Modelling individual amyotrophic lateral sclerosis disease courses in different centers using the D50 progression model

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Introduction: The routinely used Progression Rate (PR) index presumes that progression in ALS is linear and remains fixed over time. However, progression in ALS is both curvilinear and vastly heterogeneous (Fig. 1).

Methods: A sigmoidal decay function was used to describe the transition from full health to maximum disease for 4,080 patients of different European centers. The model yields following key descriptive parameters:
1) **D50**: Time taken for ALSFRS-score to drop to 24 and
2) **dx**: Constant of ALSFRS-R decay (Fig. 2A)
3) **Relative D50 (rD50)**: calculated open-ended value describing individual disease course covered in reference to D50.
4) **D50** can also be used to mathematically derive disease phases.
5) **Calculated functional state** at any time-point of the disease course
6) **Calculated functional loss** mathematically derived slope of the curve at any time-point of the disease course (Fig. 2B)

Results

Discussion And Conclusions:
The D50 model provides meaningful descriptors of overall disease aggressiveness, local disease activity, and a unified linear scale to describe disease progression. It a) offers alternative reference points to disease specific events, b) allows the staging of individual events, c) provides a way to pseudo-longitudinally interpret cross-sectional data and d) efficiently compares the composition of cohorts from different geographic regions.
However, D50 and dx correlation strongly depends on the input of ALSFRS-R count where the model forces a fixed ratio by using a single value. Deeper analysis have to assess a reasonable cut-off for D50 in order to cope with very slow progressors.

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