Chou Kelvin (Orcid ID: 0000-0002-2597-7315)

Word Count: 1680

How different aspects of motor dysfunction influence day-to-day function in Huntington disease

Noelle E. Carlozzi, PhD,[1] Stephen G., Schilling, PhD,[1,2] Nicholas R Boileau, MPH,[1]

Kelvin L. Chou., MD,[3] Joel S. Perlmutter, MD,[4] Samuel Frank, MD,[5]

Michael K. McCormack, PhD,[6] Julie C. Stout, PhD,[7] Jane S. Paulsen, PhD,[8]

Jin-Shei Lai, PhD,[9] and Praveen Dayalu, MD[3]

Running Title:
Motor Symptoms and Day-to-Day Functioning in HD

[1] Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA
[2] Institute for Social Research, University of Michigan, Ann Arbor, MI, USA
[3] Department of Neurology, University of Michigan, Ann Arbor, MI, USA
[4] Departments of Neurology, Radiology, Neuroscience, Physical Therapy and Occupational Therapy, Washington University in St. Louis, St. Louis, MO, USA
[5] Beth Israel Deaconess Medical Center, Boston, MA, USA
[6] Department of Psychiatry, Rutgers-Robert Wood Johnson Medical School, Piscataway, NJ, USA and Department of Pathology, Rowan-SOM, Stratford, NJ, USA
[7] School of Psychological Sciences, Monash University, Clayton, Victoria, Australia
[8] Departments of Psychiatry, Neurology, and Psychological and Brain Sciences, The University of Iowa, Iowa City, IA, USA
[9] Department of Medical Social Sciences, Northwestern University, Chicago, IL, USA

Address reprint requests to:
Noelle E. Carlozzi, Ph.D.
University of Michigan
Department of Physical Medicine & Rehabilitation
North Campus Research Complex
2800 Plymouth Road
Building NCRC B14, Room G216
Ann Arbor, MI 48109-2800

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/mds.27866

Phone: (734) 763 – 8917
Fax: (734) 763-7186
Email: carlozzi@med.umich.edu

Acknowledgments: This work was supported by the National Institutes of Health (NIH), National Institute of Neurological Disorders and Stroke (R01NS077946) and the National Center for Advancing Translational Sciences (UL1TR000433). In addition, a portion of this study sample was collected in conjunction with the Predict-HD study. The Predict-HD was supported by the NIH, National Institute of Neurological Disorders and Stroke (R01NS040068), the NIH, Center for Inherited Disease Research (provided supported for sample phenotyping), and the CHDI Foundation (award to the University of Iowa). We thank the University of Iowa, the Investigators and Coordinators of this study, the study participants, the National Research Roster for Huntington Disease Patients and Families, the Huntington Study Group, and the Huntington's Disease Society of America. We acknowledge the assistance of Jeffrey D. Long, Hans J. Johnson, Jeremy H. Bockholt, Roland Zschiegner, and Jane S. Paulsen. We also acknowledge Roger Albin, Kelvin Chou, and Henry Paulsen for the assistance with participant recruitment. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

HDQLIFE Site Investigators and Coordinators: Noelle Carlozzi, Praveen Dayalu, Stephen Schilling, Amy Austin, Matthew Canter, Siera Goodnight, Jennifer Miner, Nicholas Migliore (University of Michigan, Ann Arbor, MI); Jane Paulsen, Nancy Downing, Isabella DeSoriano, Courtney Shadrick, Amanda Miller (University of Iowa, Iowa City, IA); Kimberly Quaid, Melissa Wesson (Indiana University, Indianapolis, IN); Christopher Ross, Gregory Churchill, Mary Jane Ong (Johns Hopkins University, Baltimore, MD); Susan Perlman, Brian Clemente, Aaron Fisher, Gloria, Obialisi, Michael Rosco (University of California Los Angeles, Los Angeles, CA); Michael McCormack, Humberto Marin, Allison Dicke (Rutgers University, Piscataway, NJ); Joel S Perlmutter, Stacey Barton, Shineeka Smith (Washington University in St. Louis, St. Louis, MO); Martha Nance, Pat Ede (Struthers Parkinson's Center); Stephen Rao, Anwar Ahmed, Michael Lengen, Lyla Mourany, Christine Reece, (Cleveland Clinic Foundation, Cleveland, OH); Michael Geschwind, Joseph Winer (University of California – San Francisco, San Francisco, CA), David Cella, Richard Gershon, Elizabeth Hahn, Jin-Shei Lai (Northwestern University, Chicago, IL).

Abstract

Purpose: This study examined the relationships between different aspects of motor dysfunction (chorea, dystonia, rigidity, incoordination, oculomotor dysfunction, dysarthria, and gait difficulties) and functional status in persons with Huntington disease (HD).

Methods: 527 persons with HD completed the UHDRS Motor, Total Functional Capacity and Functional Assessment.

Results: Confirmatory factor analysis indicated that a 4-factor model provided a better model fit than the existing 5-factor model. Exploratory factor analysis identified 4 factors from the motor scale: Dystonia, Chorea, Rigidity, and a General Motor Factor. Regression indicated that dystonia (β's=-0.47 and -0.79) and rigidity (β's=-0.28 and -0.59) had strong associations with function, whereas chorea had modest correlations (β's=-0.16 and -0.15).

Conclusions: Dystonia and rigidity have stronger relationships with functional status than chorea in persons with HD. Findings underscore the need for further research regarding the effects of dystonia and rigidity on functioning.

Key Words: Health-related quality of life; HDQLIFE; Huntington disease; chorea; dystonia; motor function

Huntington disease (HD) is an autosomal dominant neurodegenerative disease characterized by progressive motor, behavioral, and cognitive decline.[1] Motor dysfunction is multifaceted, involves all body regions, and profoundly affects day-to-day function. Most studies and interventions focus on chorea,[2, 3] which can appear as fidgety, jerky, or dance-like movements. Chorea and dystonia are the only motor symptoms known to respond to pharmacotherapy.[4-6] By mid- to late-stage HD, motor problems steadily worsen[1, 7] even if chorea remains controlled.[8] Motor dysfunction is a major driver of functional loss in HD.[7, 9, 10]

The UHDRS Motor Scale is one of the most commonly used assessments in HD. While the motor scale includes clinician ratings of eye movements, chorea, dystonia, rigidity, speech, gait, postural stability, and bradykinesia, prior research suggests that the motor scale could be consolidated and further improved.[11, 12] The present study builds on this research by examining UHDRS motor and function ratings in a large sample of people with HD. The goal was twofold: 1) to repeat a factor analysis on the UHDRS motor scale, comparing it with the 5 factors identified previously,[11] and 2) to determine which motor factors best relate to functional status in HD.

Methods

Participants. Five-hundred-twenty-seven individuals with premanifest or manifest HD were included in this analysis. Participants were at least 18 years of age, able to read and comprehend English, and capable of providing informed consent. Participants were recruited

from eight HD treatment centers and through the Predict-HD study.[13] Electronic medical records,[14] the National Research Roster for HD, and community outreach were utilized to bolster recruitment efforts.

Measures.

The UHDRS motor scale is a 15-item clinician rating scale.[15] Total scores (TMS) range from 0 (no motor difficulties) to 124 (greater motor difficulties). Participants with a diagnostic confidence level on this scale of 4 (≥99% confidence of unequivocal motor signs) were classified as manifest HD.

The UHDRS Total Functional Capacity (TFC) [16] is a 5-item clinician rating of day-to-day functional status. TFC scores were used to examine functional status and to classify manifest HD participants as either early-stage (sum scores of 7-13) or later-stage (sum scores of 0-6).

The UHDRS Functional Assessment (FA) includes 25-items for common tasks related to occupation, finances, average daily living, domestic chores, and care level. Clinician-rated scores range from 0-25 (higher scores indicate better function; *Note.* FA scores were missing for the n=170 Predict-HD participants that were enrolled in this study given established ceiling effects in premanifest HD).

The Stroop Color Word Interference Test [17] provides measures of psychomotor speed and executive function; higher scores reflect better performance. We examined raw scores on the two processing speed components (Color raw score plus Word Naming raw score).

Statistical Analyses. Confirmatory factor analysis (CFA) was used to determine whether we could replicate the published 5-factor structure.[11] Good fit was defined as: 1) comparative fit index (CFI)>0.90, 2) root mean square error of approximation (RMSEA)<0.1,[18-21] and 3) residual correlations <.15.[22-24] This was followed by an exploratory factor analysis (EFA) with a PROMAX rotation. Eigenvalues >1 and the number of factors before the break in the scree plot helped identify discrete factors. Item loadings (criterion >0.4) established which items belonged to which factor. In cases with substantial cross-loadings, the item with the highest loading was retained. Given that the existing 5-factor model was based solely on a sample of manifest HD participants,[11] CFA was conducted using only manifest HD participants in this sample; EFA was conducted using the combined sample. These analyses were conducted using MPLUS 6.11.[25]

Linear regression (using SAS 9.4) was used to examine the relationship of the identified factors (through the procedure described above) and functional outcomes (TFC and FA). Eight sets of simple linear regression models were conducted; each of the four factors that were identified as part of the previous analysis were regressed on both outcomes of interest (TFC and FA). Two separate multiple linear regression models were conducted that included multiple predictors (the discrete factors identified in the previous analysis) and the criterion measure (TFC or FA). All

simple linear regression and multiple regression models were conducted twice: once without covariates, then again with Stroop added as a covariate.

Results

Table 1 provides descriptive data for the sample.

The initial CFA (in manifest HD participants) did not support the existing 5-factor model (CFI=0.93; TLI=0.93; RMSEA=0.14). The follow-up EFA (using the full sample) supported a four factor model (Table 2). CFA (using the full sample) on this new 4-factor model indicated a small improvement in model fit (CFI=0.94; TLI=0.94; RMSEA=0.13). Akaike Information Criterion (AIC) provided additional support for the four factor model over the five factor model (AIC=12,945.58 in 5-factor model verses AIC=12,769.22 in the 4-factor model) with regard to manifest participants. Factor 1 included the 7 chorea items (i.e., Chorea); Factor 2 included the 5 dystonia items (i.e., Dystonia); Factor 3 consisted of 2 rigidity items (i.e., Rigidity); and Factor 4 consisted of the remaining 17 items representing general motor function (i.e., General).

Findings from the simple linear regression models indicated that each of the four factors were significant predictors of the Total Functional Capacity and the Functional Assessment scale (Supplemental Table A). When cognition was considered in the models, the pattern of findings was the same except for chorea (which was no longer a significant predictor of the Functional Assessment Scale; Supplemental Table B). We thus concluded that more dystonia, rigidity, and general motor manifestations are associated with worse function.

Next, all four factors plus cognition were entered into the same multiple linear regression model. The general factor was removed from the model due to its high collinearity. Therefore, the refined multiple linear regression model examined the impact that chorea, dystonia, and rigidity had on overall function (as evaluated by the TFC and FA) while controlling for cognition. For this combined model (controlling for cognition) dystonia and rigidity remained significant predictors of both the TFC and FA; dystonia was the stronger of the two predictors for both (Supplemental Table C).

Discussion

The purpose of this study was to examine the factor structure of the UHDRS Motor Scale, and to determine which motor factors are most associated with functional status in people with HD. To this end, our analyses indicated that a 4-factor model provided a slightly superior fit to the previously published 5-factor structure [11]. Additionally, the factor structure of the 4-factor model was more readily interpretable than the factor structure of the 5-factor model. Our model included all chorea items on a single factor, whereas the chorea factor from Siesling's model did not include the face or buccal-oral-lingual items (in the Siesling model these factors loaded with the dysarthria, pronate/supinate right hand, and retropulsion test items).[11] Furthermore, while both models included a more general factor, the rigidity items cross-loaded on this factor for the Siesling model (these items clearly comprised a solitary factor in our findings), as did the dysarthria and pronate supinate-right hand items (which clearly loaded on our general factor).[11] We suspect that the substantial discrepancy in sample size likely contributes to the

different outcomes of the two studies (we included 527 premanifest and manifest participants, whereas the Siesling study only included 69 manifest participants), and we suspect that the Siesling analysis may have been underpowered (i.e., given that minimal sample size criteria for EFA is typically ~5 people per item analyzed[26-28]). Future studies are needed to evaluate replicability of our results.

A strength of this study is the large cross-sectional sample across the full TFC spectrum, and not just earlier disease. The TFC score in particular inexorably declines as HD advances;[29] in fact, it is used as a surrogate for disease severity and stage after motor diagnosis. The positive association of all identified individual motor factors with lower function is not surprising; HD is a progressive disease and all individual motor features are expected to appear, then worsen, to varying degrees with time. What is novel in our analysis is the *relative* associations of individual motor factors with functioning (and, thereby, disease stage). We found the most striking association between dystonia (accounting for 9% and 14% of the variance in TFC and FA, respectively, after controlling for cognition) and functioning. Rigidity (accounting for 1% of the variance for both TFC and FA after controlling for cognition) and chorea (accounting for 1% of the variance in TFC and FA) more weakly related to functioning and disappeared entirely when cognition was added to the model. This suggests that although chorea is the hallmark motor manifestation of HD, and one of the only motor manifestations with FDA-approved treatments,[4-6] it is not necessarily the most functionally debilitating motor abnormality. Thus, treatments that target dystonia and rigidity have potential to substantially improve function in these individuals.

We acknowledge several study limitations. While this study employed multi-site data collection, participants reflected a convenience sample that may not be readily generalizable to the broader HD population. Furthermore, our results do not imply that dystonia and rigidity are necessarily major drivers of HD functioning. It may be that these are motor markers of later-stage disease which themselves do not contribute much to loss of function. The general factor encompasses a large and diverse set of motor elements, including eye movements, speech, motor sequencing, upper limb coordination, gait, and balance. Many of these are clearly critical to human function; their elimination in the combined regression model was due to the strong correlation of this factor with the other three factors, not due to their lack of importance.

Despite these limitations, findings suggest that research examining motor function in HD should focus more broadly on the multifaceted nature of motor dysfunction including dystonia and rigidity. Although chorea can impair day-to-day function in these individuals, dystonia and rigidity may have a greater impact on function. As such, more extensive longitudinal analysis of motor progression, including disease-specific quality of life measures such as HDQLIFE Chorea[30, 31] and HDQLIFE Speech and Swallowing [30, 32], would shed light on how specific motor factors contribute directly to various facets of function loss. Our study also underscores the need for further research regarding the effects of dystonia and rigidity on functioning in HD.

Author Roles:

Carlozzi, N.E.:	Study Principal Investigator; Data Collection Site; Oversight for Statistical Analysis; Initial draft of Method, Results and Discussion; Incorporation of revisions

Schilling, S.G.	Study Co-Investigator; Primary Statistician responsible for the factor analysis and summary of results; Oversight of data analysis; Review and Feedback on manuscript drafts
Boileau, N. R.	Study Research Coordinator; Data Analyst Responsible for supplemental analyses; Assistance with Methods and Results Sections; Review and Feedback on manuscript drafts; Assistance synthesizing manuscript edits
Chou, K.L.	Study Collaborator; Review and Feedback on manuscript drafts (specific contributions with regard to framing the introduction and discussion in the context of the current HD literature)
Perlmutter, J.S.	Study Co-Investigator; Review and Feedback on manuscript drafts (specific contributions with regard to framing the introduction in the context of the current HD literature)
Frank, S.	Study Consultant; Review and Feedback on manuscript drafts (specific contributions with regard to framing the discussion in the context of the current HD literature)
McCormack, M.	Study Co-Investigator; Review and Feedback on manuscript drafts (specific contributions to the Introduction)
Stout, J.C.	Study Consultant; Assistance with presenting the results in a manner that is readily understandable for the journal audience; Review and Feedback on manuscript drafts
Paulsen, J.S.	Study Co-Investigator; Predict-HD Principal Investigator; Review and Feedback on manuscript drafts with a focus on the HD literature and presentation of findings
Lai, J.-S.	Study Co-Investigator; Project Statistician; Critical review of the analysis plan; Review and Feedback on manuscript drafts
Dayalu, P.	Study Co-Investigator; Initial Draft of Abstract; Assistance Writing the Introduction and Discussion Including Integration of Findings with Existing HD Literature; Review and Feedback on manuscript drafts

References

1. Walker, F.O., *Huntington's disease.* Lancet, 2007. **369**(9557): p. 218-28.
2. Albin, R.L., et al., *Striatal and Nigral Neuron Subpopulations in Rigid Huntingtons-Disease - Implications for the Functional-Anatomy of Chorea and Rigidity-Akinesia.* Annals of Neurology, 1990. **27**(4): p. 357-365.
3. Coyle, J.T. and R. Schwarcz, *Lesion of Striatal Neurons with Kainic Acid Provides a Model for Huntingtons-Chorea.* Nature, 1976. **263**(5574): p. 244-246.
4. Marshall, F.J., et al., *Tetrabenazine as antichorea therapy in Huntington disease - A randomized controlled trial.* Neurology, 2006. **66**(3): p. 366-372.
5. Huntington Study Group, et al., *Effect of deutetrabenazine on chorea among patients with Huntington disease: a randomized clinical trial.* JAMA, 2016. **316**(1): p. 40–50.
6. Huntington Study Group, *Effect of Deutetrabenazine on Chorea Among Patients with Huntington Disease.* JAMA, 2016. **316**(1): p. 40-50.
7. Dayalu, P. and R.L. Albin, *Huntington disease: pathogenesis and treatment.* Neurol Clin, 2015. **33**(1): p. 101-14.
8. Pagan, F., Y. Torres-Yaghi, and M. Altshuler, *The diagnosis and natural history of Huntington disease.* Handb Clin Neurol, 2017. **144**: p. 63-67.
9. Feigin, A., et al., *Functional decline in Huntington's disease.* Mov Disord, 1995. **10**(2): p. 211-4.
10. Ross, C.A., et al., *Determinants of functional disability in Huntington's disease: role of cognitive and motor dysfunction.* Mov Disord, 2014. **29**(11): p. 1351-8.
11. Siesling, S., et al., *A shortened version of the motor section of the Unified Huntington's Disease Rating Scale.* Mov Disord, 1997. **12**(2): p. 229-34.
12. Vaccarino, A.L., et al., *An item response analysis of the motor and behavioral subscales of the unified Huntington's disease rating scale in huntington disease gene expansion carriers.* Mov Disord, 2011. **26**(5): p. 877-84.
13. Paulsen, J.S., et al., *Preparing for preventive clinical trials - The Predict-HD study.* Archives of Neurology, 2006. **63**(6): p. 883-890.
14. Hanauer, D.A., et al., *Supporting information retrieval from electronic health records: A report of University of Michigan's nine-year experience in developing and using the Electronic Medical Record Search Engine (EMERSE).* Journal of Biomedical Informatics, 2015. **55**: p. 290-300.
15. Huntington Study Group, *Unified Huntington's Disease Rating Scale: reliability and consistency.* Mov Disord, 1996. **11**(2): p. 136-42.
16. Shoulson, I. and S. Fahn, *Huntington disease - Clinical care and evaluation.* Neurology, 1979. **29**(1): p. 1-3.
17. Stroop, J.R., *Studies of interference in serial verbal reactions (Reprinted from Journal Experimental-Psychology, Vol 18, Pg 643-662, 1935).* Journal of Experimental Psychology: General, 1992. **121**(1): p. 15.
18. Kline, R.B., *Principles and Practice of Structural Equation Modeling, Second Edition*. 2005, New York: Guilford Press.
19. Bentler, P.M., *Comparative Fit Indexes in Structural Models.* Psychological Bulletin, 1990. **107**(2): p. 238-246.

20. Hu, L.T. and P.M. Bentler, *Cutoff Criteria for Fit Indexes in Covariance Structure Analysis: Conventional Criteria Versus New Alternatives.* Structural Equation Modeling-a Multidisciplinary Journal, 1999. **6**(1): p. 1-55.
21. Hatcher, L., *A step-by-step approach to using SAS for factor analysis and structural equation modeling*. 1994, Cary, NC: SAS Institute, Inc.
22. McDonald, R.P., *Test theory: A unified treatment.* 1999, Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
23. Reise, S.P., J. Morizot, and R.D. Hays, *The role of the bifactor model in resolving dimensionality issues in health outcomes measures.* Quality of Life Research, 2007. **16 Suppl 1**: p. 19-31.
24. Cook, K.F., M.A. Kallen, and D. Amtmann, *Having a fit: Impact of number of items and distribution of data on traditional criteria for assessing IRT's unidimensionality assumption.* Quality of Life Research, 2009. **18**(4): p. 447-60.
25. Muthén, L.K. and B.O. Muthén, *Mplus User's Guide*. 2011, Los Angeles, CA: Muthén & Muthén.
26. Bryant, F.B. and P.R. Yarnold, *Principal components analysis and exploratory and confirmatory factor analysis*, in *Reading and understanding multivariate statistics*, L.G. Grimm and R.R. Yarnold, Editors. 1995, American Psychological Association: Washington, DC. p. 99-136.
27. Gorsuch, R.L., *Factor Analysis*. 1983, Hillsdale, NJ: Lawrence Erlbaum Associates.
28. Everitt, B.S., *Multivariate analysis: The need for data, and other problems.* British Journal of Psychiatry, 1975. **126**: p. 2S7-240.
29. Marder, K., et al., *Rate of functional decline in Huntington's disease.* Neurology, 2000. **54**(2): p. 452.
30. Carlozzi, N.E., et al., *HDQLIFE: Development and assessment of health-related quality of life in Huntington disease (HD).* Qual Life Res, 2016. **25**(10): p. 2441-55.
31. Carlozzi, N.E., et al., *The development of a new computer adaptive test to evaluate chorea in Huntington disease: HDQLIFE Chorea.* Qual Life Res, 2016.
32. Carlozzi, N.E., et al., *HDQLIFE: the development of two new computer adaptive tests for use in Huntington disease, Speech Difficulties, and Swallowing Difficulties.* Qual Life Res, 2016.

Table 1

Demographic data for the HDQLIFE participants

Variable	Premanifest (*n*=204)	Early (*n*=198)	Late (*n*=125)	All (*n*=527)
Age (Years)*				
M (SD)	42.7 (12.0)	51.4 (12.7)	54.7 (12.0)	48.8 (13.2)
Sex				
Female	65.4	53.5	57.6	59.0
Male	34.6	46.5	42.4	41.0
Ethnicity*				
Not Hispanic or Latino	92.7	92.9	96.8	93.7
Hispanic or Latino	1.5	4.6	0.8	2.5
Not Provided	5.9	2.5	2.4	3.8
Race (%)*				
White	97.5	96.5	92.8	96.0
African American	0.0	2.0	6.4	2.3
Other	2.0	1.5	0.0	1.5
Unknown	0.5	0.0	0.8	0.2
Education (Years)*				
M (SD)	15.9 (2.9)	14.7 (2.8)	14.2 (2.6)	15.1 (2.9)
Marital Status*				
Single, Never Married	15.8	15.2	11.8	14.6
Married	67.4	52.9	61.3	60.5
Separated/Divorced	13.8	25.1	23.5	20.4
Widowed	0.0	2.6	3.4	1.8
Living with Partner	3.0	4.2	0.0	2.7
Years Since Diagnosis		(*n*=154)	(*n*=75)	N=230
M (SD)	--	3.14 (3.74)	5.99 (4.62)	4.05 (4.25)

CAG Repeats*	(*n*=190)	(*n*=145)	(*n*=56)	(n=391)
M (SD)	42.2 (2.9)	43.1 (3.9)	44.4 (6.6)	42.9 (4.1)

Note. Entries in the table represent percentage of participants unless otherwise specified; * indicates that there were significant group differences for this variable.
Premanifest participants (M = 42.7, SD = 12.0) were significantly younger than early-stage (M = 51.4, SD = 12.7), who were significantly younger than late-stage participants (M = 54.7, SD = 12.0; F [2, 524] = 44.25, p< .0001); early-stage (M = 14.7, SD = 2.8) and late-stage (M = 14.2, SD = 2.6) participants had 1 to 1.5 years less education relative to premanifest HD participants (M = 15.9 years, SD = 2.9; (F [2, 502] = 15.78, p< .0001); late stage had more African Americans than early-stage and premanifest groups (Fisher's exact p=.0005); early-stage had fewer married participants than premanifest or late-stage, and premanifest had fewer widowed participants than the manifest groups (X^2[8, N = 527] = 21.9, p = .0051); there were marginal differences for gender (X^2[2, N = 527] = 5.27, p = .07), and ethnicity (Fisher's Exact p=.06).

Table 2

Factor loadings for the Total Motor Scale

Item	Factor 1 Chorea	Factor 2 Dystonia	Factor 3 Rigidity	Factor 4 General Factor	Siesling Factor Loading
Ocular Pursuit – Horizontal	0.049	-0.267	**(0.439)**	**0.833**	1
Ocular Pursuit – Vertical	-0.005	-0.198	**(0.422)**	**0.859**	1
Saccade Initiation – Horizontal	-0.039	-0.092	0.016	**1.013**	1
Saccade Initiation – Vertical	-0.021	-0.099	0.022	**0.997**	1
Saccade Velocity – Horizontal	-0.105	0.153	0.271	**0.783**	1
Saccade Velocity – Vertical	-0.106	0.140	0.281	**0.770**	1
Dysarthia	0.060	0.339	0.014	**0.593**	1 & 2
Tongue Protrusion	0.099	0.143	-0.053	**0.665**	1
Finger Taps – Right	0.173	0.258	-0.161	**0.690**	1
Finger Taps – Left	0.176	0.258	-0.177	**0.692**	1
Pronate/Supinate Hands – Right	0.066	0.285	-0.063	**0.716**	1 & 2
Pronate/Supinate Hands – Left	0.099	0.298	-0.067	**0.690**	1
Luria (fist-hand palm test)	0.081	0.222	-0.068	**0.622**	1
Rigidity Arms – Right	0.022	0.249	**0.820**	0.050	1 & 5
Rigidity Arms – Left	0.040	0.228	**0.805**	0.102	1 & 5
Bradykinesia – Body	-0.032	0.342	0.107	**0.581**	1 & 5
Maximal Dystonia – Trunk	0.086	**0.493**	0.194	0.234	4
Maximal Dystonia – RUE	0.059	**0.919**	0.149	-0.087	4
Maximal Dystonia – LUE	0.033	**0.919**	0.129	-0.053	None
Maximal Dystonia – RLE	-0.065	**0.906**	0.001	0.115	4
Maximal Dystonia – LLE	-0.021	**0.880**	0.040	0.092	None
Maximal Chorea – Face	**0.649**	-0.128	-0.013	**(0.440)**	2
Maximal Chorea – BOL	**0.645**	-0.155	-0.010	**(0.465)**	2
Maximal Chorea – Trunk	**0.738**	-0.046	0.053	0.230	3
Maximal Chorea – RUE	**0.916**	0.068	-0.156	0.095	3
Maximal Chorea – LUE	**0.949**	0.050	-0.161	0.063	None
Maximal Chorea – RLE	**0.969**	0.066	0.248	-0.186	3
Maximal Chorea – LLE	**0.991**	0.051	0.251	-0.197	None
Gait	0.076	**(0.431)**	0.022	**0.519**	1
Tandem Walking	0.074	0.377	0.001	**0.541**	1
Retropulsion Pull Test	0.017	0.336	0.051	**0.501**	2

Note. RUE=Right Upper Extremity; LUE=Left Upper Extremity; RLE=Right Lower Extremity; LLE=Left Lower Extremity; BOL=Buccal-Oral-Linguistic; bolding indicates primary factors loadings (values in parentheses indicate that item loaded on to more than one factor).