependency on others in

activities of daily life.[7] This group also reports that they experience a discrepancy between the care they need and the care they actually receive. Patients in disease stages 1 and 2 should be the main focus of psychoeducation, as well as gene carriers who do not yet experience any symptoms. Patients report that it can be frustrating that healthcare professionals lack knowledge about HD.[8] Specialized and educated professionals are needed in the care system for HD patients.

Driving and Huntington's disease

It is presumed that the decision to stop driving is a dynamic stepwise process rather than an overnight decision.[9] This process starts with increasing self-imposed driving restrictions, eventually resulting in complete cessation of driving. The fact that presymptomatic HD gene carriers reported that they adapt their driving behavior, for example with less nighttime driving, no motorway driving, and driving shorter distances, further supports this suggestion **(chapter 5)**. In addition, it confirms that the capability to drive a car is a topic of interest and concern in gene carriers with HD. This emphasizes the need to start the discussion about driving in the early stages of HD and reexamine it regularly. The possibility of stopping driving should be included as a discussion topic in the clinic, because the inability to drive a car affects the independence and quality of life of patients. Healthcare professionals and driver's licensing authorities have the obligation to inform patients about the process of driving cessation, the risks of continuing driving, and must provide proper guidance. HD gene carriers who stopped driving were significantly older and more often female compared to active drivers **(chapter 2)**. In general, women also tend to stop driving at a younger age compared to men, so this finding seems to be unrelated to HD.[10] However, men and women differed in their primary reasons for stopping driving **(chapter 2)**. Most males stated difficulties concentrating as their reason for stopping driving, whereas females reported feelings of anxiety as their primary reason. It is well known that patients with HD can have limited insight into their own functional decline.[11,12] However, in our study, patients and spouses gave the driving performance of HD patients similar grades, suggesting a certain level of awareness in these HD patients **(chapter 5)**. Spousal opinions often provide a more objective point of view, although they might give socially accepted answers because they rely on the patient being able to drive, or want to avoid an argument.[13,14] Children of an affected parent might provide the most accurate and reliable answers about whether driving is still safe.[15] To our knowledge, our study was the first to investigate the hypothesis that changes in driving performance already start in the early presymptomatic phase of HD. We found that the way presymptomatic gene carries drove was comparable

to that of controls, while the performance of symptomatic gene carriers was worse **(chapter 5)**. These results suggest that a genetic confirmation of HD should not be decisive for the recommendation to stop driving, but that individual symptoms have to be evaluated. In our opinion, the goal should be to let HD gene carriers drive for as long as this is still safe and not advise revoking the driver's license based on genetic confirmation alone.

Predicting driving performance

The findings of our study confirm that deteriorated cognition influences driving performance more than motor dysfunction **(chapter 6)**. Especially slower speed of information processing and postural sway and instability are associated with alterations in driving. The SDMT and Body Sway tests emerged as significant predictors of driving performance in our study **(chapter 6)**. These are both relatively short tests that can easily be administered with a low burden for the patient. In previous studies, the SDMT has been identified as a sensitive biomarker to detect early cognitive deterioration, and decreased psychomotor speed is one of the earliest cognitive changes observed in patients with HD.[16–18] The fact that the SDMT was also a suitable predictor of driving competence in previous studies suggests that this test is a robust predictor of changes in driving and we would recommend including it in a screening assessment **(chapter 4)**. Neuropsychological screening batteries could provide a better estimation of who should be referred for an official on-road driving test than a medical examination alone. Since HD is a heterogeneous disorder, where cognitive impairments can be more debilitating compared to the characteristic motor signs, a multidisciplinary approach seems mandatory when assessing driving ability. Specialists from disciplines other than neurology, such as psychologists or occupational therapists, should be involved in the evaluation of fitness to drive. Cognitive tests should, therefore, be embedded in the standard clinical driving evaluation. Using guidelines that have been proposed for other neurodegenerative disorders, such as Alzheimer's (AD) and Parkinson's disease (PD), seems unwarranted. Prediction models established for AD cannot necessarily be used in HD due to the different etiology and clinical expression,[19] emphasizing the need for specialized consensus guidelines limited to HD. Multiple neuropsychological tests have been proposed to predict driving errors, but there is currently no validated standardized battery that can be used.[20,21] To embed cognitive tests in the clinic, cut-off scores are necessary and these are currently still lacking. The use of one single test is not recommended and composite test batteries have been suggested to better discriminate between safe and unsafe drivers.[22] We propose at

least including the SDMT in the yet to be developed HD specific clinical screening battery.

In contrast to cognitive impairment, psychiatric behavior was unrelated to driving performances (chapter 6). It is possible that psychiatric symptoms are more manageable with medication and, therefore, have less influence on driving skills. Furthermore, depressed mood, apathy, and anxiety might result in the patient deciding to stop driving voluntarily. Thus, psychiatric symptoms could influence driving behavior, but probably at a different level than the actual driving performance. In patients with PD, higher levels of anxiety were associated with their decision to stop driving.[23] Anxiety and feelings of insecurity were also among the primary reasons reported by HD gene carriers (chapter 2). Being overcautious may be a compensation for anxiousness, which could explain the fact that patients with HD tend to drive more slowly and below the speed limit compared to controls (chapter 5). The total motor score of the Unified Huntington's Disease Rating Scale did not contribute to the prediction of driving skills, while this score is the most frequently used rating scale in HD, as well as the primary outcome measure in most clinical trials (chapter 6). Previous findings also showed that motor functioning, measured with this scale, was not predictive of driving performance.[20] For the clinical screening of driving fitness, the total motor score would be insufficient.

Driving simulator

We chose to use a driving simulator in our study, because it provides the opportunity to test driving skills in a standardized and reproducible environment. In addition, it is safer to test certain conditions with a simulator rather than putting the participants in potentially hazardous and uncontrollable situations on the road. Although on-road evaluations are the gold standard and reflect real world circumstances, they lack generalizability and the challenges differ from individual to individual. In addition, there is variability in routes and vehicles.[24,25] A validation study in HD showed that simulators have a good concurrent validity when compared to on-road tests, especially for the measurement of operational driving skills, such as vehicle control.[26] At the moment, in our opinion, it is not sufficient to use only a driving simulator when a definite decision about driving cessation has to be made, but it can complement the clinical evaluation of driving competence. In the Netherlands, novice drivers are trained with a driving simulator before their first on-road experience. Better test results in the simulator have been related to higher chances of passing the driving test the first time.[27] The results of one study indicated that simulator training is potentially useful in drivers with PD, showing improved scores on an on-road test

after simulator training.[28] In addition, PD patients who failed the on-road driving test before the training, passed the test post-training.[29] Thus, in the future, it might be effective to use a driving simulator as a training tool in HD. Since our study revealed that patients with HD have most difficulties operating a car and with adapting to certain road situations (chapter 5), training these driving skills could potentially increase the on-road driving capabilities.

A disadvantage of using simulators is the occurrence of simulator sickness, which is comparable to the symptoms of motion sickness. Although our findings illustrated that patients with HD were not more susceptible to developing symptoms of simulator sickness than controls, the occurrence of this phenomenon limits the usage of a driving simulator (chapter 7). Female gender and older age were associated with increased simulator sickness, whereas cognitive and motor functioning were unrelated to dropout due to simulator sickness. Symptoms of simulator sickness mostly occurred during the urban driving scenario, which is characterized by sharper turns and more sudden stops (chapter 7). However, we are of the opinion that these types of scenarios should be further optimized to properly test situations that require a high mental workload. Reducing the duration of the simulator assessments or taking more breaks in between sessions could alleviate the symptoms of simulator sickness.[30]

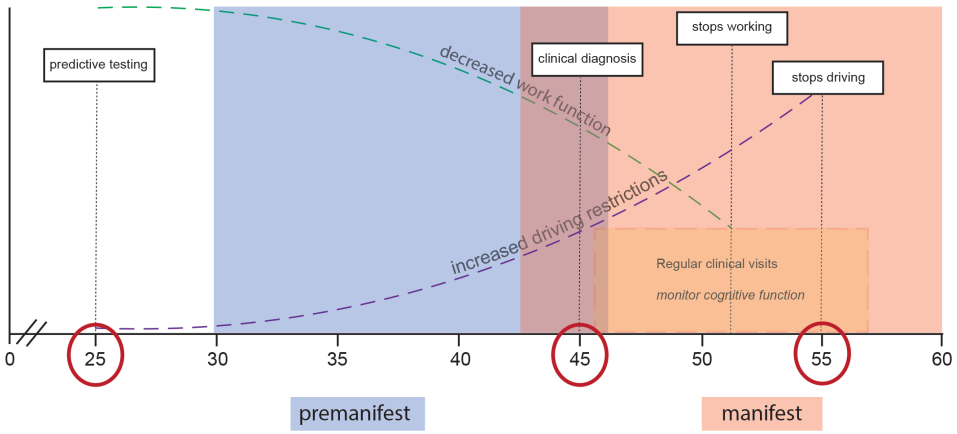
Recommendations and future perspectives

More studies are necessary to validate our findings and compare the simulator results with on-road assessments. Because of the progressive nature of HD, longitudinal studies should be performed to establish a reasonable follow-up period for retesting driving ability. The current lack of cut-off scores for cognitive tests has to be tackled. Investigating driving in a naturalistic driving setting, using a dashcam, could provide an opportunity to examine driving behavior during multiple occasions and in the patient's own car.[24]

Since there is currently no cure for HD, the focus of treatment is on improving quality of life and providing the necessary support to patients and families. Maintaining independence through employment and driving, for as long and as safely as possible, has a substantial influence on a patient's own general functioning and their family. Because the symptomatic onset of HD mostly occurs during midlife, the disease can affect various activities of daily life, such as work, driving, and social relationships, at a relatively young age. Based on the main findings of this thesis, a proposed schematic timeline for when, during the course of HD, to discuss working and driving in the clinic, is shown in Figure 1. During the earliest phase of HD,

shortly after predictive testing, gene carriers should be informed about how the signs of HD can affect the capability to work and drive a car. This could be done via a brochure that describes the possible issues that patients with HD may be confronted with in daily life as the disease progresses. When the clinical diagnosis is established, physicians (e.g., neurologists) and other healthcare professionals, such as psychologists and occupational therapists, should again inform the patient and their spouses about the influence of HD on employment and driving ability. Psychoeducation will increase the awareness about what changes might occur in work and driving, how these relate to signs of HD, and the safety of themselves and others. Regarding work adjustments, lowering the work demands or reducing the number of hours might be a first solution. Discussing alternative options of transportation is important to help patients adjust to the loss of independence when they decide to stop driving. In general, during the earliest manifest stages, driving performance will not yet be altered and patients might be able to compensate for changes in driving by increasing the number of restrictions or adapting their car. For example, they can decide not to drive during rush hour, not to drive during nighttime, or to change to a car with automated transmission. For patients who visit the outpatient clinic, annual monitoring of cognitive decline is recommended. At the moment, a longitudinal, international, observational study is collecting data on demographics, motor, cognitive, and neuropsychiatric signs to improve the understanding and monitor the progression of HD (Enroll-HD).[31,32] The neuropsychological test battery included in this study has the potential to be used as a screening tool to monitor changes in cognition related to work and driving. If cognitive function further deteriorates, patients should be advised to stop driving voluntarily, for their own safety and that of others. Voluntarily deciding to stop driving gives a feeling of autonomy, contrary to a forced revocation of a driver's license when a formal driving test is performed.

FIGURE 1



Hypothetical schematic timeline for the discussion of working and driving in the clinic. The influence of Huntington's disease on employment and driving should be discussed regularly, starting at an early stage, shortly after predictive testing, again after the clinical diagnosis has been given and during follow-up visits. Cognitive function should be monitored with a standardized assessment battery. Specialists from multiple disciplines, such as neurologists, psychologists and/or occupational therapists, should be included in the examination of fitness to work and drive.

CONCLUSIONS

This thesis addresses the topics working and driving ability as being relevant in HD. Our results consistently showed that the cognitive and behavioral changes in HD are more debilitating in daily life than the characteristic motor signs. Healthcare professionals should be educated about the different stages of HD, to allow them to provide appropriate information to patients and families when discussing possible changes in work and driving as a result of the disease. The driving performance of presymptomatic HD gene carriers and controls was comparable, suggesting that individual evaluation is warranted and that the decision to stop driving should not solely be based on disease stage or a genetic confirmation. Multidisciplinary screening, using a HD-specific test battery, is recommended and should be embedded in the clinic.

REFERENCES

1. Downing N, Smith MM, Beglinger LJ, et al. Perceived stress in prodromal Huntington disease. *Psychology and Health*. 2012;27(2):196-209.
2. McCabe MP, Roberts C, Firth L. Work and recreational changes among people with neurological illness and their caregivers. *Disability and Rehabilitation*. 2008;30(8):600-610.
3. Downing NR, Williams JK, Paulsen JS. Couples' attributions for work function changes in prodromal Huntington disease. *Journal of Genetic Counseling*. 2010;19:343-352.
4. Koerts J, König M, Tucha L, Tucha O. Working capacity of patients with Parkinson's disease - A systematic review. *Parkinsonism and Related Disorders*. 2016;27:9-24.
5. Bombard Y, Palin J, Friedman JM, et al. Beyond the patient: The broader impact of genetic discrimination among individuals at risk of Huntington disease. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2012;159:217-226.
6. Goh AMY, You E, Perin S, et al. Predictors of Workplace Disability in a Premanifest Huntington's Disease Cohort. *The Journal of Neuropsychiatry and Clinical Neurosciences*. 2018;30:115-121.
7. van Walsem MR, Howe EI, Ruud GA, Frich JC, Andelic N. Health-related quality of life and unmet healthcare needs in Huntington's disease. *Health and Quality of Life Outcomes*. 2017;15(6):1-10.
8. Etchegary H. Healthcare experiences of families affected by Huntington disease: Need for improved care. *Chronic Illness*. 2011;7(3):225-238.
9. Kowalski K, Love J, Tuokko H, MacDonald S, Hultsch D, Strauss E. The influence of cognitive impairment with no dementia on driving restriction and cessation in older adults. *Accident Analysis and Prevention*. 2012;49:308-315.
10. Siren A, Hakamies-Blomqvist L, Lindeman M. Driving Cessation and Health in Older Women. *Journal of Applied Gerontology*. 2004;23(1):58-69.
11. Hoth KF, Paulsen JS, Moser DJ, Tranel D, Clark LA, Bechara A. Patients with Huntington's disease have impaired awareness of cognitive, emotional, and functional abilities. *Journal of Clinical and Experimental Neuropsychology*. 2007;29(4):365-376.
12. Sitek EJ, Thompson JC, Craufurd D, Snowden JS. Unawareness of deficits in Huntington's disease. *Journal of Huntington's Disease*. 2014;3:125-135.
13. Brown LB, Ott BR, Papandonatos GD, Sui Y, Ready RE, Morris JC. Prediction of On-Road Driving Performance in Patients with Early Alzheimer's Disease. *Journal of American Geriatric Society*. 2005;53:94-98.
14. Meuser TM, Carr DB, Unger EA, Ulfarsson GF. Family reports of medically impaired drivers in Missouri: Cognitive concerns and licensing outcomes. *Accident Analysis and Prevention*. 2015;74:17-23.
15. Bixby K, Davis JD, Ott BR. Comparing caregiver and clinician predictions of fitness to drive in people with Alzheimer's disease. *American Journal of Occupational Therapy*. 2015;69:1-7.
16. Lemiere J, Decruyenaere M, Evers-Kiebooms G, Vandenbussche E, Dom R. Cognitive changes in patients with Huntington's disease (HD) and asymptomatic carriers of the HD mutation--a longitudinal follow-up study. *Journal of Neurology*. 2004;251(8):935-942.
17. Stout JC, Paulsen JS, Queller S, et al. Neurocognitive signs in prodromal Huntington disease. *Neuropsychology*. 2011;25(1):1-14.
18. Stout J, Jones R, Labuschagne I, et al. Evaluation of longitudinal 12 and 24 month cognitive outcomes in premanifest and early Huntington's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*. 2012;83:687-694.

19. Piersma D, de Waard D, Davidse R, Tucha O, Brouwer W. Car drivers with dementia: different complications due to different aetiologies? *Traffic Injury Prevention*. 2016;17(1):9-23.
20. Devos H, Nieuwboer A, Tant M, de Weerdt W, Vandenberghe W. Determinants of fitness to drive in Huntington disease. *Neurology*. 2012;79:1975-1982.
21. Hennig BL, Kaplan RF, Nowicki AE, Barclay JE, Gertsberg AG. We can predict when driving is no longer safe for people who have HD using standard neuropsychological measures. *Journal of Huntington's Disease*. 2014;3:351-353.
22. Bennett JM, Chekaluk E, Batchelor J. Cognitive Tests and Determining Fitness to Drive in Dementia: A Systematic Review. *Journal of the American Geriatrics Society*. 2016:1-14.
23. Turner LM, Liddle J, Pachana NA. Parkinson's Disease and Driving Cessation: a journey influenced by anxiety. *Clinical Gerontologist*. 2017;40(3):220-229.
24. Ott B, Papandonatos G, Davis J, Barco P. Naturalistic validation of an on-road driving test of older drivers. *Human Factors*. 2012;54(4):663-674.
25. Davis JD, Papandonatos GD, Miller LA, et al. Road test and naturalistic driving performance in healthy and cognitively impaired older adults: Does environment matter? *Journal of the American Geriatrics Society*. 2012;60(11):2056-2062.
26. Devos H, Nieuwboer A, Vandenberghe W, Tant M, de Weerdt W, Uc E. Validation of driving simulation to assess on-road performance in Huntington disease. In: *Proceedings of the Seventh International Driving Symposium on Human Factors in Driver Assessment, Training, and Vehicle Design*. ; 2013:241-247.
27. de Winter JCF, de Groot S, Mulder M, Wieringa PA, Dankelman J, Mulder JA. Relationships between driving simulator performance and driving test results. *Ergonomics*. 2009;52(2):137-153.
28. Uc E, Rizzo M, Anderson S, Lawrence J, Dawson J. Driver rehabilitation in Parkinson's disease using a driving simulator: a pilot study. In: *Proceedings of International Driving Symposium Human Factors Driver Assessment, Training, and Vehicle Design*. ; 2011:248-254.
29. Devos H, Morgan JC, Onyeamaechi A, et al. Use of a driving simulator to improve on-road driving performance and cognition in persons with Parkinson's disease: a pilot study. *Australian Occupational Therapy Journal*. 2016;63:408-414.
30. Domeyer JE, Cassavaugh ND, Backs RW. The use of adaptation to reduce simulator sickness in driving assessment and research. *Accident Analysis and Prevention*. 2013;53:127-132.
31. The Enroll-HD Study Group. Enroll-HD: A Prospective Registry Study in a Global Huntington's Disease Cohort. A CHDI Foundation Project. Enroll-HD Study Protocol, Version 1.0 2011-September-09.; 2011. https://www.enroll-hd.org/.
32. Landwehrmeyer GB, Fitzer-Attas CJ, Giuliano JD, et al. Data analytics from Enroll-HD, a global clinical research platform for Huntington's disease. *Movement Disorders: Clinical Practice*. 2016:212-224.

8