

Application of an Item Response Theory Model to describe Amyotrophic Lateral Sclerosis Functional Rating Scale Data

Åsa M. Johansson¹, Inez de Greef², Bernard Muller², Piet H. van der Graaf¹

¹Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands

²Treeway B.V., Rotterdam, The Netherlands

Objective

To develop an Item Response Theory (IRT) model, which describes Amyotrophic Lateral Sclerosis (ALS) Functional Rating Scale (ALSFRS) data.

Conclusion

Several IRT models describing ALSFRS data were developed. The final model will be used in a disease progression model for ALS, to evaluate the effect of new therapies.

Background

ALSFRS

- 10-12 tasks
- 5 levels of fulfilment (0-4)

PRO-ACT¹

- ALSFRS data from 4,838 ALS patients
- In total 42,775 ALSFRS evaluations
- 33,431 evaluations from patients with limb onset.

IRT modelling

- Links the probabilities to complete different tasks to the patient's disability level.
- The disability level is a latent trait.
- The latent trait is assumed to be normally distributed in the population.
- The latent trait can be modelled as a random effect in NONMEM, $\eta \sim N(0, 1)$.²

Methods and Results

Homogeneous graded response model³

$$P_{ik}^*(\eta) = \frac{\exp[a_i(\eta - b_{ik})]}{1 + \exp[a_i(\eta - b_{ik})]}$$

$$P_{ik}(\eta) = P_{ik}^*(\eta) - P_{ik+1}^*(\eta)$$

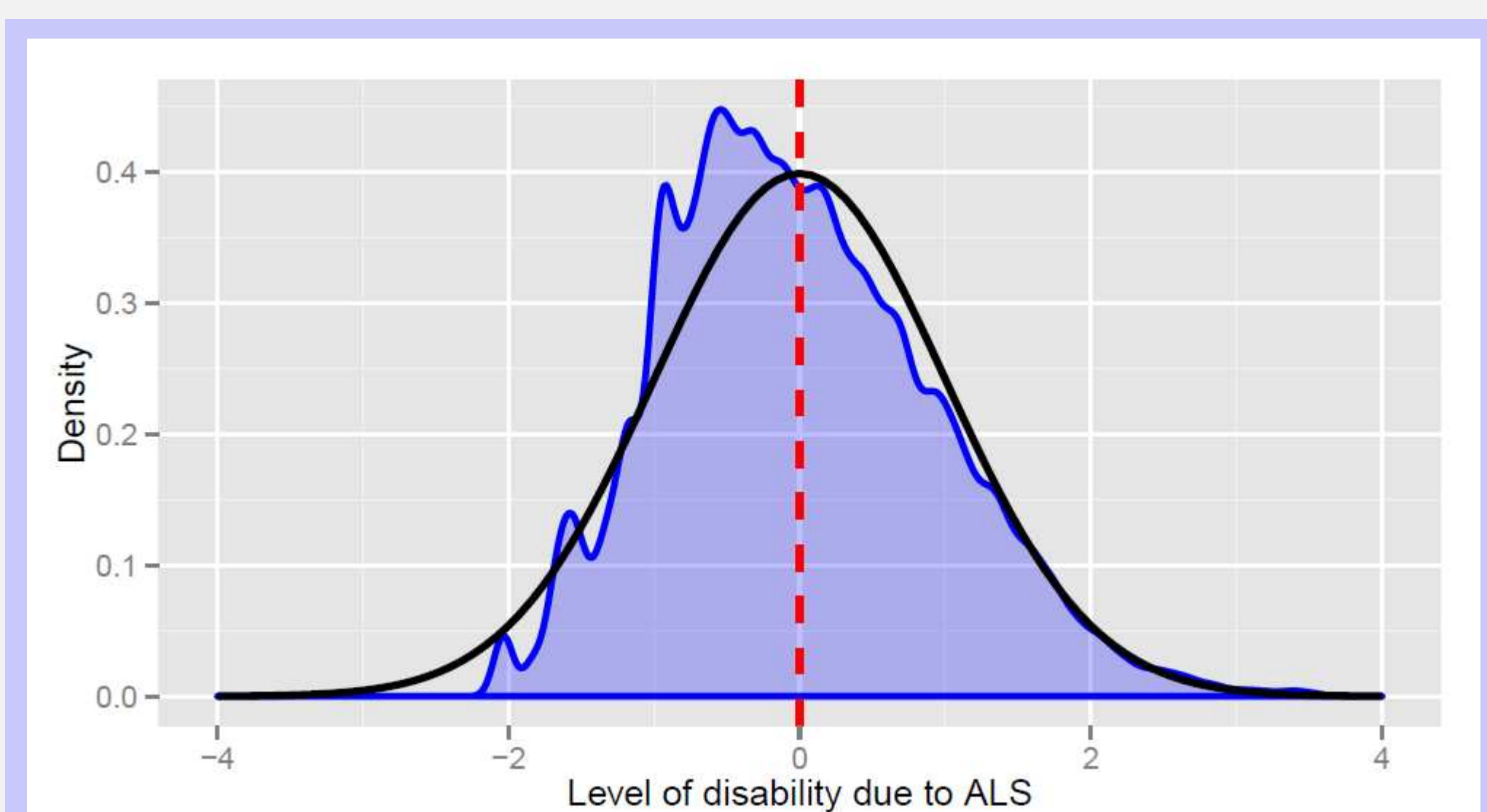


Figure 1. Distribution of the latent trait variable.

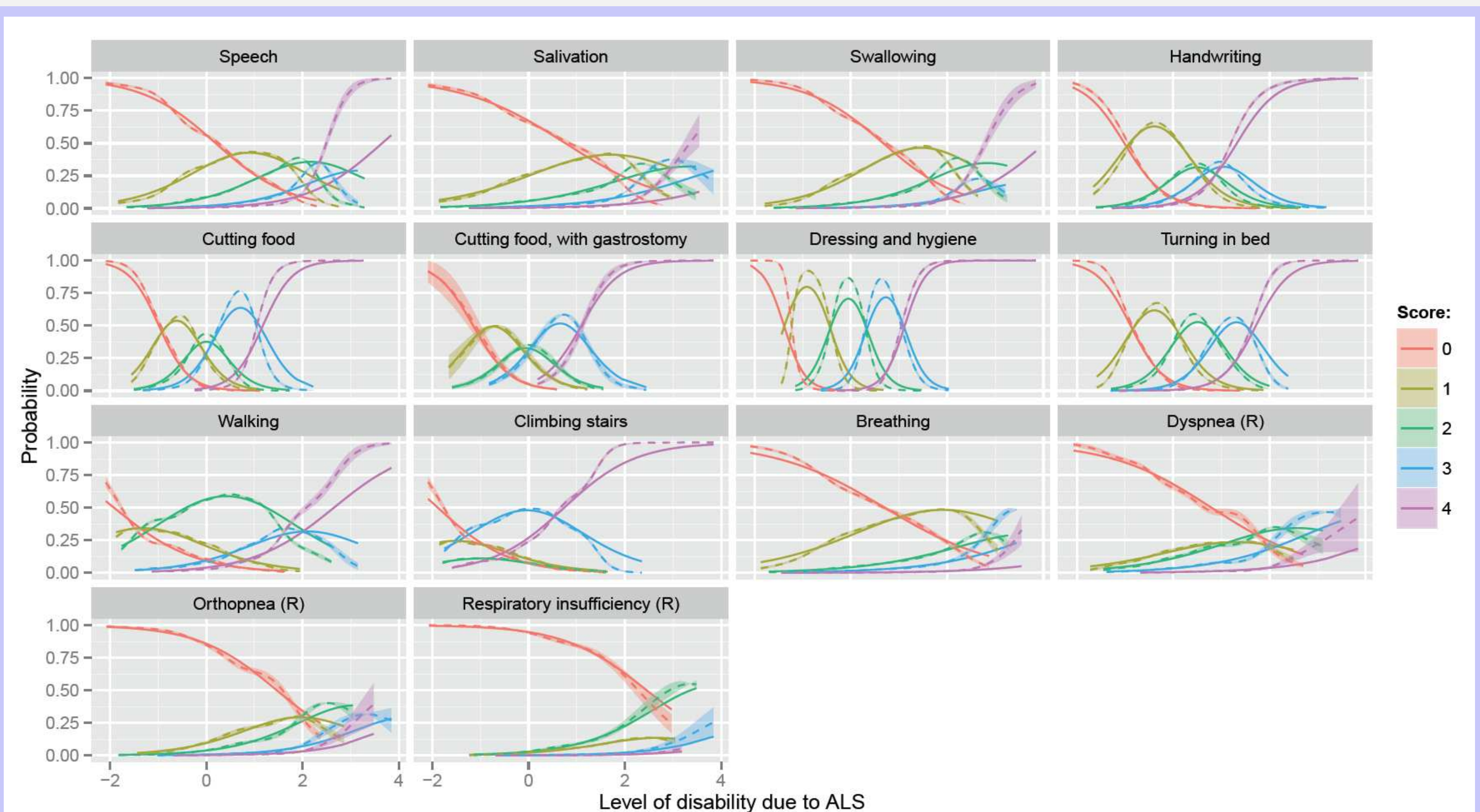


Figure 2. Observed (dashed lines and shaded areas) and predicted (solid lines) frequencies of individual ALSFRS subscores as a function of the latent trait variable.

Heterogeneous graded response model⁴

$$P_{ik}^*(\eta) = P_{ik-1}^*(\eta) * \left(\frac{\exp[a_{ik}(\eta - b_{ik})]}{1 + \exp[a_{ik}(\eta - b_{ik})]} \right)$$

$$P_{ik}(\eta) = P_{ik}^*(\eta) - P_{ik+1}^*(\eta)$$

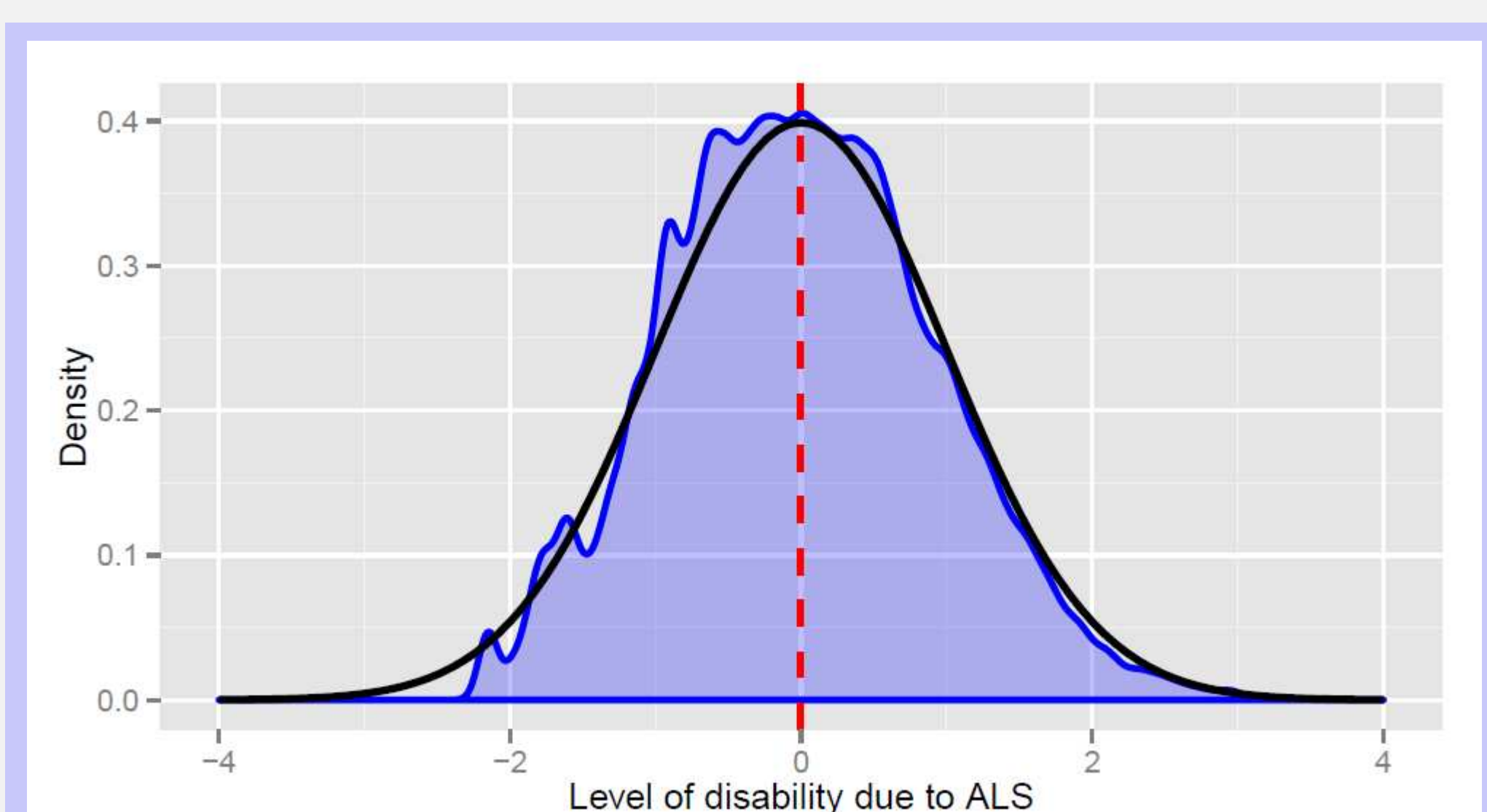


Figure 3. Distribution of the latent trait variable.

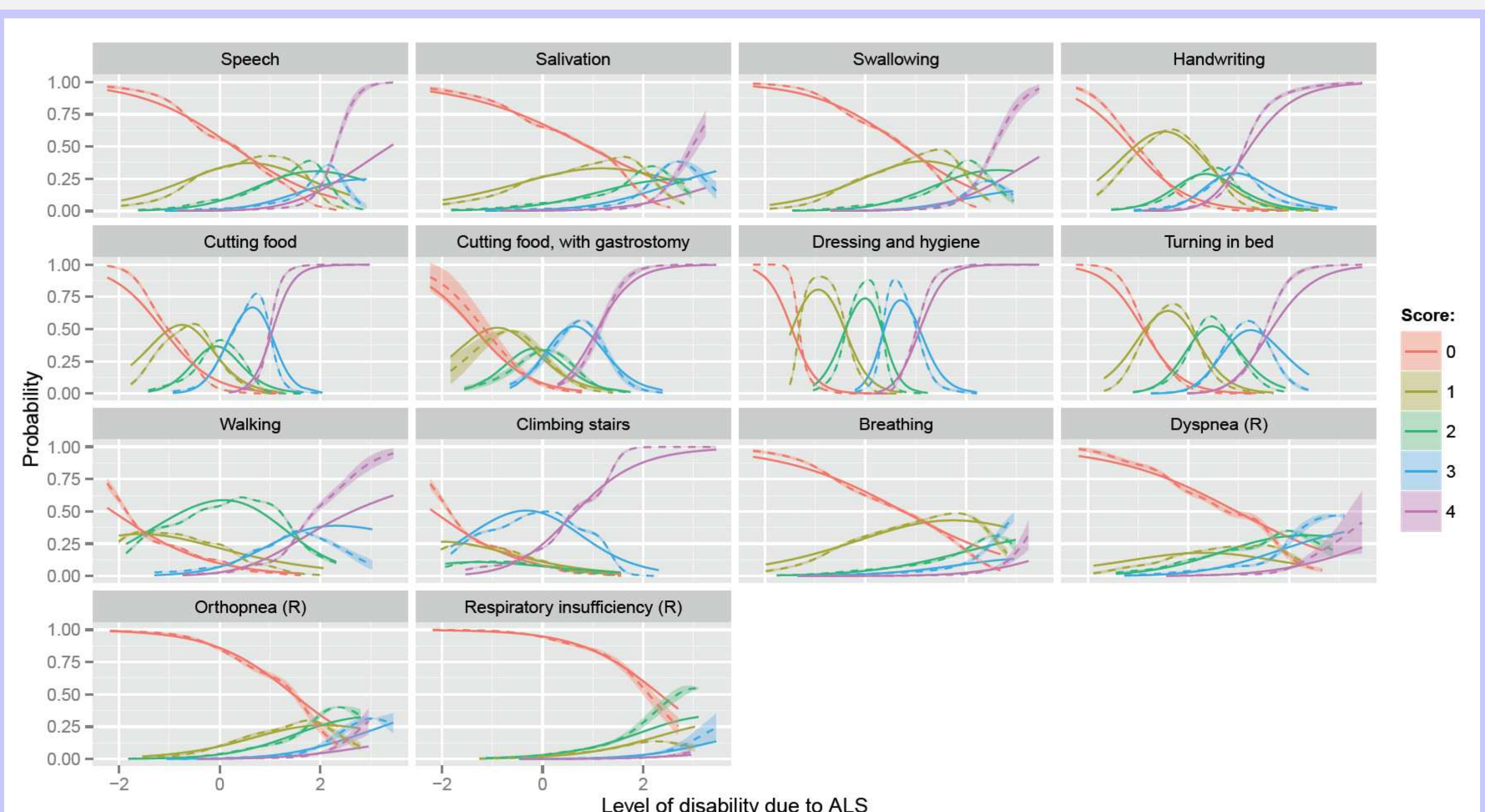


Figure 4. Observed (dashed lines and shaded areas) and predicted (solid lines) frequencies of individual ALSFRS subscores as a function of the latent trait variable.

[1] Nering M.L., Ostini R. Handbook of polytomous Item Response Theory models. Taylor & Francis Group, 2010.

[2] Ueckert S., et al. Pharmaceutical Research. 2014; 31(8): 2152-2165

[3] Samejima F. Psychometrika. 1969; Psychometrika Monograph 17.

[4] Samejima F. Psychometrika. 1995; 60: 549-572