Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Development of a Clinical Rating Scale for the Severity of Apraxia of Eyelid Opening, Either Isolated or Associated with Blepharospasm

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ABSTRACT: Background: Apraxia of eyelid opening is a movement disorder characterized by an inability to raise the eyelids without any overt contractions of the orbicularis oculi muscle. There is currently no clinical scale to rate the severity of this condition.

Objectives: To develop and validate a novel scale that considers phenomenological aspects relevant to the severity of the condition.

Methods: The study sample included 20 patients with apraxia of eyelid opening, either isolated (9 patients) or associated with blepharospasm (11 patients). To validate the scale, selected features were checked for reliability, reliable items were combined to generate the scale, and clinimetric properties were evaluated.

Results: The novel severity scale yielded acceptable reliability, scaling assumptions, internal consistency, and sensitivity to change; a lack of floor and ceiling effects; and no correlation with the blepharospasm severity rating scale.

Conclusions: We propose a severity scale that considers the most relevant apraxia of eyelid opening motor abnormalities based on objective criteria. This scale can be reliably administered by general neurologists after a brief training.

Apraxia of eyelid opening (AEO) is a disorder characterized by transient difficulty in initiating the act of lid elevation after voluntary or involuntary lid closure.[1–3] The transient inability to raise the eyelids is typically associated with a lack of visible contraction of the orbicularis oculi (OO) muscle.[1,2] This condition is also associated with compensatory frontalis muscle hyperactivity, which helps counteract the inability to raise the eyelids.[1] Two forms of AEO with different physiological mechanisms are currently recognized. One form is attributed to the involuntary inhibition of the levator palpebrae superioris muscle, whereas the other is attributed to involuntary contractions of the pretarsal portion of the OO muscle.[1–4] Based on the neurophysiological findings reported in these patients, some authors have suggested that AEO is a form of dystonia.[4–6]

AEO may manifest as an isolated condition or in association with other movement disorders, including blepharospasm (BSP).[3,4,7] The frequency of lid closure episodes may be affected by conditions that worsen or improve dystonic spasms, such as stress, voluntary/involuntary OO muscle contractions, or attention-demanding tasks such as writing or speaking.[1,3,4] In addition, sensory trick, a highly specific feature of dystonia, has been documented in both patients with AEO associated with BSP[4,5] and in patients with isolated AEO.[3] The interference of AEO with normal lid opening and vision may adversely affect activities of daily life. A clinical improvement in AEO attributed to involuntary tonic contraction of the pretarsal portion of the OO can now be obtained with the pretarsal injection of botulinum toxin

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(BoNT).[8,9] However, because there is no clinical scale for rating AEO severity, clinical evaluation of the condition is challenging. Similarly, it is difficult to evaluate BoNT effects. In this study, we developed and validated a novel scale to rate AEO severity that may be useful in evaluating severity and treatment efficacy in patients with isolated AEO or AEO associated with BSP.

Methods

The AEO Severity Scale (AEOSS) was developed and validated in a multistep procedure. In the first step, phenomenological AEO features potentially related to the severity of the condition were analyzed by the authors. Of note, the transient inability to reopen the eyes at will with the preserved ability to open them and keep them open at other times, which is the diagnostic criterion for AEO,[1,3,4] was not considered in our attempt to rate severity. Likewise, frontalis muscle hyperactivity during AEO episodes was considered a compensatory phenomenon counteracting the inability to raise the eyelids and was therefore not included in the severity assessment. Although the duration of AEO episodes may vary among patients and within the same patient,[1,3] the authors agreed that the duration and frequency of AEO episodes were objective clinical features reflective of the severity of the condition. Based on the duration of AEO-related eyelid closure in our population, the following 3 types of AEO episodes were identified: brief episodes lasting <3 seconds, intermediate episodes lasting 3 to 5 seconds, and prolonged episodes lasting >5 seconds. The authors also considered that AEO episodes may occur spontaneously, and the frequency of AEO-related lid closure episodes may be increased by voluntary/involuntary OO muscle contraction and reduced by attention-demanding tasks.[1,3,4] Therefore, the items we selected for inclusion in the scale were duration of AEO episodes categorized as brief, intermediate, or prolonged; frequency of AEO episodes as assessed by counting the number of AEO episodes during a given time; the occurrence of spontaneous AEO episodes and/or induction of AEO episodes by slight/forceful eye closure; and the occurrence of AEO during writing or speaking (Table 1). Because sensory trick may impact on the disability associated with the severity of this condition, we also included sensory trick among the scale items. Therefore, the items we selected for inclusion in the scale were duration of AEO episodes categorized as brief, intermediate, or prolonged; frequency of AEO episodes as assessed by counting the number of AEO episodes during a given time; the presence of effective sensory trick; the occurrence of spontaneous AEO episodes and/or induction of AEO episodes by slight/forceful eye closure; and the occurrence of AEO during writing or speaking (Table 1).

In the second step, the selected items were tested for interobserver and intraobserver reliability. To this aim, 21 Italian outpatients with AEO (12 women and 9 men aged 63 ± 12.3 years) were video recorded at least 4 months after the last BoNT injection according to a standardized video protocol that lasted approximately 5 minutes and reproduced all the aforementioned distinctive phenomenological features (Table 2). The number of AEO episodes during the last 120 seconds (while the patient was at rest with the eyes open) was counted to assess the frequency of AEO episodes.

Video recordings were reviewed by three movement disorder experts (G.D., G.F., and A.C.) and 1 general neurologist (A.M.) who did not know the patients. Before the study, the general neurologist received brief training on conditions characterized by transient involuntary bilateral eye closure, including BSP, blinking, and AEO. A sudden OO muscle contraction causing eyelid rim narrowing/closure associated with eyebrow lowering below the superior orbital margin was classified as an OO spasm; a bilateral, synchronous, short-duration (<1 second) OO muscle contraction causing a transient eyelid drop (without eyebrow movements) was considered a blink; and a delay in reopening the eyelids after involuntary closure associated with no overt OO contractions and the raising of the eyebrows above the superior orbital margin was considered AEO.[10] Video recordings of patients were also rated a second time by 1 of the neurologists 5 months later. Reliability was measured by κ statistics and the intraclass correlation coefficient as appropriate using Stata statistical software, version 11 (StataCorp, College Station, TX). $\kappa > 0.4$ and intraclass correlation coefficient > 0.75 indicated satisfactory agreement.[11,12]

In the third step, the items that achieved acceptable reliability were incorporated into the scale. We assumed that both duration

TABLE 1 Items included in the preliminary version of the Apraxia of Eyelid Opening Severity Scale: interobserver reliability (κ statistics) and item-to-total correlations (Spearman ρ)

Item	Interobserver Agreement (κ Value, *P*)	Item-to-Total Correlation, Spearman ρ
During the episodes of eye closure attributed to apraxia of eyelid opening, eyelid reopening is delayed by:		
<3 seconds	0.72, <0.0001	0.2
3 seconds to 5 seconds	0.74, <0.0001	0.53
>5 seconds	1.0, <0.0001	0.59
Apraxia of eyelid opening occurs:		
Spontaneously	0.65, 0.0001	0.77
After forceful voluntary lid closure	−0.02, 0.56	−0.08
After slight voluntary lid closure	0.61, 0.0005	0.36
Apraxia of eyelid opening occurs during:		
Writing	0.78, <0.0001	0.39
Speech	0.85, <0.0001	0.33
Effective sensory trick	0.71, <0.0001	0.44

TABLE 2 Standardized clinical examination and video protocol

1. Patient at rest, eyes open (10 seconds).
2. Patient voluntarily performs a forceful eye closure followed by eye reopening (repeated 5 times, 1 cycle/s).
3. Patient at rest, eyes open (10 seconds).
4. Voluntary gentle eye closure followed by eye reopening (repeated 5 times, 1 cycle/s).
5. Patient at rest, eyes open (10 seconds).
6. The physician asks the patient the following questions: Are you able to facilitate eye opening? How? By willpower alone? Or do you need to touch your eyes, face, or neck?
7. The patient answers the questions (at least 50 seconds).
8. The physician asks the patient to write a stereotyped sentence 3 times ("Today is a nice sunny day.").
9. Patient at rest, eyes open (at least 150 seconds). In the past 120 seconds, the number of apraxia of eyelid opening episodes is counted. Patients are instructed to avoid geste antagoniste.

TABLE 3 Apraxia of Eyelid Opening Severity Scale

Item	Scoring System
No apraxia of eyelid opening	0
Apraxia of eyelid opening	
(D1) is delayed by ≤5 seconds	1
(D2) Is delayed by >5 seconds	2
(F) Count number of episodes of apraxia of eyelid opening (last 2 minutes of the video recording, patient at rest, eyes open) and calculate the correspondent tertile:	
I tertile = 1–2/min	1
II tertile = 2.1–5/min	2
III tertile = >5 minutes	3
(G1) Apraxia of eyelid opening occurs	
Only after gentle voluntary lid closure	1
Spontaneously and after gentle voluntary lid closure	2
Apraxia of eyelid opening occurs	
(G2) During speech	1
(G3) During writing	1
(G4) Effective sensory trick:	
Yes	0
No	1

Total score: (D1 + D2) + F + G1 + (G2 + G3) + G4.

and frequency contribute to AEO severity. To rate duration, we first assigned a basic score to each type of AEO episode: prolonged episodes lasting >5 seconds were given higher basic scores than brief episodes lasting <3 seconds and intermediate episodes lasting 3 to 5 seconds. To rate frequency, we counted AEO episodes occurring during the last 120 seconds of the video recording. The number of AEO episodes was then transformed into tertiles obtained from the frequency distribution of the variable in the population being studied. Duration and frequency scores were graded whenever possible by other AEO-associated features, including effect of sensory trick, occurrence of spontaneous AEO episodes and/or induction of AEO episodes by gentle eye closure, and occurrence of AEO during writing and/or speaking. The total severity score was calculated by adding the subscores of all items (Table 3).

In the fourth step, we evaluated clinimetric properties of the scale, including item-to-total correlation,[13,14] internal consistency,[15] floor and ceiling effects,[16] and sensitivity to change. Because of the lack of other existing scales for rating AEO severity, we could not check for convergent validity. However, we assessed the correlation between the AEOSS and the Blepharospasm Severity Rating Scale (BSRS)[10] in the patients presenting with both AEO and BSP. All patients with AEO associated with BSP and 5 of 9 patients with isolated AEO underwent BoNT treatment. However, only 10 of these patients (4 with isolated AEO and 6 with AEO and BSP) were reevaluated 1 month after BoNT treatment. The study was approved by the institutional review board, and all patients provided written informed consent.

Results

Study Population

A total of 20 patients participated in the study, of which 9 had isolated AEO and 11 had AEO and BSP. Regarding the duration of AEO-related eyelid closure, brief episodes lasting <3 seconds were present in all patients except 1, intermediate episodes lasting 3 to 5 seconds were present in 7 patients, and prolonged episodes lasting >5 seconds were present in 4 patients. Stratification of the number of AEO episodes counted during the last video segment into tertiles yielded 6 patients in the first tertile (1–2 episodes/min), 9 patients in the second tertile (2.1–5 episodes/min), and 3 patients in the third tertile (>5 episodes/min). Tactile sensory trick was effective in reducing AEO duration in 7 patients. Regardless of duration and frequency, AEO manifested either spontaneously or after gentle eye closure in 9 patients, and both spontaneously and after voluntary gentle eye closure in 12 patients. Finally, AEO episodes were observed during writing in 3 patients, during speech in 1 patient, and during both writing and speech in 1 patient.

Interrater and Intrarater Reliability of the Items

The 4 observers yielded satisfactory interobserver reliability ($\kappa > 0.4$) on the following items: duration of AEO episodes, occurrence of spasms during writing and speaking, presence of sensory trick, and occurrence of AEO episodes either spontaneously or after gentle voluntary eye closure (Table 1). Likewise, the number of AEO episodes in the last 2 minutes of the video recording reached satisfactory reliability (intraclass correlation coefficient > 0.81). In contrast, AEO occurring after forceful voluntary eye closure yielded unsatisfactory interobserver reliability (Table 1) and was therefore excluded from the final version of the AEOSS. Repeat rating yielded acceptable intrarater reliability for all items ($\kappa > 0.73$).

Scale Generation and Clinimetric Properties

The initial version of the scale included both duration and frequency as items reflective of AEO severity. Duration and frequency scores were graded whenever possible by occurrence of spontaneous AEO episodes and/or induction of AEO episodes by eye closure, occurrence of AEO during writing and/or speaking, and effect of sensory trick.

Based on the assigned scoring system (Table 3), most items achieved an item-to-total correlation greater than the criterion 0.30 (Table 1). Only "AEO occurrence after forceful voluntary lid closure" and "brief AEO episodes" yielded weak scaling assumptions (Table 1). Therefore, these 2 items were not included in the final version of the scale.

In the 20 patients, the final version of the AEOSS yielded a mean total severity score of 5.2 (range, 3–8; standard deviation, 1.6). No patient reached the theoretical minimum or maximum score values (a score of 2 or 10, respectively). The minimum and maximum scores we observed in this population were obtained by 4 patients and 2 patients, respectively. Assessing the internal consistency of the AEOSS yielded a satisfactory Cronbach's α value (0.75). No significant correlation was found between total severity score and age or disease duration (data not shown). No correlation emerged between the AEOSS and BSRS in the 10 patients who manifested both AEO and BSP ($\rho = -0.1$, $P = 0.8$); the finding was confirmed even when a BSRS item relative to the presence of AEO was omitted from analysis ($\rho = -0.1$, $P = 0.8$). Finally, comparison of the total severity score before and after BoNT treatment in 10 patients (4 with isolated AEO and 6 with AEO and BSP) showed a significant 38% decrease in the AEOSS score after BoNT (5.2 ± 1.7 vs. 3.2 ± 2.3, $P = 0.004$).

Discussion

In this article, we discuss the development and validation of a novel scale for rating AEO severity. We first identified clinical features potentially relevant in scoring AEO severity. Thereafter, selected items were checked for reliability, reliable items were combined to generate the scale, and clinimetric properties were evaluated.

Among the clinical items potentially useful in rating AEO severity, 5 contributed to the final version of the scale. Duration and frequency of AEO-related eyelid closure are the core clinical hallmarks of AEO severity, whereas occurrence of AEO episodes spontaneously and/or after gentle voluntary eye closure, occurrence of AEO during writing/speaking, and effective sensory trick may be useful features to grade clinical severity. The items included in the final version of the scale were reliable and had satisfactory scaling assumptions.[13,14] The item "brief AEO episodes" had a weak scaling assumption and was therefore excluded. Likewise, the item "AEO occurring after forceful voluntary eye closure" yielded both unsatisfactory reliability and a weak scaling assumption and was therefore not considered in the final scale. The weakness of this item probably reflected confounding by the OO spasms that voluntary forceful eye closure can elicit in patients with both AEO and BSP (52% of study participants).

Internal consistency was acceptable for the present scale, which has a relatively small number of items, particularly when considering that Cronbach's α is also dependent on the number of items.[15] The lack of participants with a total score near the bottom or top of the scale also ruled out floor and ceiling effects. In patients manifesting both AEO and BSP, we did not find any correlation between the AEOSS and BSRS. This indicates that the present scale explores domains that are not considered in the BSRS. Furthermore, although the BSRS contains an item assessing the presence of AEO,[10] our results did not change when this item was omitted.

Because of the lack of other scales for rating AEO severity, we could not assess the convergent validity of the present scale. The comparison of total severity scores at baseline and 4 weeks after BoNT treatment likely reflects the sensitivity to change of the AEOSS. The 38% decrease in AEOSS score after BoNT treatment likely indicates a reduced response of patients with AEO to BoNT treatment compared with patients with BSP, in whom a more marked amelioration of symptoms is often reported.[8,9,17] In this regard, AEO and BSP may coexist in some patients, although different pathophysiological mechanisms underlie involuntary inhibition of the levator palpebrae superioris muscle and involuntary contractions of the pretarsal portion of the OO muscle. Indeed, AEO attributed to involuntary levator palpebrae inhibition shows less response to BoNT than AEO as a result of pretarsal OO overactivity and BSP.[8,9,17]

The scale also contains other advantageous features. Selected items can be easily administered and measured during a brief clinical examination lasting approximately 5 to 10 minutes. Because of the variable duration of AEO episodes in different patients or within the same patient over time, we were aware that any stratification of AEO duration would be arbitrary. The final scale distinguished brief/intermediate (≤5 seconds) and prolonged (>5 seconds) AEO episodes, an approach that likely reflects the AEO severity spectrum as well as clinimetric assessment. Some AEO-associated features were included in the scale as further clinical determinants of severity.

The present study has limitations, the most relevant of which is probably the small sample size. However, AEO is a rare condition that manifests as an isolated entity or in association with other conditions, including BSP.[2–4,18] We developed a scale for patients with isolated AEO or AEO associated with BSP. Because of the small size of the subsamples, we could not provide a stratified analysis to separately assess patients with isolated AEO and AEO associated with BSP. Nevertheless, we considered the selected scale items to be applicable to both isolated AEO and AEO associated with BSP. In addition, the lack of correlation between the AEOSS and BSRS in patients manifesting both AEO and BSP excluded confounding by patients with BSP. In designing the scale, we did not consider the inability to read or watch television or other functional disability items

attributed to AEO because such features are more likely consequences rather than determinants of AEO severity. The score distribution in the study sample did not consider the complete range of total scoring because we did not have patients scoring the highest 2 points. This may suggest that the study sample was not completely representative of all severity stages. To score the upper 2 points, patients would need to manifest all types of AEO episodes and almost all determinants of severity. Although these patients are not frequent, the scale we propose would theoretically detect even these severe forms of AEO. Because some authors[4–6,19,20] have suggested that AEO is a dystonia of the pretarsal portion of the OO muscle, future studies may also include electromyography recordings of the levator palpebrae superioris and the OO muscles to better characterize patients.

In conclusion, we propose a severity scale that considers some relevant aspects of AEO abnormalities; is based on objective criteria; and yields acceptable reliability, scaling assumptions, internal consistency, sensitivity to change, lack of floor and ceiling effects, and no correlation with the BSRS. A further advantage is that the scale can be reliably administered by general neurologists after a brief training on the most common forms of transient bilateral involuntary eye closure conditions. Because of the size and composition of the study sample, the proposed scale needs to be validated in a larger sample spanning the entire clinical spectrum of AEO (including AEO associated with parkinsonism in addition to isolated AEO and AEO associated with BSP). A modified Delphi approach might be appropriate to better identify phenomenological aspects possibly related to the severity of AEO associated with parkinsonism. However, this is the first attempt to design a multi-item tool assessing the severity of this rare condition. Future multicenter collaborations are needed to refine and validate the scale in a larger sample of patients with AEO in different clinical settings.

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.

G. Ferrazzano: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B
A. Muroni: 1C, 2B, 2C, 3A, 3B
A. Conte: 1A, 1B, 2A, 2B, 2C, 3A, 3B
T. Ercoli: 1C, 2B, 2C, 3A, 3B
G. Tamburini: 1C, 2B, 2C, 3A, 3B
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Disclosures

Ethical Compliance Statement: The experimental procedure was conducted in accordance with the Declaration of Helsinki and was approved by the local institutional review board. All participants signed a written informed consent form. All authors confirm that they have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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