Comparison of Huntington's disease in Europe and North America

Michael Orth[1], Juliana Bronzova[1], Christine Tritsch[1], E. Ray Dorsey[2], Joaquim J. Ferreira[3], Armin Gemperli[4], and the EHDN REGISTRY and HSG COHORT Investigators

[1]Department of Neurology, Ulm University Hospital, Ulm, Germany
[2]Department of Neurology, University of Rochester Medical Center, Rochester, NY
[3]Clinical Pharmacology Unit, Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon, Portugal
[4]Department of Health Sciences and Health Policy, University of Lucerne, Lucerne, Switzerland, and Swiss Paraplegic Research Nottwil, Nottwil, Switzerland

EUROPEAN HUNTINGTON'S DISEASE NETWORK
Advancing Research, Conducting Trials, Improving Care

Background

In a rare disorder such as Huntington's disease (HD) a global network of clinical trial sites with access to patients speeds up recruitment into clinical trials. We tested the hypothesis that demographics, *HTT* genotype, clinical spectrum and progression are similar in HD participants of two large observational HD studies, the European Huntington's Disease Network's European REGISTRY study and the North American COHORT study.

Methods

- Cross-sectional data **REGISTRY**: 7,398 participants (1,125 (15.2%) premanifest, 6,273 (84.8%) manifest HD). **COHORT:** 1,499 participants (175 pre-HD (11.7%), 1,324 manifest HD (88.3%)).
- Longitudinal data was available for total motor score or cognitive performance in more than 50% of REGISTRY participants and more than 70% of COHORT participants.
- Participants were assessed clinically using the Unified Huntington's Disease Rating Scale (UHDRS).
- Statistics: Outcomes were compared between COHORT and REGISTRY via difference with confidence intervals constructed using large-sample statistics based on the t-distribution for means and relative frequencies. The association between the dichotomous education level and study was verified using Fisher's exact test. Linear regression analyses were performed to ascertain associations.

Results

Cross-sectional data

- Demographics, *HTT* genotypes, phenotype and progression, were similar in the two studies (Figure 1).
- REGISTRY had a larger proportion of late stage HD participants than COHORT (UHDRS TFC stages 4 and 5) and a smaller proportion of stage 2 participants. In all stages the proportion of participants with higher education was higher in COHORT than in REGISTRY.
- Differences in cognitive performance between REGISTRY and COHORT were due to disease stage and education differences but not to language

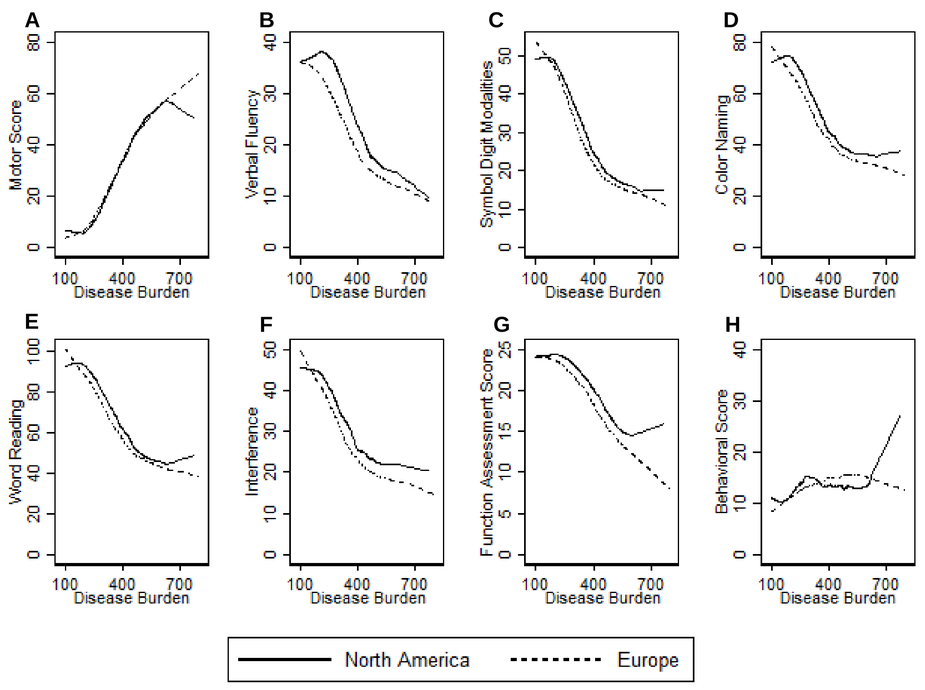

Figure 1: Association of disease burden score and phenotype ratings in COHORT and REGISTRY. A. UHDRS motor score. B-F. UHDRS cognitive scores. G. UHDRS function assessment score. H. UHDRS behavioural score.

Disease progression

- The most robust annualised change was evident for UHDRS total motor score (TMS) and word reading while change in other cognitive test scores was small (adjusted for disease burden scores at baseline; Table 1).
- Progression was similar between studies for TMS and cognitive scores (Table 1). Similar to cross-sectional data, COHORT participants had higher cognitive scores than REGISTRY participants throughout the study.

	COHORT	REGISTRY	Difference
UHDRS motor score	3.10 (2.59, 3.60)	2.64 (2.46, 2.82)	0.46 (-0.16, 1.08)
Symbol Digit Modalities	-0.59 (-0.96, -0.22)	-0.40 (-0.57, -0.24)	-0.19 (-0.64, 0.25)
Verbal Fluency	0.06 (-0.35, 0.47)	0.01 (-0.17, 0.19)	0.05 (-0.38, 0.48)
Color Naming	-1.02 (-1.55, -0.50)	-0.87 (-1.09, -0.65)	-0.16 (-0.76, 0.44)
Word Reading	-1.86 (-2.52, -1.21)	-1.48 (-1.76, -1.19)	-0.39 (-1.15, 0.37)
Interference	-0.73 (-1.12, -0.35)	-0.35 (-0.51, -0.19)	-0.39 (-0.82, 0.04)

Table 1: Change in clinical scores per year of study participation

Medication

- Patients in Europe were prescribed anti-dyskinetics more frequently, and anti-depressants less frequently, than in North America (Table 2).

	Premanifest			Manifest		
	COHORT	REGISTRY	P-Value	COHORT	REGISTRY	P-Value
	N=175	N=1,125		N=1,324	N=6,273	
Medication class	n (%)	n (%)		n (%)	n (%)	
Anti-dyskinetic	2 (1.1)	8 (0.7)	0.543	119 (9.0)	1,344 (21.8)	<0.001
Anti-depressant	77 (44.0)	169 (15.0)	<0.001	989 (74.7)	2,824 (45.8)	<0.001
Anti-dementia	10 (5.7)	9 (0.8)	<0.001	145 (11.0)	145 (2.4)	<0.001
Nutritional suppl.	69 (39.4)	63 (5.6)	<0.001	490 (37.0)	385 (6.2)	<0.001
Other	65 (37.1)	897 (79.7)	<0.001	231 (17.4)	2,622 (42.5)	<0.001

Table 3: Medication class by study. P-values were derived using large-sample statistics based on the t-distribution.

- In either study, participants on anti-dyskinetic medication had higher UHDRS total motor scores, worse function assessment scores and worse cognitive scores than those taking anti-depressants or no medication. In contrast, motor, function assessment and cognitive scores were broadly similar in participants taking anti-depressants or no medication.
- The differences in cognitive performances between languages were small.

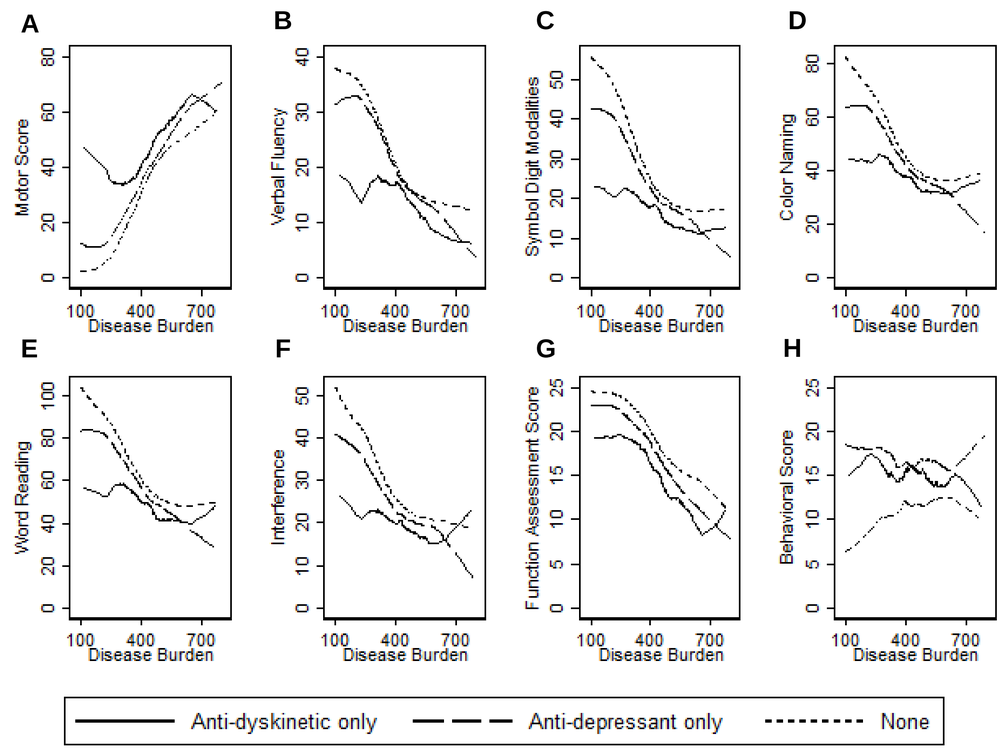

Figure 2: Medication and the association of disease burden score and phenotype ratings in COHORT and REGISTRY. A. UHDRS motor score. B-F. UHDRS cognitive scores. G. UHDRS function assessment score. H. UHDRS behavioural score. Solid lines: Anti-dyskinetics alone. Dashed lines: Anti-depressants alone. Dotted lines: no anti-dyskinetics or anti-depressants.

Conclusions

Our data suggest that HD patients, and the way they are assessed, are similar across two continents with different cultures and languages.

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