Relationship of Pre-morbid IQ and Education to Progression of Alzheimer’s Disease

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Background
• Education is a strong predictor of AD incidence
• Education and tests of cognitive performance are highly correlated
• Studies of the role of education on rate of cognitive decline after a diagnosis of AD have not yielded consistent results
• Since education and pre-morbid intellectual functioning are highly correlated, a direct measure of pre-morbid IQ may be better than education as a predictor of cognitive decline in AD

Hypothesis
• Pre-morbid IQ is a better predictor of cognitive decline, global progression, and overall survival than education in patients with probable AD

Methods
• Setting and Study Population
  – Baylor Alzheimer’s Disease Center, Houston
  – Electronic database of initial and follow-up clinical and neuropsychological assessments maintained for more than 1600 patients diagnosed according to NINCDS-NDRDA criteria
  – Database established in 1989, new patients accrued continuously since that time
  – Vital status of all patients ascertained through phone follow-up of contacts and/or death index searches
• Inclusion criteria
  – Diagnosis of probable AD
  – An AMNART test administered within six months of the baseline visit
  – At least one annual follow-up visit with neuropsychological assessment

Study Variables
• Outcome Variables
  – Baseline and follow-up MMSE scores
  – Baseline and follow-up ADAS-Cog scores
  – Baseline and follow-up Clinical Dementia Rating (CDR) scores
  – Vital status
• Predictor Variables
  – Age at baseline visit to center
  – Sex
  – Race/ethnicity
  – Years of education
  – Estimated duration of symptoms before baseline visit
  – Nelson Adult Reading Test (American version) raw score
• Statistical Analysis
  – Analysis was restricted to the first six testing sessions, since the small number of individuals with more than six assessments could distort regression model fit
  – Linear random effects models used to test hypotheses regarding education, pre-morbid cognitive ability and decline on MMSE and ADAS-Cog scores
  – Cox proportional hazards regression with robust variance estimation used to identify predictors of all-cause mortality
  – Quadratic term for time included to account for non-linear change
  – Time by baseline AMNART and time by education interaction terms tested as warranted
  – Graphs of fitted regression lines produced using STATA

Results
• 478 patients met inclusion criteria. Baseline characteristics of the study population shown in Table 1.
• When the raw AMNART score was not in the model, education was a significant predictor of cognitive performance, but was not associated with differential rate of decline (education by time interaction term not significant).
• The raw baseline AMNART was significantly associated with performance on the MMSE, ADAS-Cog and CDR Sum of Boxes scores, and the rate of decline was more rapid in persons with a below average AMNART score (see Table 2 and graphs of fitted regression lines).
• Education was not a significant predictor of test performance or global function when the raw baseline AMNART was included in the regression models.
• Neither education nor the baseline AMNART score were significant predictors of all cause mortality (Table 3).

Conclusions
• A measure of pre-morbid IQ is preferable to a predictor of cognitive performance and rate of cognitive decline than education in persons diagnosed with probable AD
• Neither pre-morbid IQ nor education is associated with overall survival after a diagnosis of probable AD

Implications
• Baseline differences in cognitive performance and global function associated with pre-morbid IQ are preserved over long-term follow-up
• The difference in the slope of decline associated with higher pre-morbid IQ is relatively small, and the practical impact on outcomes such as nursing home placement and/or caregiver burden needs further study
• A measure of pre-morbid IQ is preferable to education as a predictor of AD outcomes