Measurement Tools to Assess Outcomes

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Computational Neurobiology Laboratory Salk Institute for Biological Studies Computational Neurology Center Institute for Neural Computation UCSD ... So once we define a patient population for a trial...

i.e. a "context of use" (COU)

...how should we assess trial outcome?

i.e. the "clinical outcome assessment" (COA)

Implicit in outcome assessment: measuring SEVERITY



- 1. Compare before and after (e.g. TWSTRS(before) - TWSTRS(after))
- 2. After intervention, assay "change" (e.g. PGI-C)

Measuring severity of WHAT?



(i.e. "concept(s) of interest" (COI))

Measuring severity: WHO?

FDA categories of clinical outcome assessments (COAs) based on **WHO** is doing the measuring:

ClinRO: clinician reported outcome
 (i.e. clinical rating scales)

ObsRO: observer reported outcome

- (someone other than health professional or patient)
- PRO: patient reported outcome
 - (a.k.a. patient centered outcomes, PCOs)

Clinical rating scales: BSP

A. As part of broader (e.g. whole body) scales:

- 1. GDRS: Global Dystonia Rating Scale
- 2. BFM: Burke-Fahn Marsden Scale

- B. Specific to BSP:
 - 1. JRS: Jankovic Rating scale
 - 2. BSRS: Blepharospasm Severity Scale
 - 3. Blepharospasm Mini (aka BPT: Blepharospasm Phenotyping Tool)

Clinical rating scales: CD

A. As part of broader (e.g. whole body) scales:

- 1. GDRS: Global Dystonia Rating Scale
- 2. BFM: Burke-Fahn Marsden Scale

- B. Specific to CD:
 - 1. Tsui scale
 - 2. TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale
 - 3. TWSTRS-2

Clinical rating scales: LD

A. As part of broader (e.g. whole body) scales:

- 1. GDRS: Global Dystonia Rating Scale (larynx)
- 2. BFM: Burke-Fahn Marsden Scale (speech/swallowing)

- B. Specific to LD:
 - SDAI (?): SD Attribute Inventory (binary, but many features)
 ?

Rating scales are subjective

Humans:

- ClinRO: clinician reported outcome
- ObsRO: observer reported outcome
- PRO: patient reported outcome
- Based on human judgment, i.e. subjective
- Concerns about intra- and inter-rater reliability
 - The issue isn't accuracy per se, but <u>consistency</u> (subjective isn't wrong, just highly variable)



Can we supplement rating scales with OBJECTIVE measures?



How do we define "objective"?: each measurement does **not** depend on human judgement

Terminology gymnastics:

- "technology-based objective measures" (TOMs, Espay 2016 Mov Disord; to distinguish from subjective methods labeled as "objective"?)
- "digital methods"
 - but digital implementations of subjective measures, e.g. "electronic CRSs"; apps being developed for PROs, etc.)

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- how about a ruler?
- "digital health technology" (FDA; so "digital health technology RO"?)

Objective measures for dystonia

Why video? (vs. IMUs, 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!
- Enables telehealth, remote access, more frequent assays during ADLs

CMOR:

the Computational Motor Objective Rater

Overall Approach:

- Develop software that leverages advances in AI (e.g. computer vision and machine learning/deep learning)
- Quantify phenomena of interest ("COIs")
- Test CMOR's convergent validity with clinical ratings severity

Scope:

- BSP and CD: videos from clinical exam
- LD: videos from laryngoscopic exam

CMOR for eye closure in BSP



(with Berman, Jinnah, Hallett, Perlmutter)

CMOR for head deviation in CD



CMOR for vocal fold dynamics in LD







(with Berke and Mendelsohn, UCLA)

Al vs. Neurologist: an artificial dichotomy



CONTROVERSY

CLINICAL PRACTICE

Will Artificial Intelligence Outperform the Clinical Neurologist in the Near Future? Yes

Roongroj Bhidayasiri, MD, FRCP* 💿

Will Artificial Intelligence Outperform the Clinical Neurologist in the Near Future? No

Christopher G. Goetz, MD*

Measuring severity: the patient perspective

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Iterative scale design for PROs



In "context of use" (BoNT cycles), we need more frequent measures

Figure 2. Fluctuations in severity over time and complications of therapy.



Weekly, multi-cycle assessments



Link PRO's to objective measures based on in-clinic videos



All assessments depend on the "tasks"

we need to be careful about **WHAT** is happening **during** the measurements (part of the COU ?)

especially for the dystonias; the moment-to-moment motor features depend on:

- sensory input
- attention
- task



one FDA clinical outcome assessments (COA) category:

- PerfO: performance outcome
 - based on "standardized task(s) according to a set of instructions"

FDA Co-stars

- CO*:
 - clinical outcome assessments (COAs)
 - measuring concepts of interest (COIs)
 - in contexts of use (COUs)
- re: the measures
 - should be validated BEFORE trials begin
 - helpful to discuss the measures with FDA representatives *prior to* designing trials
- COA Qualification Program
 - early days? Table of Qualified COAs is:
 - short
 - all PROs
 - closest thing to Neurology:
 Major Depressive Disorder Scale



Collaborators and Sponsors Dy

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Thank you

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