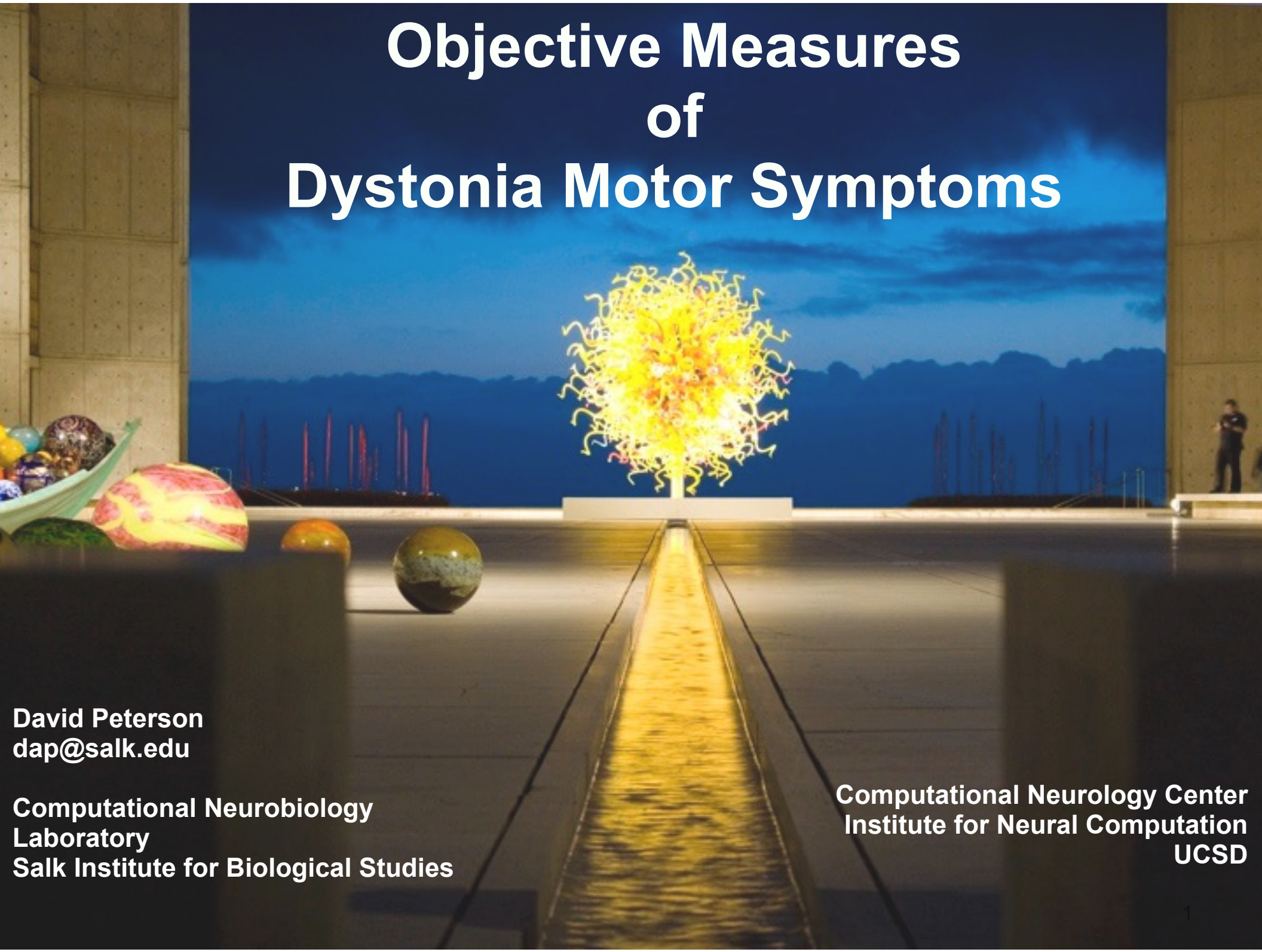
Objective Measures of Dystonia Motor Symptoms



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Quantifying motor symptom severity from videorecordings

Overarching Goal:

Objectively measure severity of motor symptoms in isolated dystonia

Scope:

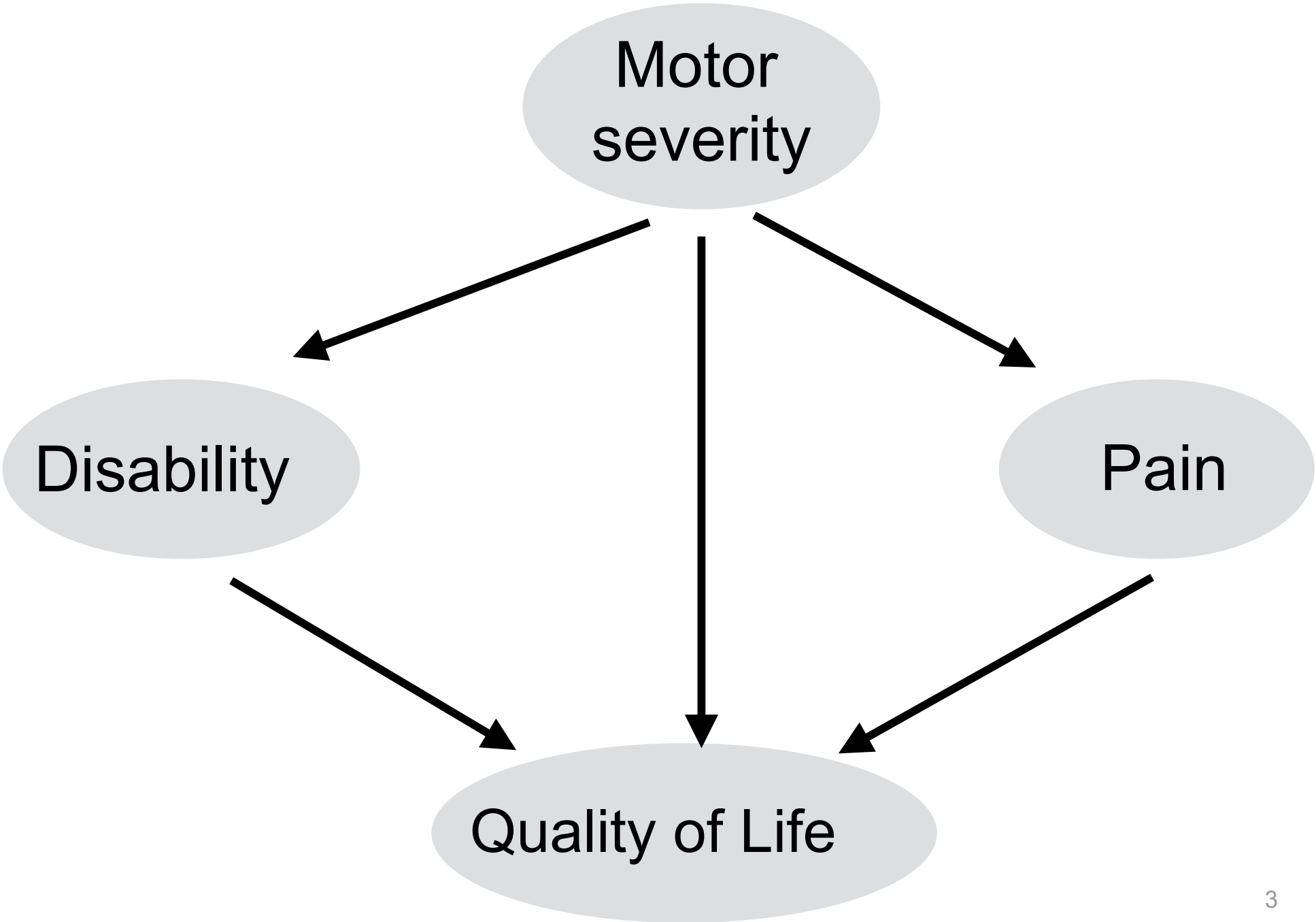
- blepharospasm (BSP)
- cervical dystonia (CD)
- laryngeal dystonia (LD)

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?



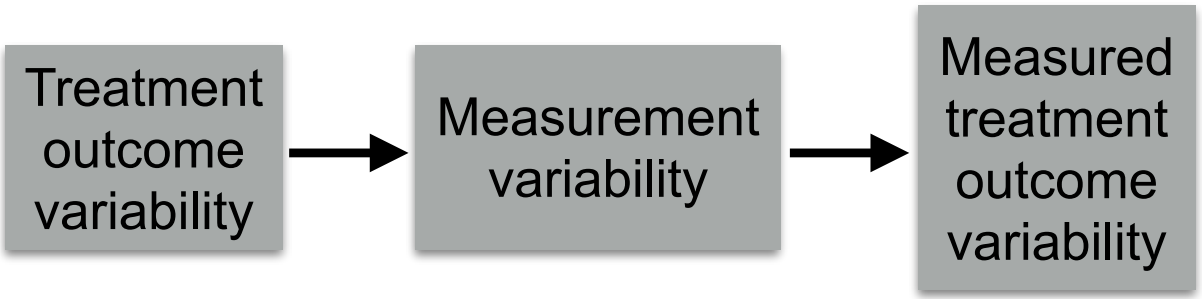
Why is it important to measure severity?

- 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)

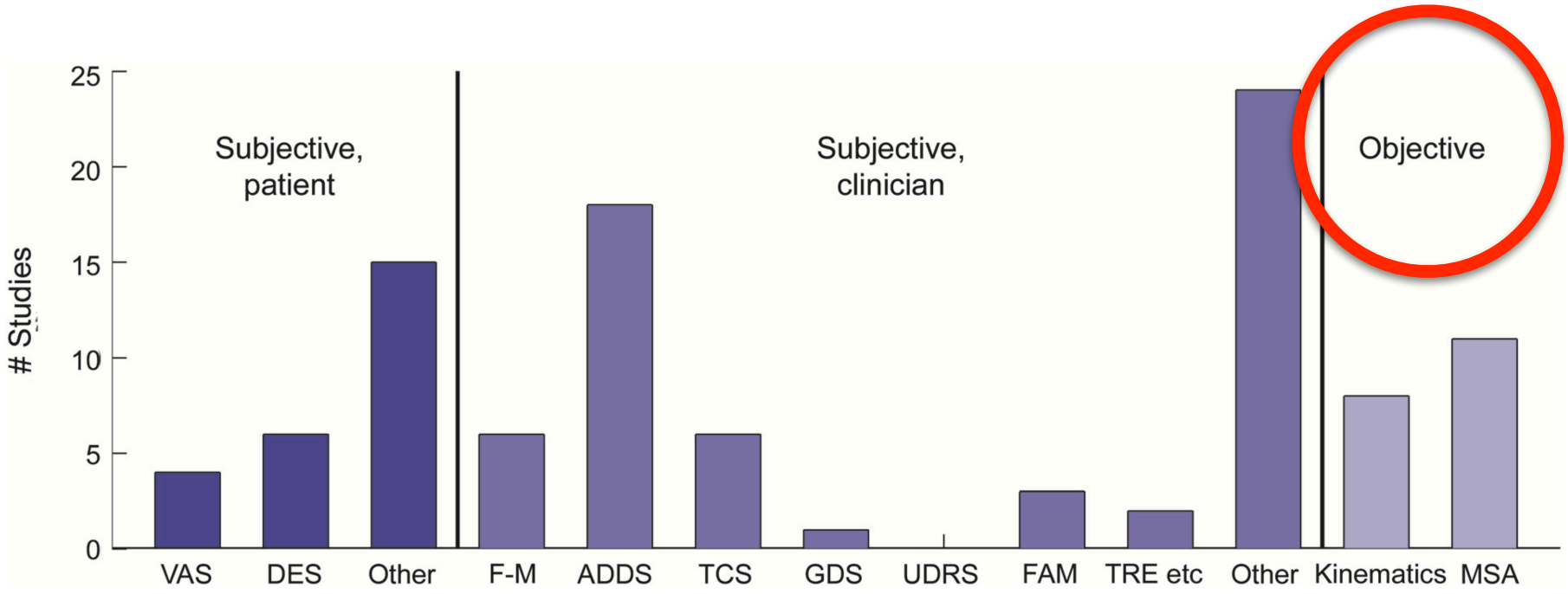
- Most clinical rating scales:
  - map descriptions to numbers:
    (none = 0, mild = 1, moderate = 2, severe = 3, etc.)

  - 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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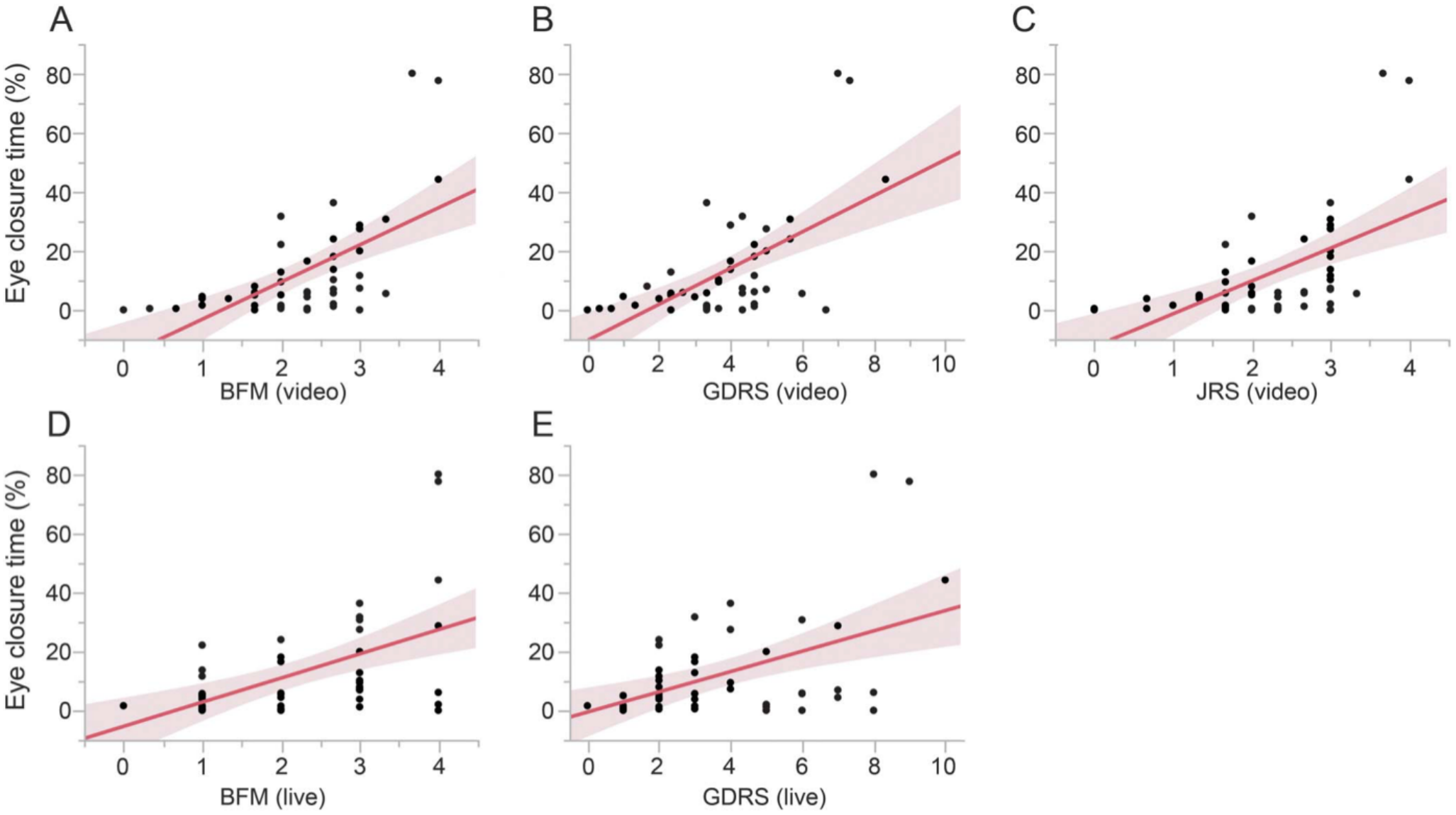
ABSTRACT

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)

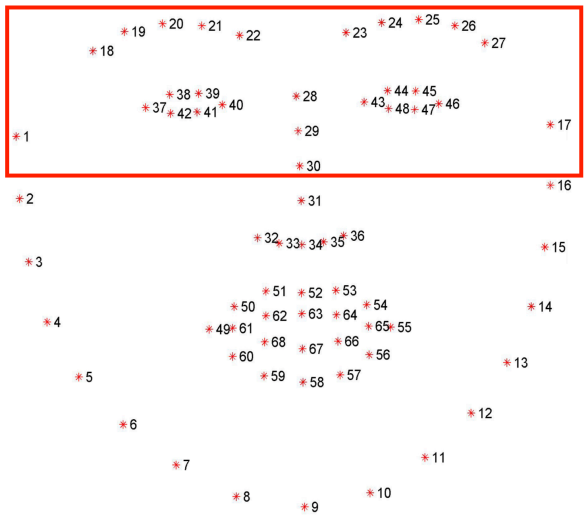


Peterson et al. 2016 Neurology

BSP: beyond eye closure

(with Brian Berman and Mark Hallett)

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



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

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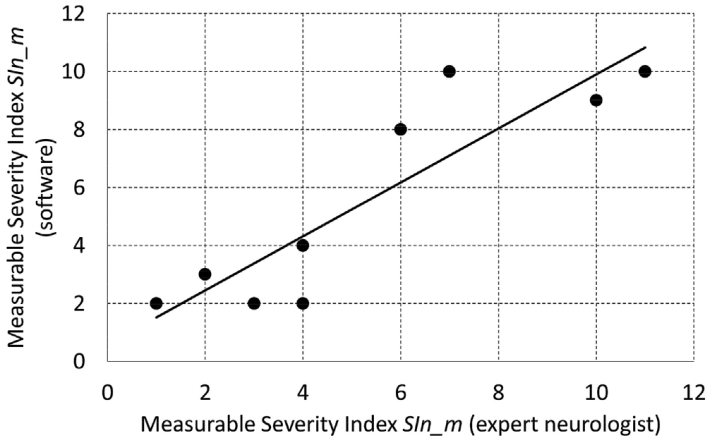
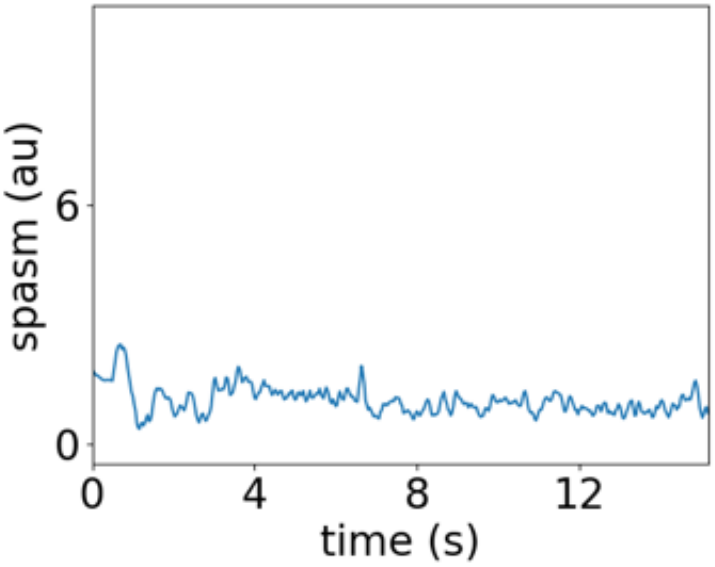
(N = 9)

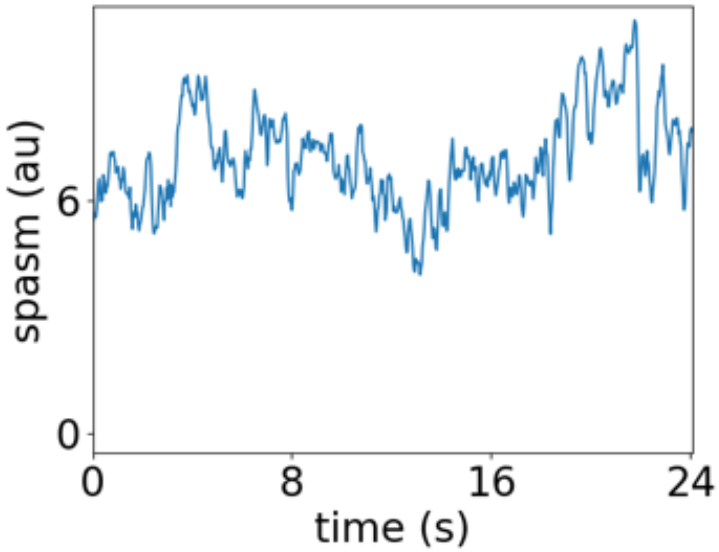


BSP: spasms

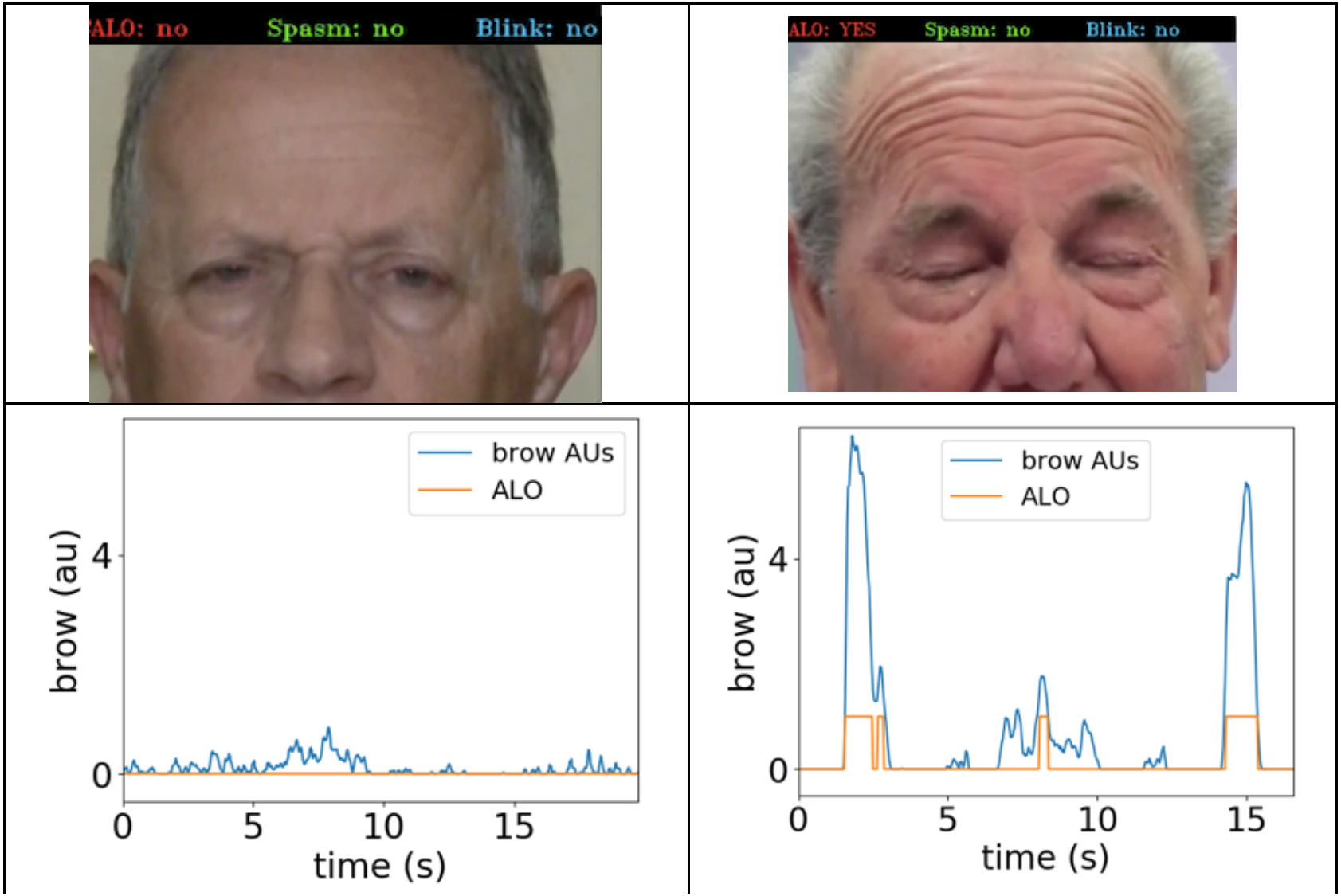

ALO: no
Spasm: no
Blink: no


ALO: no
Spasm: YES
Blink: no


spasm (au)
6
0
0
4
8
12
time (s)

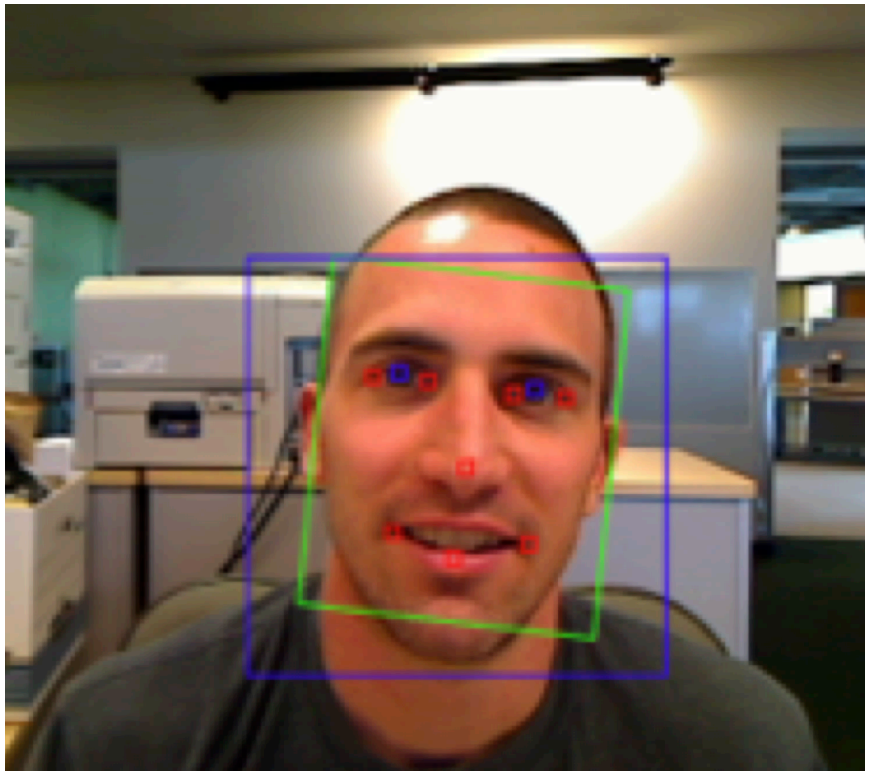

spasm (au)
6
0
0
8
16
24
time (s)

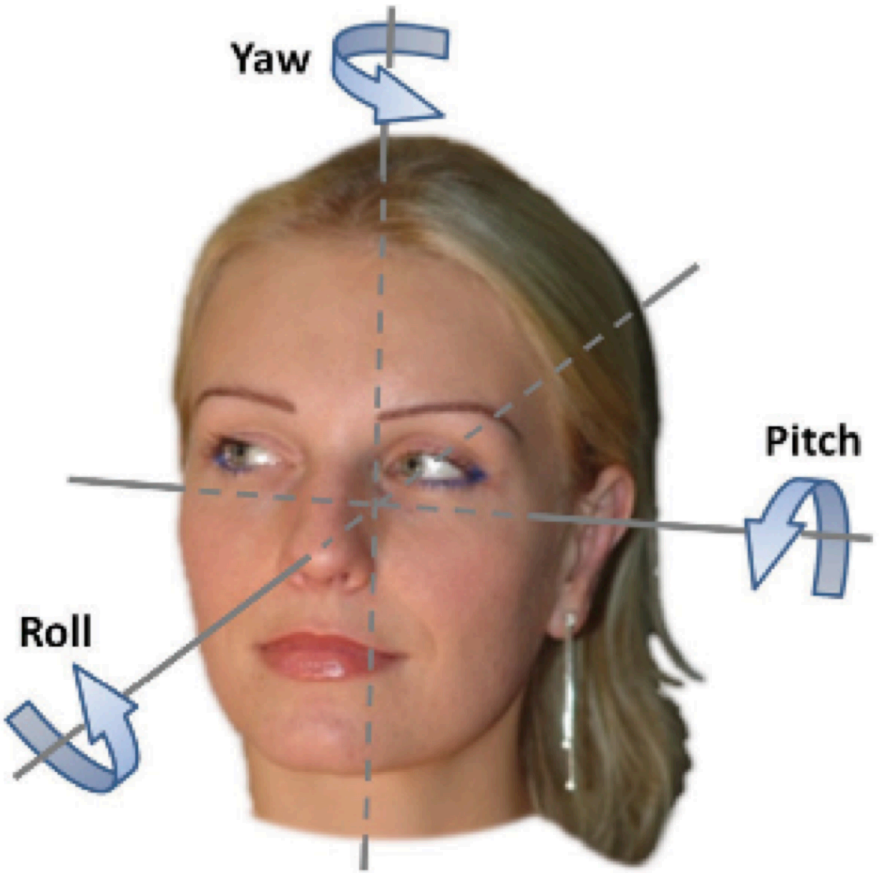
BSP: apraxia of lid opening



CD: capturing head posture

(with Cindy Comella and Glenn Stebbins)



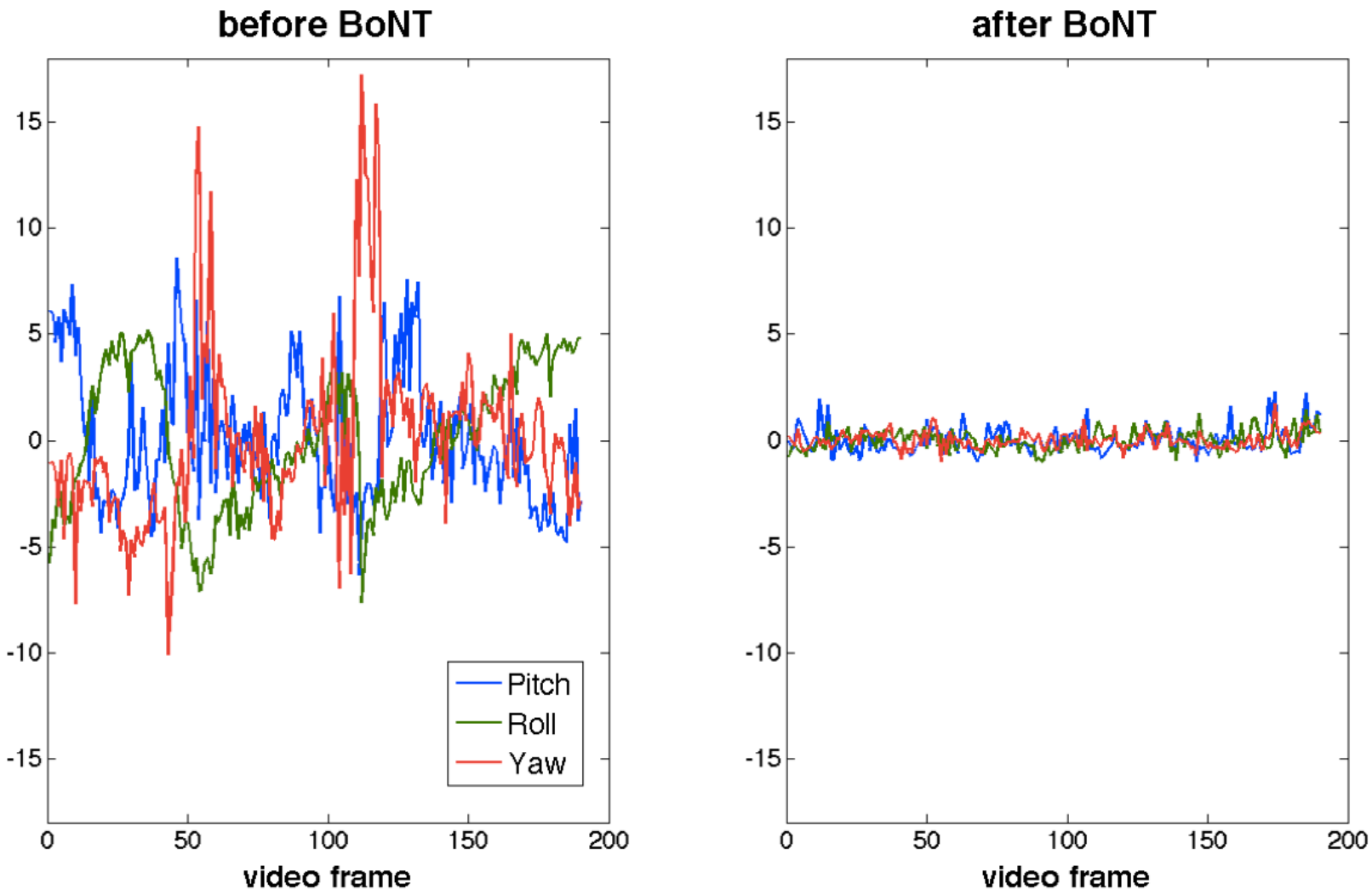


anterocollis / retrocollis	pitch
laterocollis	roll
horizontal rotation	yaw

from Figure 1, Storer et al. 2009

CD: BoNT treatment sensitivity

CMOR

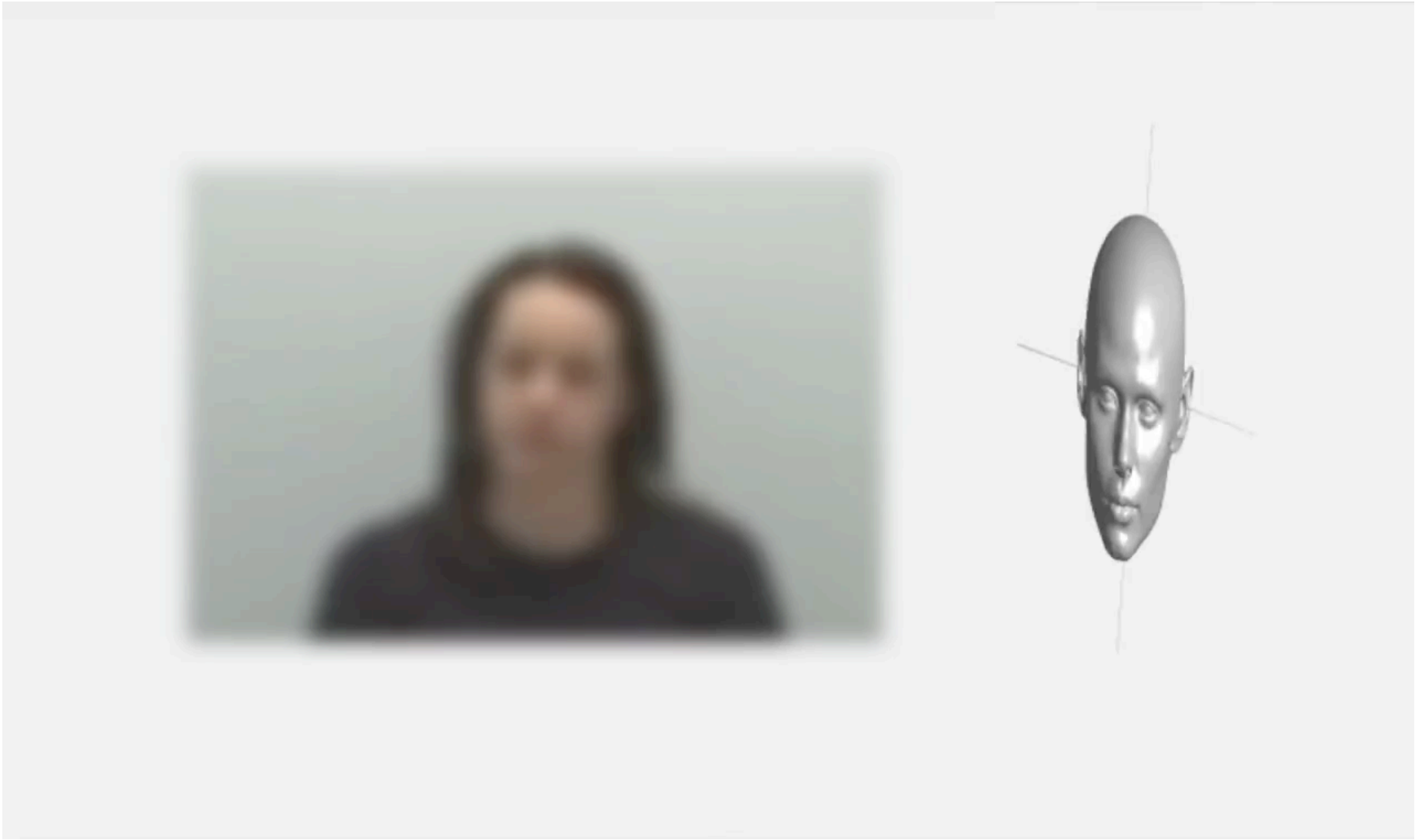


Head pose dynamics before (left), and four weeks after (right), BoNT (angle, zero-meaned).

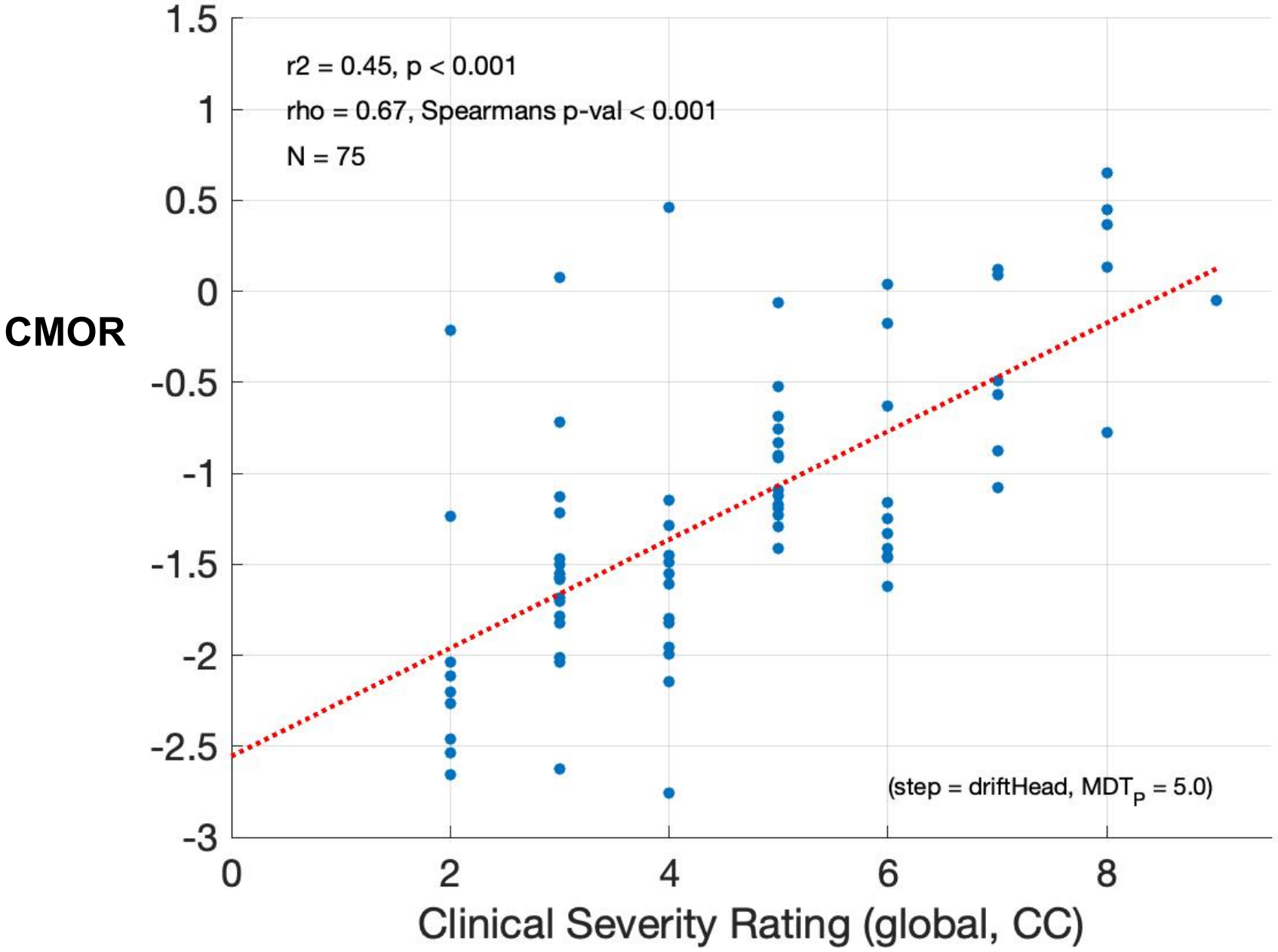
[Patient Anonymous 2, frames 300:489 and 1876:2065]

Head tremor in CD

(Qiyu Chen, Jeanne Vu)



CD: Capturing head tremor severity

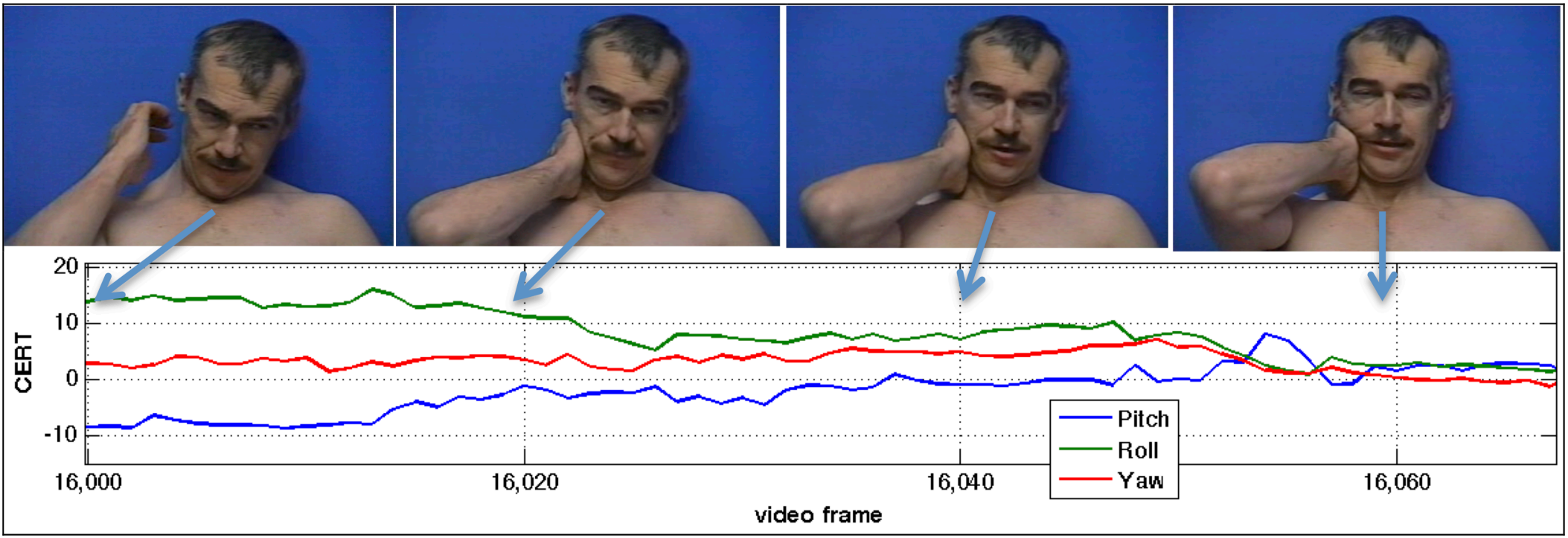


Vu et al, MDS-PAS Abstract, 2020

The “sensory trick” in CD

(Elizabeth Cisneros)

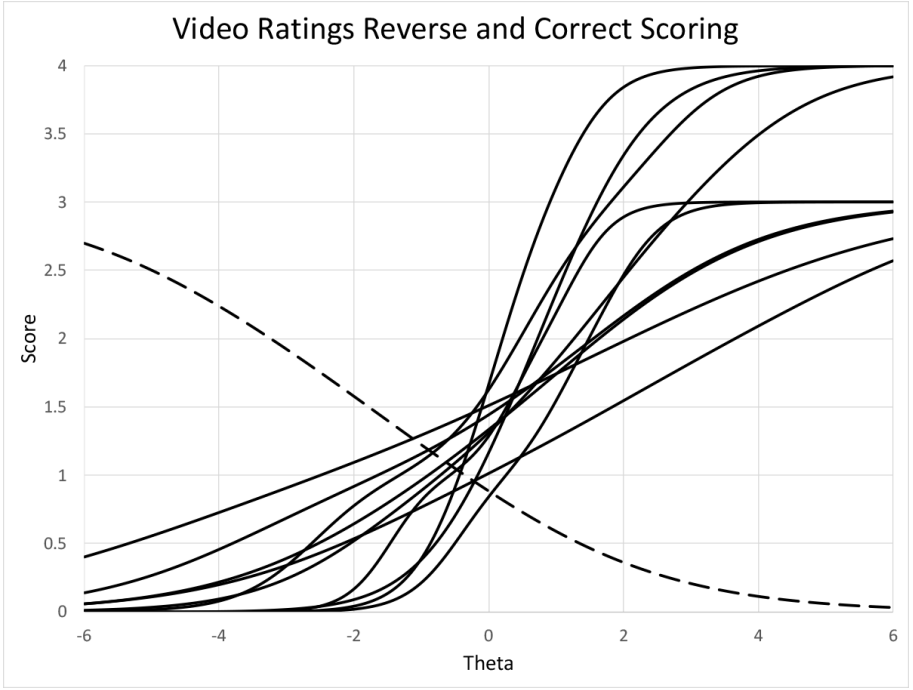
… can transiently normalize head posture:

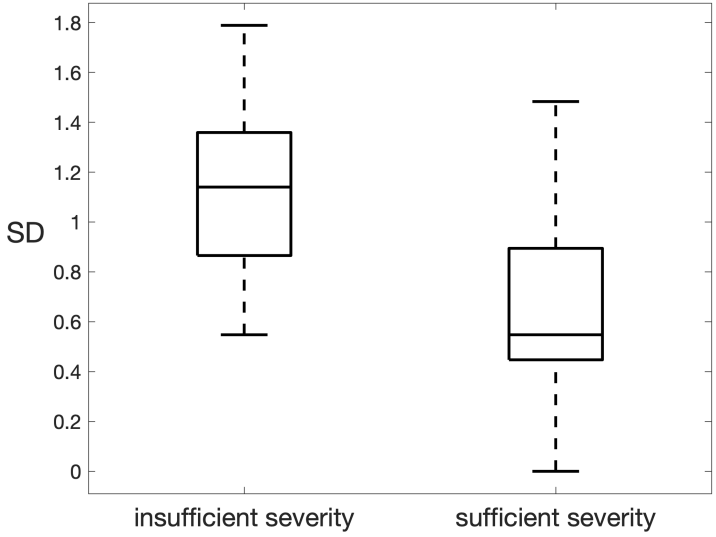


images from video frames taken at 670 msec intervals (frames 16000, 16020, 16040, and 16060); *Patient TWSTRS SUBJ 3*

Sensory trick clinical ratings are so…. tricky

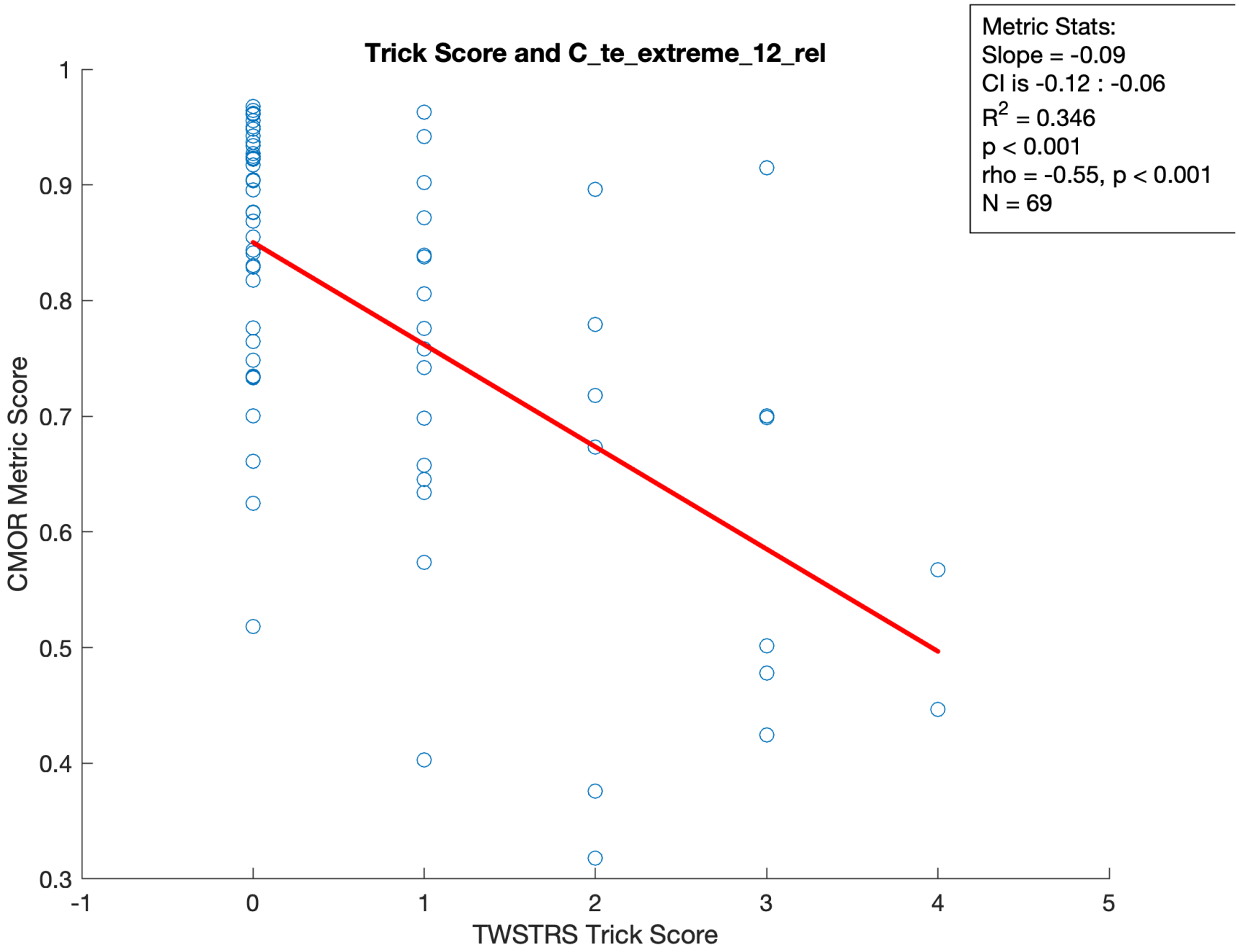
patient:	score_1	score_2	score_3	score_4	score_5
1	4	4	0	0	4
2	0	0	1	0	0
3	2	2	1	1	1
4	1	2	1	2	1
5	0	1	0	1	2
6	3	2	0	0	4





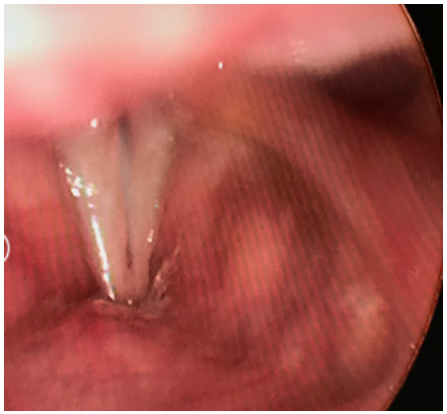
Cisneros et al. (under review)

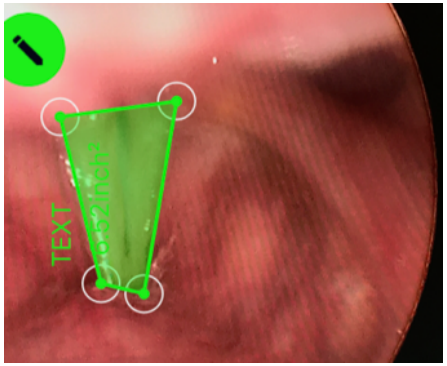
Capturing the sensory trick efficacy with CMOR

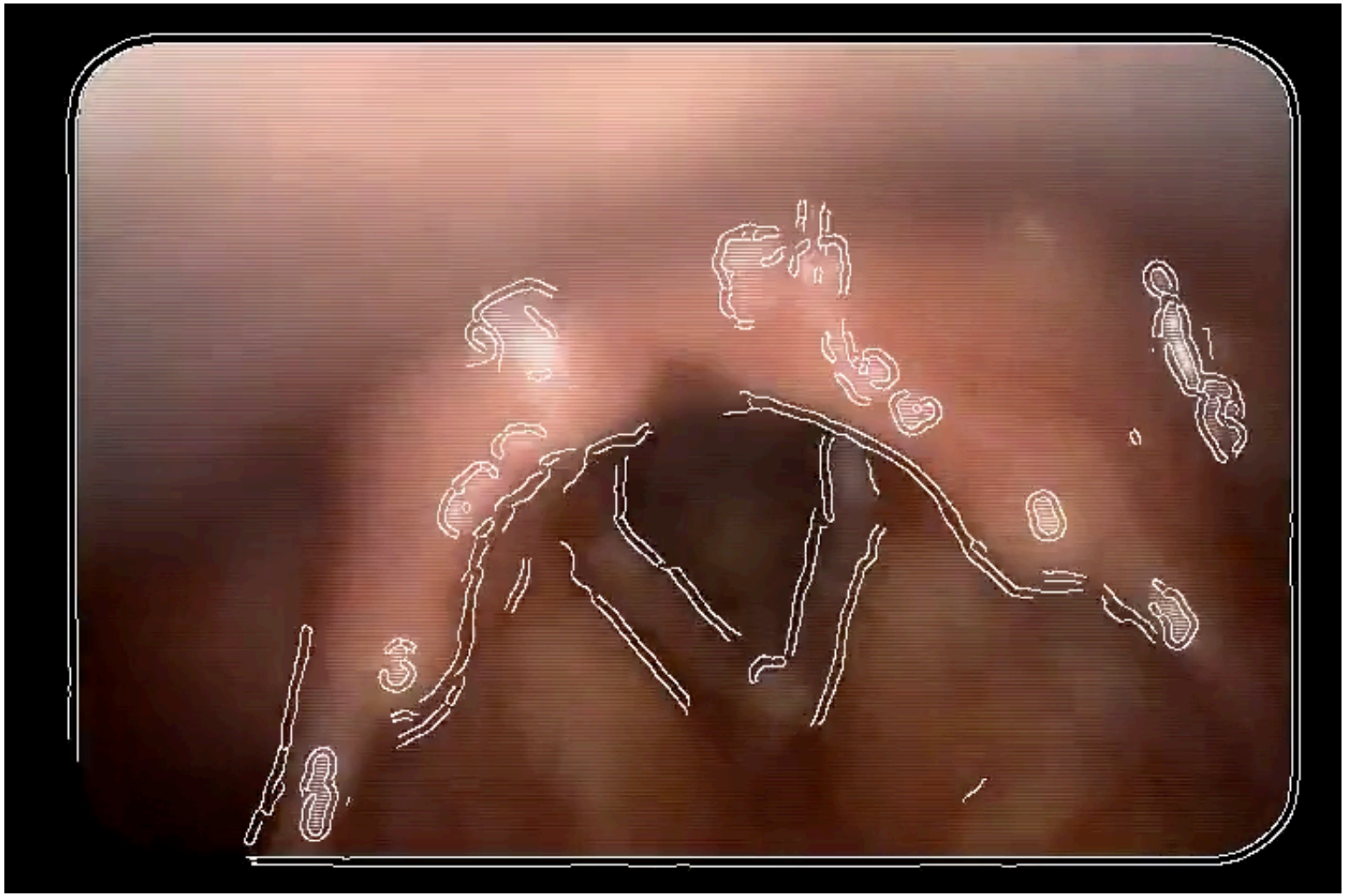


LD: is severity evident in vocal fold dynamics (as seen in nasolaryngoscopic videos)?

(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

Buz Jinnah, Emory

Joel Perlmutter and Jo Wright, WUSTL

Mark Hallett, NINDS

Giovanni Defazio, Antonella Macerollo U Bari

Marni Bartlett, Apple

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Jake Whitehill, Worcester Polytechnic

Cindy Comella, Glenn Stebbins Rush University Medical Center

Brian Berman, U Colorado

DMRF

Dystonia Coalition

NIH NCATS (U54-NS11602)

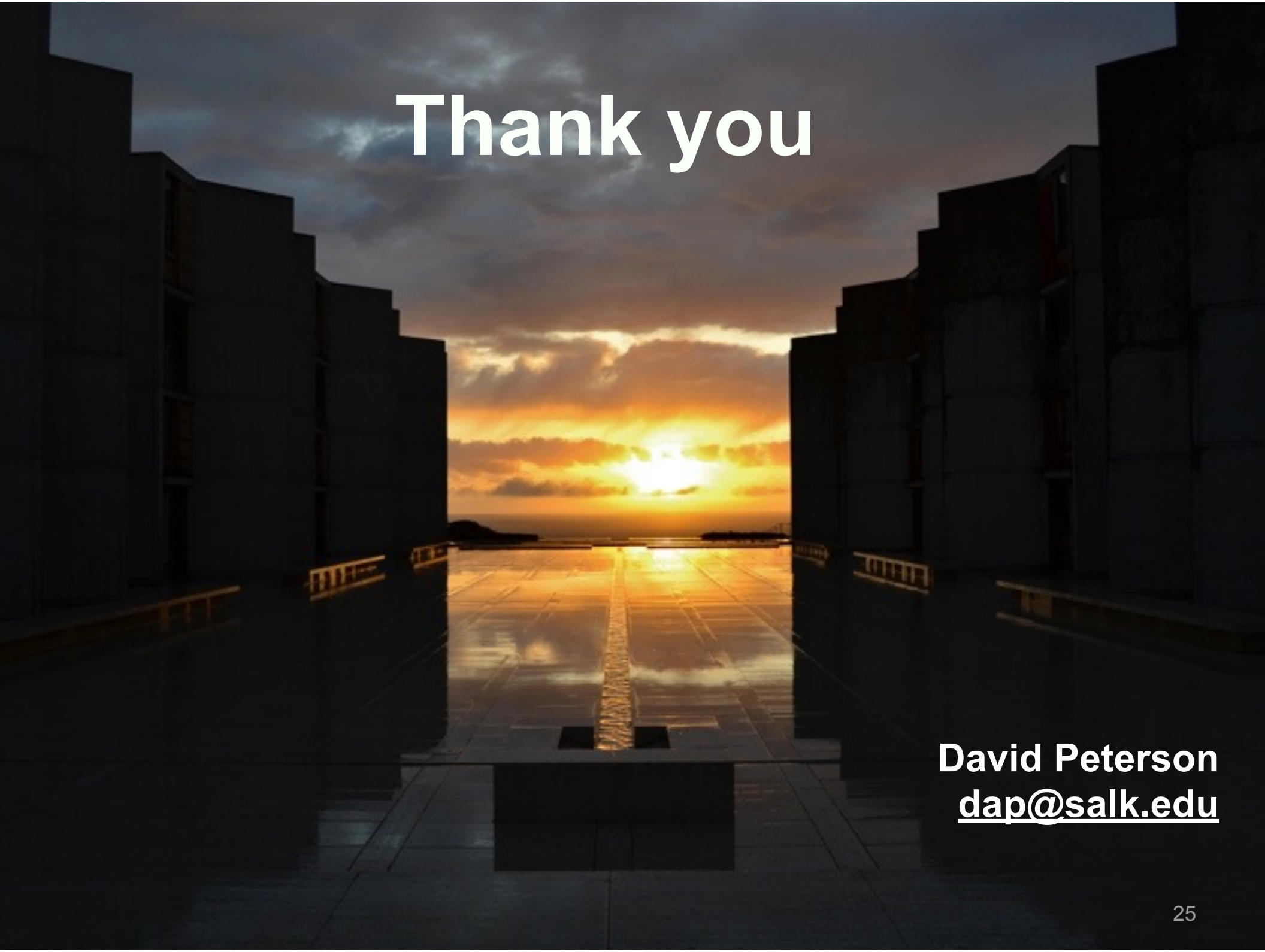
RARE DISEASES CLINICAL RESEARCH NETWORK

Benign Essential Blepharospasm Research Foundation

NIH NIMH (5T32-MH020002)

DoD CDMRP

CDMRP Department of Defense


Thank you
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