Modeling the Neuropsychiatric Inventory (NPI) – Strengths and Weaknesses of a Multidimensional Item Response Theory Approach

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Objectives: The NPI is a behavior instrument widely used in clinical trials of antidementia agents. It measures the severity and frequency of 12 non-cognitive symptoms of dementia ranging from agitation/aggression to changes in appetite and eating behaviors. From the perspective of the data analysis, this multi-faceted score represents a challenge requiring a balance of clinical complexity and statistical parsimony.

The objectives of this work were to investigate the strengths and weaknesses of a multidimensional item response theory model (MDIRT) for simultaneous, longitudinal modeling of the NPI frequency and severity outcomes in an Alzheimer’s population.

Methods: NPI item frequency and severity scores collected over time from 954 patients receiving a placebo treatment were collated from several Pfizer clinical trials. The patient data was used to build a MDIRT model describing the probability of each frequency and severity score as a function of multiple patient-specific latent variables and item-specific discrimination parameters. The longitudinal evolution of the score was described using a linear disease progression model with latent variable-specific slopes.

Model selection and evaluation were performed using simulation based diagnostics and objective function value (OFV) using NONMEM 7.3 for parameter estimation and R for creation of diagnostics.

Results: Based on OFV, a MDIRT model with three latent variables provided the best description of the data. The three dimensional model accurately reflected the correlations in the data between items, between frequency and severity component as well as over time. Different rates of disease progression were identified for different latent variables.

Conclusions: MDIRT models constitute an attractive approach to describe multifaceted composite scores like the NPI with a minimal set of assumptions. From a practical perspective, model complexity might constitute a hurdle.

Figure 1: Schematic representation of a version of the model with subjects moving over time in a hypothetical 2D latent variable space partitioned by item-specific decision boundaries.