Objective Measures of Dystonia Motor Symptoms

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Quantifying motor symptom severity from videorecordings

Overarching Goal:
Objectively measure severity of motor symptoms in isolated dystonia

Scope:
- blepharospasm (BSP)
- cervical dystonia (CD)
- laryngeal dystonia (LD)

Overall Approach:
- Develop software that recognizes motor abnormalities using video recordings (“CMOR”, the Computational Motor Objective Rater)
- Test CMOR’s convergent validity with clinical ratings of severity
Why a focus on motor symptoms?

Motor severity

- Disability
- Pain

Quality of Life
Why is it important to measure severity?

- epidemiological data
- research into mechanisms
  (imaging, neurophysiology, histopathology, genetics)

- Natural history (progression, spread)

- **Clinical trials**: pre-/post-treatment
  (new oral meds?, DBS, BoNT, rTMS, etc.)
How is severity currently measured?: clinical rating scales (CRS)

- Most clinical rating scales:
  - map descriptions to numbers:
    (none = 0, mild = 1, moderate = 2, severe = 3, etc.)

- are based on human judgement, i.e. subjective
  - Some trials exhibit improvements in objective measures but not with CRSs (Ralf Reilmann, MDS 2018)

- Concerns about intra- and inter-rater reliability
  - The issue isn’t accuracy per se, but consistency (subjective isn’t wrong, just highly variable)
Distribution of subjective and objective severity measure use: an example

(review of 73 publications on musician’s FHD that quantified motor symptoms)

Peterson et al. 2013 Neurol

(see also Morris 2018 Mov Disord: acoustics for embouchure)
Why video? 
(vs. kinematics, EMG, etc.)

• Clinical utility
  • Minimal additional resource requirements
    • equipment
    • expertise
    • time
  • Pervasive in movement disorders

• Less physically obtrusive 
  (vs. markers, EMG electrodes, etc.)
  • minimize observer effect!

• Obvious extension to mobile platforms
BSP: eye closure

Objective, computerized video-based rating of blepharospasm severity

Neurology 2016

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Marian S. Bartlett, PhD
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ABSTRACT

Objective: To compare clinical rating scales of blepharospasm severity with involuntary eye closures measured automatically from patient videos with contemporary facial expression software.

Methods: We evaluated video recordings of a standardized clinical examination from 50 patients with blepharospasm in the Dystonia Coalition’s Natural History and Biorepository study. Eye closures were measured on a frame-by-frame basis with software known as the Computer Expression Recognition Toolbox (CERT). The proportion of eye closure time was compared with 3 commonly used clinical rating scales: the Burke-Fahn-Marsden Dystonia Rating Scale, Global Dystonia Rating Scale, and Jankovic Rating Scale.

Results: CERT was reliably able to find the face, and its eye closure measure was correlated with all of the clinical severity ratings (Spearman $\rho = 0.56$, 0.52, and 0.56 for the Burke-Fahn-Marsden Dystonia Rating Scale, Global Dystonia Rating Scale, and Jankovic Rating Scale, respectively, all $p < 0.0001$).
Convergent validity with clinical ratings (BFM, GDRS, JRS)
BSP: beyond eye closure
(with Brian Berman and Mark Hallett)

- Blinks
- Spasms (of various duration)
- Apraxia of eyelid opening

A neural network-based software to recognise blepharospasm symptoms and to measure eye closure time

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(N = 9)
BSP: spasms

The three major features of BSP: excessive blinking, spasms of the orbicularis oculi (OO) and other periocular muscles, and apraxia of lid opening (ALO; defined below) – are included as separate items for the BSP Severity Rating Scale (BSRS; Defazio 2015). It was developed and validated with a separate cohort of 70 BSP patients. In brief, blinks are defined as movement limited to the eyelid, do not involve the orbital portion of the OO or other surrounding muscles, and are normally very short. Spasms are defined as complete or partial lid narrowing with accompanying evidence of activation of additional facial muscles beyond the pre-tarsal OO, as evidenced by additional movements of other regions of the face during eye closures, such as downward movement of the eyebrow or upward movement of the lower eye region, often leading to either a squinting or “squinching” appearance (see Fig. 6). The severity rating is based on the duration and intensity of spasms. ALO is defined as failure of eye opening, despite voluntary attempts to open the eyes, as evidenced by delayed eyelid opening combined with frontalis muscle activation and corresponding upward movement of the eyebrow (see Fig. 7) or use of the fingers or a “sensory trick” to open the eyes.

We have constructed provisional “event detectors” for each of the 3 BSP features with simple heuristics based on the operational definitions in the BSRS and the BSRS training videos. Briefly, blinks will be detected as eye closures identical to our previous report on CERT and eye closure in BSP (Peterson 2016), but excluding periods with simultaneous spasms or ALO. Spasms will be defined as reduced eye opening (a lower threshold for closure than used for full blinks) in Fig. 6.
**BSP: apraxia of lid opening**

The basic template for our approach is depicted in Fig. 5. For each **Aim**, we will evaluate our computational video-based metrics' diagnostic accuracy by testing our hypothesis that the metrics can distinguish the two groups. We should make clear that we are not trying to determine which is more accurate – the CMOR category or the clinical category. Indeed, there is no ground truth or gold standard method for diagnosing BSP.

**BSP “features”**

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CD: capturing head posture
(with Cindy Comella and Glenn Stebbins)

from Figure 1, Storer et al. 2009
CD: BoNT treatment sensitivity

Head pose dynamics before (left), and four weeks after (right), BoNT (angle, zero-meaned).

[Patient Anonymous 2, frames 300:489 and 1876:2065]
Head tremor in CD

(Qiyu Chen, Jeanne Vu)
CD: Capturing head tremor severity

$r^2 = 0.45, p < 0.001$

$\rho = 0.67, \text{Spearman's } p\text{-val} < 0.001$

$N = 75$

$\text{(step } = \text{driftHead, } MDT_p = 5.0)\text{.}$

Vu et al, MDS-PAS Abstract, 2020
The “sensory trick” in CD

(Elizabeth Cisneros)

... can transiently normalize head posture:

images from video frames taken at 670 msec intervals (frames 16000, 16020, 16040, and 16060);  Patient TWSTRS SUBJ 3
Sensory trick clinical ratings are so.... tricky

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Video Ratings Reverse and Correct Scoring

Cisneros et al. (under review)
Capturing the sensory trick efficacy with CMOR

**Metric Stats:**
- Slope = -0.09
- CI is -0.12 : -0.06
- $R^2 = 0.346$
- $p < 0.001$
- $\rho = -0.55$, $p < 0.001$
- $N = 69$
LD: is severity evident in vocal fold dynamics (as seen in nasolaryngoscopic videos)?

(with Gerald Berke and Abie Mendelsohn)
Broader Relevance and future directions

Subtyping:
- CD: “jerky” vs. “regular” tremor
  (ET consensus definition took 6 years)
- LD: ADSD v. ABSD ? tremor?

Basic research on mechanisms
- more temporally precise motor correlates?
- genotyping ←——→ phenotyping

Telemedicine and mobile implementation
- Including integration with PCO initiatives
Collaborators and Sponsors

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DoD CDMRP
Thank you