Validity of semantic memory test as predictor of change in ADAS-cog scores in MCI

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Abstract

There are many clinical trials evaluating disease modifying agents in subjects with mild cognitive impairment (MCI). This poster examines the predictive value of a neuropsychiatric test used to characterize the cognitive deficit in MCI in comparison to a well validated assessment commonly used in Alzheimer's disease trials. ROC analysis was used to compare the neuropsychiatric tests. Preliminary statistical analyses from a multinational trial suggest the Free and Cued Selective Recall Reminding test does not reliably predict short-term longitudinal change in the Alzheimer's disease Assessment Scale-cognitive subscale in the MCI population.

Background

Neuropsychiatric test batteries are utilized to measure cognitive performance in many indications. In a multinational study for MCI a neuropsychiatric test battery included a novel assessment for some sites, the Free and Cued Selective Recall Reminding test (FCSRT)[1]. This reminding test for verbal episodic memory is an adaptation of the Grober & Buschke paradigm to diagnose MCI phenotype[2]. The FCSRT test is considered a very sensitive and specific assessment for the diagnosis of prodromal Alzheimer's Dementia (AD). This test may distinguish early AD from subtypes of MCI were conversion to AD is less common. For the purposes of this clinical trial, the FCSRT was administered for diagnostic purposes and was not utilized as an outcome measure. The inclusion criteria were free recall score $\leq$ 20 and a total recall score of $\leq$ 40. The focus of this review was the ability of the FCSRT to track short-term changes in the Alzheimer's disease Assessment Scale-cognitive subscale (ADAS-cog).

Methods

The analyses were conducted on subjects who completed a screening FCSRT, qualified for randomization and subsequently provided an ADAS-cog at baseline and at week 24. Descriptive statistics were generated on the FCSRT. Change scores were computed for baseline ADAS-cog and week 24 resulting in a variable of increase or decrease in ADAS-cog. The change score for each patient was compared to the baseline FCSRT's free recall score and total recall score. Receiver operating characteristics (ROC curves) were generated on the change score variable of the ADAS-cog and free recall score and total score of the FCSRT using all patients randomized, regardless of treatment group assignment. ROC analysis tests for sensitivity and specificity of models based on the theory of signal detection. An excellent model would have an area under the curve of .9 – 1 while a test that was a poor model would result in an area under the curve of .5-.6.

Results

The ADAS-cog scores for 93 subjects increased at week 24, while the scores for 117 subjects decreased. (See Table 1 for a summary of scores on free recall and total recall by change score of ADAS-cog). In this study, the FCSRT for either free recall and total recall appeared to be poor predictors of subsequent ADAS-cog performance.

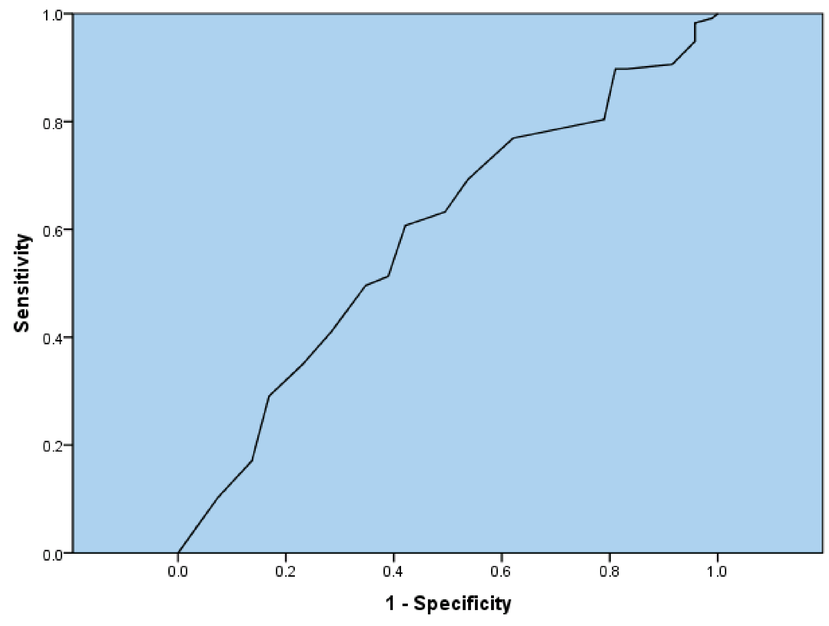
	Free Recall Score	Total Recall Score
Increase in ADAS-cog in 24 weeks (n=93)	11.60 (5.26)	28.52 (8.65)
Decrease in ADAS-cog in 24 weeks (n=117)	13.24 (5.24)	31.23 (8.80)

Table 1. Means (Standard Deviations) of neuropsychiatric assessments.

Results cont'd

The area under the curve for the free recall scores was .588 (see Figure 1 for ROC), and the area under the curve for the total recall score of FCSRT was .606 (Table 2).

Figure 1. ROC Curve of Free Recall Scores and ADAS-cog change.



	Area Under the Curve	Standard Error
Free Recall	.588	.039
Total Recall	.606	.039

Table 2. Comparing ROC curves.

Conclusions

A cross-sectional, screening FCSRT failed to mirror subsequent change in ADAS-cog scores over 24 weeks for this multinational MCI trial. A limitation of the above study is that the FCSRT was only used as a screening measure and was not administered at subsequent weeks so that so that correlations in change could be directly linked. Also, the time reference was limited to 24 weeks, which may be inadequate to demonstrate changes in either measure. Please note these preliminary analsyes were generated using blinded data. Further analysis should include a logistic regression to see if each instrument contributes to a subject's decreased cognitive abilities.

References:
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