Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Measurement Properties of Clinical Scales Rating the Severity of Blepharospasm: A Multicenter Observational Study

Giovanni Defazio, MD, PhD,[1] Mark Hallett, MD,[2] Alfredo Berardelli, MD,[3,4] Joel S. Perlmutter, MD,[5] Brian D. Berman, MD, MS,[6] Joseph Jankovic, MD,[7] Tobias Bäumer, MD,[8] Cynthia Comella, MD, FAAN,[9] Tommaso Ercoli, MD,[1] Gina Ferrazzano, MD, PhD,[3] Susan H. Fox, MBChB, MRCP, PhD,[10] Han-Joon Kim, MD, PhD,[11] Emile Sami Moukheiber, MD,[12] Sarah Pirio Richardson, MD,[13] Anne Weissbach, MD,[7,14] Angelo F. Gigante, MD, PhD,[15,*] and Hyder A. Jinnah, MD, PhD[16]

Abstract: Background: Several scales have been proposed to clinically evaluate the Motor Severity of Blepharospasm (BSP) but information about their measurement properties as a multicenter instrument is limited.

Objective: To compare the measurement properties of four clinical scales in rating the severity of BSP in a large sample of patients from multiple sites.

Methods: The Burke–Fahn–Marsden Scale (BFMS), the Global Dystonia Severity Rating Scale (GDRS), the Jankovic Rating Scale (JRS), and the Blepharospasm Severity Rating Scale (BSRS) were administered to 211 patients across 10 sites who were also requested to self-complete the Blepharospasm Disability Index (BDI). Measurement properties to be assessed included inter−/intra-observer agreement, item-to-total correlation, internal consistency, floor and ceiling effect, convergent/discriminant validity, and adherence to the distribution of BDI.

Results: The BFMS had unsatisfactory measurement properties, the GDRS had acceptable reliability but other properties could not be completely testable; the JRS had satisfactory measurement properties but the scale did not accurately reflect the distribution of disability parameter (BDI) in the sample, and the BSRS had satisfactory measurement properties and also showed the best adherence to the distribution of BDI in the assessed sample.

Conclusion: The comparison of the measurement properties of four rating scales to assess the motor state of the BSP in a large sample of patients from multiple sites showed that the GDRS should be used to simultaneously assess BSP and dystonia in other body parts, while the JRS (easier to use) and BSRS (better to discriminate severity) should be used to assess BSP alone.

Blepharospasm (BSP) is an adult-onset focal dystonia characterized by involuntary bilateral, synchronous, orbicularis oculi (OO) muscle contractions leading to partial/total eyelid rim closure.[1,2] Spasms may be brief or prolonged, are aggravated by bright light, wind and stress, or voluntary muscle contraction, and are usually reduced by attention-demanding tasks such as

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy; [2]Human Motor Control Section, NINDS, NIH, Bethesda, MD, USA; [3]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy; [4]IRCCS NEUROMED, Pozzilli, Italy; [5]Neurology, Radiology, Neuroscience, Physical Therapy, Occupational Therapy, Washington University in St. Louis, St Louis, MO, USA; [6]Virginia Commonwealth University, Richmond, VA, USA; [7]Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, TX, USA; [8]Institute of Systems Motor Science, University of Luebeck, Luebeck, Germany; [9]Rush University Medical Center, New Philadelphia, OH, USA; [10]Toronto Western Hospital, Krembil Brain Institute, University of Toronto, Toronto, ON, Canada; [11]Department of Neurology and Movement Disorder Centre, Seoul National University Hospital, Seoul, South Korea; [12]Department of Neurology, Johns Hopkins University, Baltimore, MD, USA; [13]Department of Neurology, University of New Mexico, Albuquerque, NM, USA; [14]Institute of Systems Motor Science and Institute of Neurogenetics, University of Lübeck, , Lübeck, Germany; [15]Section of Neurology, San Paolo Hospital, Bari, Italy; [16]Department of Neurology and Human Genetics, Emory University, Atlanta, GA, USA

***Correspondence to:** Dr. Angelo F. Gigante, Section of Neurology, Department of Medical Sciences and Public Health, San Paolo Hospital, Bari, Italy; E-mail: angelo.gigante@yahoo.it

Keywords: Blepharospasm, dystonia, rating scale, measurement properties, severity of illness index.
Received 6 March 2022; revised 24 June 2022; accepted 9 July 2022.
Published online 15 August 2022 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.13530

talking and singing; additional motor features include increased blinking, apraxia of eyelid opening (AEO) and dystonia in other body parts.[3–5] As in other type of dystonia, there may also be sensory features including dry eyes, sensations of grittiness or sand in the eyes, photophobia, and alleviating maneuvers (sensory tricks).[6–8] Precise tools to rate improvement or deterioration of motor symptoms are important to assess a patient's condition and the outcome after treatment. Clinician-rated scales that have been proposed to evaluate the motor severity of BSP belong to two categories: the first category includes scales specifically developed for BSP, like the Jankovic Rating Scale (JRS)[9,10] and the Blepharospasm Severity Rating Scale (BSRS)[2]; the second category refers to scales that comprehensively measure dystonia severity in all body parts, like the Burke–Fahn–Marsden Rating Scale (BFMS)[11] and the Global Dystonia Severity Rating Scale (GDRS).[12]

Although each scale underwent validation procedures, several measurement properties were not assessed or were assessed in limited populations. The BSRS is the only scale that presents acceptable parameters of reliability (inter and intra-rater agreement, internal consistency, item-to-total correlation), convergent and discriminant validity, and floor-and-ceiling effect, resulting from the assessment of a homogeneous population of 68 patients with idiopathic BSP from a single country (Italy).[2] The BFMS, the first scale proposed for scoring the severity of dystonia, was evaluated in a small sample of patients with multifocal/generalized dystonia by four raters who provided reliability and concurrent validity data for the total score but not for dystonia in single body parts.[11] Data from a randomized, double-blind, controlled clinical trial in 300 BSP patients from Europe and Israel were used to evaluate the measurement properties of the JRS: excellent internal consistency, inter-observer agreement and convergent validity were observed, but the study did not provide information on other measurement properties.[9] A further, more recent study performed in the USA and Canada compared measurement properties of BFMS and GDRS in 100 patients: both scales showed excellent internal consistency and inter-observer agreement, but other measures were not evaluated.[12] Therefore, information about the measurement properties of these scales in a large sample of BSP patients from multiple sites is still lacking.

In this paper, we compared the measurement properties of four clinical scales in rating the severity of BSP in a large sample of patients from multiple sites, to ultimately guide the choice of reliable and valid BSP rating scales to be used in different populations from multiple centers.

Methods

The data from the present study are part of a macro project called "Diagnostic and Rating Tools for Blepharospasm," a multicenter, international, prospective observational study of people with isolated BSP performed within the Dystonia Coalition effort (www.rarediseasesnetwork.org/dystonia/).

Subjects

Participants were enrolled across 10 sites in the USA and Europe, each recruiting 20–25 patients. Inclusion criteria, that is age 18 or more, any gender, any racial-ethnic background, and willingness and mental/physical ability to sign informed consent and participate in the protocol, were coherent with those already published by the Dystonia Coalition.[13] Informed consent was therefore obtained by all participants.

For the purposes of the study, patients needed to have isolated idiopathic BSP diagnosed by an experienced movement disorder neurologist.[14,15] Exclusion criteria were acquired BSP,[14] and co-existing medical conditions/surgical interventions that could confound BSP assessment. Concomitant medication and Botulinum NeuroToxin (BoNT) administration in the OO muscles were allowed, but patients needed to be sufficiently symptomatic at recruitment to ensure that the clinical features were evident to evaluators. The last BoNT treatment session should have been performed at least 10 weeks prior to examination. Thus, patients for whom severity scores would predictably have been zero were not included.

The final study sample included 211 patients with idiopathic BSP (65 men and 146 women aged 63.7 ± 9.2 years; age at BSP onset, 51.8 ± 10.8 years). Focal BSP was detected in 80 patients, BSP as part of a segmental/multifocal dystonia in 131 patients.

Study Procedure

All patients were assessed by four severity scales including the BFMS,[11] the GDRS,[12] the JRS,[9,10] and the BSRS.[2] Raters from different countries all used the original, English version of each scale.[2,9–12] The BFMS comprehensively measure dystonia severity in 10 body parts. Severity grading is based on a severity factor ranging from 0 (no dystonia) to 4 (maximum dystonia severity) multiplied by a provoking factor that rates the relation of dystonia to action, from 0 (no dystonia at rest or with action) to 4 (dystonia at rest). The score obtained for eyes was finally multiplied by 0.5. In the GDRS, dystonia severity in 10 body areas is rated by a Likert type scale, with ratings from 0 to 10 (0 is no dystonia, 1 minimal, 5 moderate and 10 severe dystonia). BSP is addressed in the eye/upper face subscore of the GDRS. The JRS ranges from 0 to 8 points (sum score) and includes two categories: severity (from 0 = none to 4 = severe) and frequency (from 0 = none to 4 = functionally "blind" due to persistent eye closure). Finally, the BSRS included seven clinical items. Among them, degree and duration of eyelid closure caused by spasms and frequency of spasms were the core clinical hallmarks of BSP severity while increased blinking, presence of AEO, and occurrence of spasms during writing were useful to grade severity.

Blepharospasm patients were also asked to complete the Blepharospasm Disability Index (BSDI),[9] a disease- specific patient-rated disability scale that measures impairment of specific activities of daily living caused by BSP. BSDI consists of six items rating specified activities (vehicle driving, reading, watching television, shopping, walking, and doing everyday activities), scored as a 5-point Likert scale relating to the severity of

impairment (0, no impairment; 4, no longer possible due to illness), as well as a "not applicable" option. The range of scores is zero to 24, with higher scores indicating a greater disability. In our sample, mean BSDI rating was 8.1 ± 5.4.

Participants were also video-recorded according to a standardized protocol[13] that reproduced all the major and distinctive features identified by the clinical examination, including standard maneuvers triggering eyelid spasms, demonstrating a sensory trick if present, and assessing blink rate. The video-recording protocol also included examination of all body sites during several tasks, allowing manifestation and detection of OO spasms under several conditions.

Analysis of Measurement Properties

Measurement properties we assessed included inter/intra-observer agreement,[16,17] item-to-total correlation,[18] internal consistency (the contribution of each single item to the total score),[19] floor and ceiling effect,[20] and convergent/discriminant validity.[21]

Inter−/intra-rater agreement was measured among six independent raters (from the centers participating in the project) who assessed 43 out of 211 randomly selected videos of BSP patients. Since examination of 43 video-recordings from each rater would be excessively time-consuming, we adopted the following procedure to compare raters' judgment: (1) raters did not rate videos from their own sites; (2) each video was rated by three different people; (3) each rater assessed 15 randomly assigned videos; (4) ratings from each rater were compared with average ratings from the other raters who examined the same videos by the first rater. Results of the six comparisons were averaged. For intra-rater assessment, each of the six raters was asked to re-evaluate five videos, at least 2 weeks following the first rating. Raters could not see their prior ratings. Results of the six intra-rater assessments were averaged. Intra- and inter-rater agreement was measured by the intraclass correlation coefficient (ICC). ICCs exceeding 0.91 are considered to be very good, with values between 0.71 and 0.9 viewed as good, values between 0.51 and 0.70 viewed as moderate, values between 0.31 and 0.5 viewed as poor, and values below 0.3 viewed as bad.[16] A sample of 43 subjects and six raters provided >80% study power to see an expected ICC >0.5 as significant ($P < 0.05$, two-tailed).[17]

With regard to the further measurement properties, these were tested on data from face to face examination of all 211 patients under the following procedures. Item-to-total correlation was considered to be acceptable if Spearman coefficient was >0.30[18,19]; internal consistency was satisfactory under Cronbach's $\alpha > 0.30$.[21] The possibility of floor and ceiling effects was ruled out when subjects with total score near to the bottom or the top of the scale did not exceed 15%.[20] Convergent validity was assessed by correlating the sumscores of each scale to the BSDI: a significant correlation indicated that the tested motor scale also explored domains that are not considered in the disability scale. Discriminant validity was assessed by correlating the sumscores of each scale to the Eye symptoms scale, a tool recording the eye symptoms possibly associated with BSP, including red eyes, burning sensation, and gritty/sandy sensation.[22] Lack of significant correlation indicated that the tested motor scale and the Eye symptom scale truly explored different domains. Adherence of each motor scale ratings to the frequency distribution of the disability score from BDSI (reflecting the degree of disability linked to BSP) in the study sample was checked by visual inspection of Kernel density distribution curves that reflected the frequency distribution of score from each scale. In addition to the quantitative assessments provided for each scale, the raters were also asked to provide subjective feedback regarding possible difficulties they encountered in applying each scale across different cases. Subjective feedback was

TABLE 1 *Results of measurement properties analysis of the four tested scales*

Scale	Inter-observer agreement [intraclass correlation coefficient (*P*)]	Intra-observer agreement [intraclass correlation coefficient (*P*)]	Item-to-total correlation (*P*)	Internal consistency (Cronbach's α)	Floor and ceiling effect (percent of patients)	Convergent validity [scale vs. Blepharospasm disability index (*P*)]	Discriminant validity [scale vs. Eye symptom scale (*P*)]
Burke–Fahn–Marsden scale	0.56 (0.0006)	0.78 (<0.0001)	≥0.63 (< 0.0001)	0.52	>18	0.37 (< 0.0001)	−0.01 (0.90)
Global dystonia rating scale	0.81 (<0.0001)	0.85 (<0.0001)	NA	NA	<10	0.35 (< 0.0001)	0.07 (0.31)
Jankovic Rating Scale	0.51 (0.0005)	0.81 (<0.0001)	≥0.92 (< 0.0001)	0.85	<9	0.45 (< 0.0001)	0.05 (0.49)
Blepharospasm Severity Rating Scale	0.86 (<0.0001)	0.83 (<0.0001)	>0.40 (< 0.0001)	0.68	<5	0.38 (< 0.0001)	0.03 (0.68)

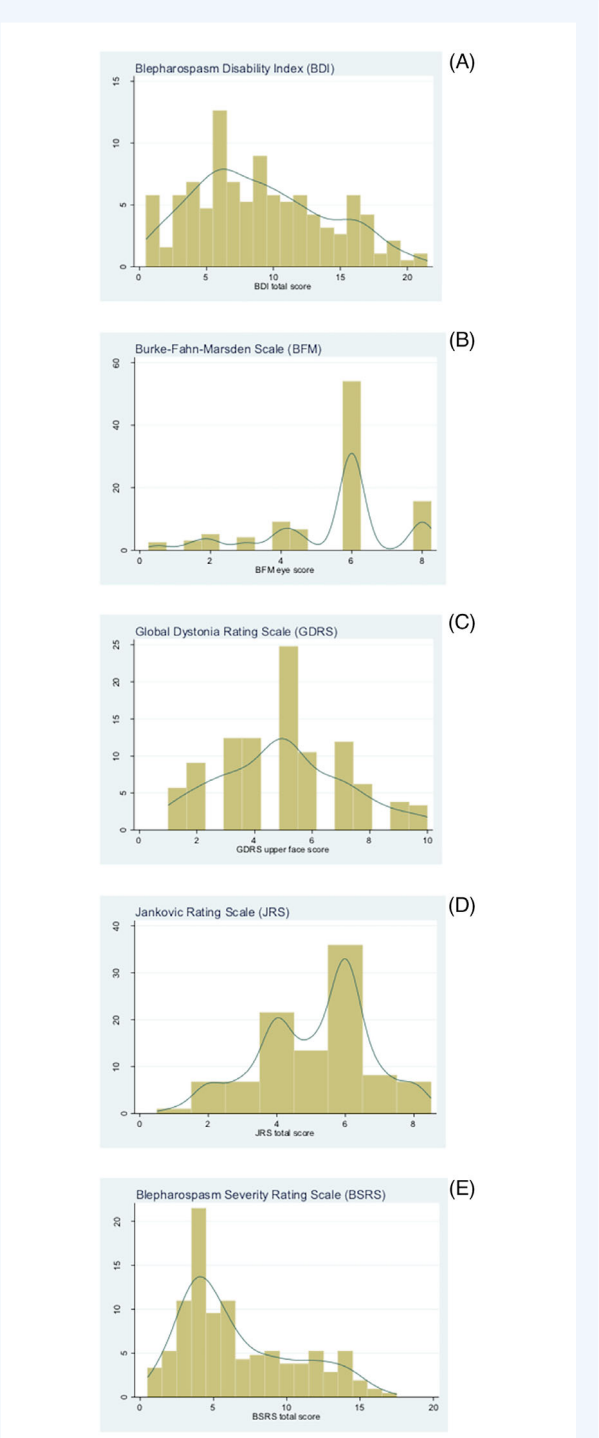

FIG. 1. Kernel density curves showing the probability density function of the scores from (**A**) the blepharospasm disability index, (**B**) the Burke–Fahn–Marsden Scale (BFMS), (**C**) the global dystonia rating scale, (**D**) the Jankovic Rating Scale (JRS), and (**E**) the Blepharospasm Severity Rating Scale (BSRS).

based on open text feedback. We did not highlight some themes in particular but merely collected the comments, if any, provided by observers.

Results

Measurement Properties

Measurement properties analysis is summarized in Table 1. On reliability assessment, all scales were characterized by significant inter-observer agreement, though to a different degree. Agreement was excellent for the JRS and the BSRS, moderate for the BFMS and the GDRS. Repeat rating of videotapes yielded acceptable intra-rater reliability for all scales and all the six observers (ICC >0.78). The BFMS, the JRS and the BSRS gained item-to-total correlation greater than the criterion 0.30 and satisfactory internal consistency. Since the eye/upper face subscale of the GDRS consisted in only one item, item-to-total correlation and internal consistency could not be tested. Floor and ceiling effect was not evident for the GDRS, the JRS, and the BSRS; by contrast, when BSP was assessed by the BFMS, more than 15% of subjects yielded minimum/maximum scores, thus suggesting a floor and ceiling effect. With regard to convergent validity, significant correlations emerged between the GDRS, the BSRS, and the JRS and the BSDI. Assessment of discriminant validity failed to reveal any significant correlation between each motor scale and the eye symptoms scale.

Kernel density curve indicating the distribution of scores from each motor severity scale was right-skewed for the BSRS (mean, 9.95; median, 8) and the BFMS (mean, 3.3; median, 2) and was left-skewed for the JRS (mean, 5.14; median, 6), with substantially no skew for the GDRS (mean, 4.95; median, 5) (Fig. 1).

Subjective Feedback by Experts

The raters identified several concerns mainly related to comprehensiveness and usability of the scales that are summarized below. The raters noted that an item for delayed eyelid opening or AEO was missing in all scales but the BSRS, despite the fact that this problem may accompany BSP and can be quite disabling. For the BFMS the raters indicated that the first two items raised the possibility that blinking without spasms may be scored as a form of dystonia. Likewise, the term "exaggerated blinking" could be interpreted as increased frequency or increased strength of blinking. The provoking factor was considered particularly problematic, because BSP almost always occurs at rest, and actions of distant body parts (such as speaking or writing) often suppress BSP rather than provoke it. The peak at score 6 on Kernel density curve (Fig. 1) likely reflected the most common severity score of 3 (which is the first to require spasm), multiplied by 4 (at rest) and then multiplied by 0.5.

For the JRS there were concerns that numerous terms could lead to differences in interpretation including "fluttering," "external stimuli," and "incapacitating." Discrimination of "eyelid spasm" from "eyelid fluttering" was viewed as subjective. Additionally, the frequency scale is confounded with elements of the severity scale. The two peaks at 4 and 6 on Kernel density curve (Fig. 1) likely reflect that severity and frequency scales overlap. So a score 2 (or 3) on severity means most likely to get

a score 2 (or 3) on frequency, which gives a sum score of 4 (or 6).

For the BSRS, raters highlighted difficulty in scoring the writing item either alive or in video because the face often cannot be seen clearly when the patient looks down to write. In addition, there were concerns that there was no item for "short" partial rim closure, even though the item was considered in the original formulation of the scale but it was later deleted because of low reliability.

Discussion

The large multicenter and international sample of BSP patients that were recently recruited by the "Diagnostic and Rating Tools for Blepharospasm" study provided the unique opportunity to assess measurement properties of four clinical scales rating the motor severity of BSP in the same patient population and using the same observers. We also provided novel information about measurement properties that had never been previously assessed in same scales.

Overall, comparison of scales showed that: (1) the BFMS has unsatisfactory measurement properties when used for assessing BSP motor severity alone; (2) the GDRS has acceptable measurement properties even though item-to-total correlation and internal consistency could not be tested; (3) the JRS has satisfactory measurement properties but the left-skewed density curve indicated that the scale did not accurately reflect BSP-related disability in the sample; (4) the BSRS also has satisfactory measurement properties and also shows the best adherence to the distribution of the disability parameter in the assessed sample, as reflected by the right-skewed density curve.

The study has several strengths. First, it included participants and physicians from several countries and languages, thus allowing cross-cultural comparison that was lacking for all scales.[2,9–12] Second, the BSP population was representative of the general population of cases in terms of demographic/clinical features and encompassed a wide spectrum of severity and disability.[1,4,6] Third, the approach we used to test reliability reflects a real life multicenter clinical study where several investigators are involved, each assessing a fraction of patients. The use of video-recorded patients to test reliability also allowed us to check the scales for remote use, though this was not our primary aim. Despite of these strengths, subjective feedback by experts highlighted a few aspects of each scale that may contribute to lowering reliability. Experts also noted that an item for delayed eyelid opening or AEO was missing in all scales but the BSRS, despite the fact that this problem may accompany BSP and can be quite disabling.

The measurement properties of the scales highlighted in the present study, together with the working context and aims, should drive the choice of the scale to be used to assess BSP motor state. The GDRS would be used when we need to simultaneously rate BSP and dystonia in other body parts while both the JRS and the BSRS can be proposed to rate BSP alone. Certainly, the JRS is easier to use but the BSRS has a wider range of score values and might better discriminate variable degree of severity.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

GD: 1A, 1B, 1C, 2A, 2B, 3A.
MH: 1A, 1B, 1C, 2C, 3B.
AB: 1A, 1B, 1C, 2C, 3B.
JSP: 1B, 1C, 2C, 3B.
BDB: 1B, 1C, 2C, 3B.
JJ: 1B, 1C, 2C, 3B.
TB: 1B, 1C, 2C, 3B.
CC: 1B, 1C, 2C, 3B.
TE: 1B, 1C, 2C, 3B.
GF: 1B, 1C, 2C, 3B.
SHF: 1B, 1C, 2C, 3B.
HJK: 1B, 1C, 2C, 3B.
ESM: 1B, 1C, 2C, 3B.
SPR: 1B, 1C, 2C, 3B.
AW: 1B, 1C, 2C, 3B.
AFG: 1B, 1C, 2B, 3B.
HAJ: 1A, 1B, 1C, 2C, 3B.

Disclosures

Ethical Compliance Statement: We received institutional approval from the Internal Review Boards of all participating clinical sites. All subjects gave written informed consent at the recruiting site according to the Declaration of Helsinki and The Common Rule. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: The authors declare that there are no conflicts of interest relevant to this work. This work was supported in part by NIH grant NS119831 and NIH grants to The Dystonia Coalition (NS065701, TR001456, NS116025) which is part of the National Institutes of Health (NIH) Rare Disease Clinical Research Network (RDCRN), supported by the Office of Rare Diseases Research (ORDR) at the National Center for Advancing Translational Science (NCATS), and the National Institute of Neurological Diseases and Stroke (NINDS).

Financial Disclosures for the Previous 12 Months: M. Hallett is an inventor of patents held by NIH for an immunotoxin for the treatment of focal movement disorders and the H-coil for magnetic stimulation; in relation to the latter, he has received license fee payments from the NIH (from Brainsway). He is on the Medical Advisory Boards of CALA

Health and Brainsway (both unpaid positions). He is on the Editorial Board of approximately 15 journals and receives royalties and/or honoraria from publishing from Cambridge University Press, Oxford University Press, Springer, Wiley, Wolters Kluwer, and Elsevier. He has research grants from Medtronic, Inc. for a study of DBS for dystonia and CALA Health for studies of a device to suppress tremor. JS Perlmutter has received research grant support from NIH (NCRR/NCATS, UNM CTSC KL21TR001448-01 and UL1TR001449) and Dystonia Coalition Projects (NIH/NINDS/ORDR) and has received publishing royalties from Springer; G. Berkmen reports no disclosure; B. Berman has received research grant support from the Dystonia Coalition (receives the majority of its support through NIH grant NS065701 from the Office of Rare Diseases Research in the National Center for Advancing Translational Science and National Institute of Neurological Disorders and Stroke), Benign Essential Blepharospasm Research Foundation, Colorado Clinical & Translational Science Institute and Center for Neuroscience, Tools4Patient, Parkinson's Foundation, and Virginia Commonwealth University School of Medicine. He is on the medical advisory board of the Benign Essential Blepharospasm Research Foundation and the National Spasmodic Torticollis Association. Brian Berman received research grant support within last 12 months from the Dystonia Coalition (through NIH grant NS065701 from the Office of Rare Diseases Research in the National Center for Advancing Translational Science and National Institute of Neurological Disorders and Stroke), Parkinson's Foundation, VCU School of Medicine, the Administration for Community Living and Dystonia Medical Research Foundation; honoraria from the MedLink Corporation and the International Parkinson and Movement Disorder Society; and consultancies from AbbVie Inc. J Jankovic has received research/training funding from AbbVie Inc; Acadia Pharmaceuticals; Allergan, Inc; Biotek; Cerevel Therapeutics; CHDI Foundation; Dystonia Coalition; Emalex Biosciences, Inc; F. Hoffmann-La Roche Ltd; Huntington Study Group; Medtronic Neuromodulation; Merz Pharmaceuticals; Michael J. Fox Foundation for Parkinson Research; National Institutes of Health; Neuraly, Inc.; Neurocrine Biosciences; Parkinson's Foundation; Parkinson Study Group; Prilenia Therapeutics; Revance Therapeutics, Inc; Teva Pharmaceutical Industries Ltd. Dr. Jankovic has served as a consultant for Eon BioPharma; Nuvelution Pharma, Inc; Teva Pharmaceutical Industries Ltd. Dr. Jankovic has received royalties from Cambridge; Elsevier; Medlink: Neurology; Lippincott Williams and Wilkins; Wiley-Blackwell; C. Comella serves on the editorial board of Clinical Neuropharmacology and Sleep Medicine. She receives compensation/honoraria for services as a consultant or an advisory committee member: Acorda Therapeutics, Allergan, Inc; Lundbeck Ltd.; Merz Pharmaceuticals; Acadia Pharmaceuticals; Ipsen Pharmaceuticals, Jazz. Pharmaceuticals, Neurocrine Biosciences Inc., Revance Therapeutic, Sunovion., EON Biopharma. She receives royalties from Cambridge University Press and Wolters Kluwer. She receives research support from the Parkinson's Disease Foundation. Susan Fox has received clinic support from the Edmond J. Safra Foundation for Parkinson Research; Parkinson Foundation and the Toronto Western and General Foundation; salary from UHN Dept of Medicine Practice Plan; research Funding from Michael J. Fox Foundation for Parkinson Research, NIH (Dystonia Coalition); Parkinson Canada; honoraria from the International Parkinson and Movement Disorder Society; Consultancy/Speaker fees from Alexion; Bial, Merck; Pharma 2B; Sunovion; Teva; Paladin; royalties from Oxford University Press. She was site PI for Clinical Trials for Alexion, Biotie, Eisai, Pharma2B, Revance. HJ Kim received travel grant support from the International Parkinson and Movement Disorder Society and Korean Movement Disorder Society and research grants support from the Institute for Information and Communications Technology Promotion, Seoul National University Hospital, New York University, and C-TRI. A Weissbach received funding from the Else Kröner-Fresenius Foundation (EKFS, 2018_A55) and the German Research Foundation (DFG, WE 5919/2-1). S Pirio Richardson has received research support from the National Institutes of Health (P20 GM109899; U54 NS116025), Department of Defense (W81XWH-19-CTRR-CTA); Pharma 2B; Addex and Eon. HA Jinnah has active or recent grant support from the US government (National Institutes of Health), private philanthropic organizations (Cure Dystonia Now), and industry (Revance Therapeutics, Inc.). Dr. Jinnah has also served on advisory boards or as a consultant for Addex, Allergan, CoA Therapeutics, Cavion Therapeutics, EnePharmaceuticals, Ipsen, Retrophin, Revance, and Takaha Pharmaceuticals. He has received honoraria or stipends for lectures or administrative work from the International Parkinson's Disease and Movement Disorders Society. Dr. Jinnah serves on the Scientific Advisory Boards for several private foundations including the Benign Essential Blepharospasm Research Foundation, Cure Dystonia Now, the Dystonia Medical Research Foundation, the Tourette Association of America, and Tyler's Hope for a Cure. He also is principal investigator for the Dystonia Coalition, which has received the majority of its support through the NIH (grants NS116025, NS065701 from the National Institutes of Neurological Disorders and Stroke TR 001456 from the Office of Rare Diseases Research at the National Center for Advancing Translational Sciences). The Dystonia Coalition has received additional material or administrative support from industry sponsors (Allergan Inc. and Merz Pharmaceuticals) as well as private foundations (The Benign Essential Blepharospasm Foundation, Cure Dystonia Now, The Dystonia Medical Research Foundation, and The National Spasmodic Dysphonia Association). Angelo F. Gigante, E. Moukheiber, T. Ercoli, T. Baumer, A. Berardelli, G. Defazio, and G. Ferrazzano report no disclosures. ■

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