Innovative approaches to delirium measurement

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Delirium in Older Adults: Finding Order in the Disorder
NIA/AGS Bench to Bedside Conference
February 9-11, 2014, Bethesda, MD
February 11, 2013
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Disclosures

• Current funding:
  R01AG030618; P01AG031720;
  R03AG045494; U01AR057954

• Other financial relationships:
  None to report.

• Conflicts of interest:
  None to report.
Measurement

• The process of assigning numbers to observations
• Allows use of tools of math on subjective observations
• Fundamental for
  – Objectivity
  – Reproducibility
  – Validity
  – Progress of science
Measurements are constructed

- People construct measures
- Measurement, *like all of science*, is a social phenomena
  - What measures are used
  - How measures are interpreted

http://abemkemet.blogspot.com/2012/06/ruler-for-ruler.html
Measurement in medicine

• Source of information
  – People
    • Patients, informants, clinicians
    • Verbal reports, performance tests, clinical exam
  – Tools, devices
    • Driven by advances technology and
    • Biological knowledge
Measurement in psychiatry

• Main goals
  – Case identification
  – Identification of risk factors
  – Severity measurement
  – Outcome assessment

• Main approaches
  – Self-report
  – Expert rating
  – Clinical observation
  – Biomarkers (imaging, function, biochemistry)
State-of-the-art in delirium measurement

• Case identification
  – Diagnostic criteria (e.g., CAM, DSM, ICD)
  – Count and cut (e.g., DRS, MDAS)

• Severity measurement
  – Count symptoms (e.g., DRS, MDAS)

• Outcome assessment
  – OPM (other people’s measures; e.g., MMSE)

Please see this excellent systematic review:
An innovation in measurement

• Item response theory (IRT)
• Undergirds major NIH-funded measurement initiatives
  – PROMIS
  – NIH Toolbox
• Relatively new approach (1952)
• Computationally intensive (slows uptake)
• But, really, just a generalized linear mixed effect model like most everything else
Item response theory (IRT)

• Statistical model that relates
  – Responses or observations of patients, to
  – Theoretical underlying quantities
• A family of statistical models
  – Not just one model
• Invented in fields of educational psychology and psychological measurement
• AKA latent trait theory
• Widely applied in health and psychiatry
Used IRT to identify the best MMSE items to screen for delirium

3 item test was best (year, date, backward spelling)

Limitation: two data sets, in 1 delirium was defined as MMSE < 24
- Used IRT to evaluate measurement properties of MMSE
- Used logistic regression to devise short form
- Short form performed poorly relative to full MMSE
• Use IRT to identify optimal screening items for CAM ratings of delirium
  ○ From among MMSE, MDAS, etc.
• Limitations
  ○ No validation
  ○ No instrument developed
Why is IRT important?

• Can be used to **harmonize** different tools
• Can be used to generate new tests that *simultaneously* optimize
  – measurement **precision** and
  – respondent **burden**
• Outcome measures with **interval measurement** properties (i.e., study change)
• Can be extended to include models for mixtures of clinical populations
  – Separate the merely demented from the delirious
Item Response Function

\[ P(y_{ij}=1 | \theta_i) = F[a_j(\theta_i - b_j)] \]
Bayesian estimates of underlying trait

Bayes modal estimates of latent ability ($\theta$) (modal a posteriori [MAP] estimates)

likelihood function for response pattern $U$ given ability $\theta$:

$$g(U|\theta) = \prod_{i}^{p} P_{i}^{Y_{i}} Q_{i}^{1-Y_{i}}$$

a posteriori likelihood function of $\eta$ given pattern $U$:

$$g(\theta|U) = \frac{\phi(\theta)g(U|\theta)}{g(U)}$$
How is IRT relevant to delirium research?
Figure 2: Dynamic biomarkers of the Alzheimer’s pathological cascade
Aβ is identified by CSF Aβ₄₂ or PET amyloid imaging. Tau-mediated neuronal injury and dysfunction is identified by CSF tau or fluorodeoxyglucose-PET. Brain structure is measured by use of structural MRI. Aβ=β-amyloid. MCI=mild cognitive impairment.
A computational neurodegenerative disease progression score: Method and results with the Alzheimer's disease neuroimaging initiative cohort

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Fig. 5. (a) Estimated biomarker dynamics as a function of the normalized ADPS. Estimation of the normalized ADPS for all ADNI subjects was carried out, and common biomarker dynamics represented by sigmoidal functions were simultaneously fitted as part of the ADPS normalization algorithm. Each sigmoidal function was scaled and flipped in order to fit on a scale going from -1 representing “Normal” to 1 representing “Abnormal”. The positions of vertical lines representing progression from Normal to MCI and MCI to AD were fitted as optimal separating thresholds between the clinical diagnoses provided in the ADNI database. (b) 90% confidence intervals for the inflection point of each biomarker.
Future innovations in delirium measurement

Measurement Models for Nominal Indicators
Opportunities

• Improved and harmonized measures
• More power
• Using measurement to test theories
  – etiology and pathogenesis
  – Mechanisms of risk and protective factors
Conclusion

• Measurement is important and complicated
• Progress requires collaboration
  – Clinical experts
  – Measurement experts
Delirium: Class vs Continuum

• Clinical experts argue delirium is a spectrum disorder

• But, sx measurements are sometimes nominal
  – absent
  – present not fluctuating not acute
  – present and (fluctuating and/or acute)
Delirium as Subtype of Impairment

• Cognition (attention, memory) is a continuum (high fn → severe imp)
• Delirious are a subpopulation of those impaired
• Subpopulation indicators:
  – Disturbance of Consciousness (awareness of surroundings)
  – Sx show fluctuation (each? any?)
  – Sx show acute onset (each? any?)
  – Presence of perceptual disturbance
  – Level of impairment
Can this be modeled?

• Linear Latent Variable Models
  – Mixture measurement model (IRT Mixture Model)
  – Assumes population traits (attention, memory) are continuous normal

• Bayesian modeling
  – More flexibility in latent trait distributions

• Examples
  – Lubke and Muthen, 2005 *Psychol Methods* **10**:21-39
  – Lubke and Neale, 2006 *Multivariate Behav Res* **41**:499
  – Muthén and Asparouhov, 2006 *Addict Behav* **31**:1050-66
Corollary

• **Better** measurement in science will lead to work that is
  – More objective
  – More reproducible
  – More validity
  – Accelerate progress
Why would we do this?

• Theory-Data-Model Fit
  – Are we forcing delirium into linear factor analysis (item response theory) box?
  – If yes, should we?

• What would be the benefit of such modeling exercises?
  – Models contribute to understanding of disorder (endo-) phenotypes
    • Clarify delirium sub-types
      – Yang et al., 2008 *Psychosomatics* 50:248-54
    • Probe meaning of ‘severity’ of delirium
  – Sufficiently accurate models can be used as screening tools (provide weights for criteria)
    • Move beyond “count and cut” screening