

Combining Cognitive Testing and Informant Report to Increase Accuracy in Screening for Dementia

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This poster was presented at the World Psychiatric Association Section of Epidemiology and Community Psychiatry Symposium at Sydney, 19-22 October, 1997

INTRODUCTION

Cognitive impairment is central to the diagnosis of dementia and the use of psychometric tests of cognitive performance forms the cornerstone of screening and assessment of the disorder. The use of informant report is a most promising alternative. This approach involves the administration of a questionnaire to a person who knows the patient well. The questionnaire inquires about aspects of memory and intellectual function in everyday situations compared to earlier in life. Correlations between these tests are moderate (see, for example, Jorm et al., 1997, Mulligan et al., 1996). Further, joint factor analyses of test and informant report items have produced separate factors for each item domain (Jorm et al., 1995).

The desirability of using both types of test when assessing patients at risk to dementia is reinforced when the complimentary shortcomings of each type of test are considered. Cognitive tests are affected by education and premorbid ability. Poorly educated patients may be misclassified as demented and well-educated subjects missed (Tombaugh and McIntyre, 1992). Cognitive testing also requires intact sensorimotor and language faculties. Informant report questionnaires have been shown to be uncontaminated by premorbid intelligence and education, and are unaffected by patients' physical disabilities. However, scores on these test may be influenced by non-cognitive factors such as the affective state of the patient and the informant, the personality of the patient and the quality of the relationship between patient and informant (Jorm, 1996).

While clinical practice in the assessment of dementia often includes an informal interview with a relative of the patient, only the administration of an informant report questionnaire enables a quantitative rating of changes observed to be made. More importantly, no procedures currently exist that allow this information to be combined formally with the results of cognitive tests administered to the patient. Informally, when test results concur, greater confidence can be had in the diagnosis based on the tests. Where informant report and cognitive testing suggest different conclusions, the optimal clinical impact of the tests is uncertain. Given the moderate correlation of the tests, such discrepancies will not be infrequent. Beyond simply resolving this problem, the opportunity may exist to combine tests in such a manner that the performance of the combination, as measured by its sensitivity, specificity and other indices, exceeds either test used alone.

The aim of this study was to determine whether information from an informant report questionnaire could be combined with a standard cognitive test to improve performance in screening for dementia in clinical settings. Reflecting this aim, the most widely used cognitive test, the Mini-Mental State Examination (MMSE; Folstein et al., 1975) and the most established informant report measure, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm and Jacomb, 1989) were used. There are a large number of ways in which two or more test scores might be combined to make an assessment or reach a screening decision.

Methods of analysis of psychometric tests as diagnostic or screening tools are generally restricted to individual tests. The development of optimal combinations of tests has received little attention. Three methods by which two test scores might be combined were considered (See "Combining Tests" box.). The choice of methods investigated was influenced by the following factors: 1) The rules should be broadly consistent with the current use of each test. 2) The method of combination should be 'transparent' to users. 3) No special equipment or resources should be needed to undertake the combination. The performance of the three rules was compared to each test used alone and between each other.

METHOD

Subjects

Subjects were patients at the Geriatric Hospital or at the Memory Clinic of the Hospitals of the University of Geneva School of Medicine. Their age ranged from 62 to 98 years (Mean 80.33, S.D. 8.12). Seventy six patients were women and thirty were men.

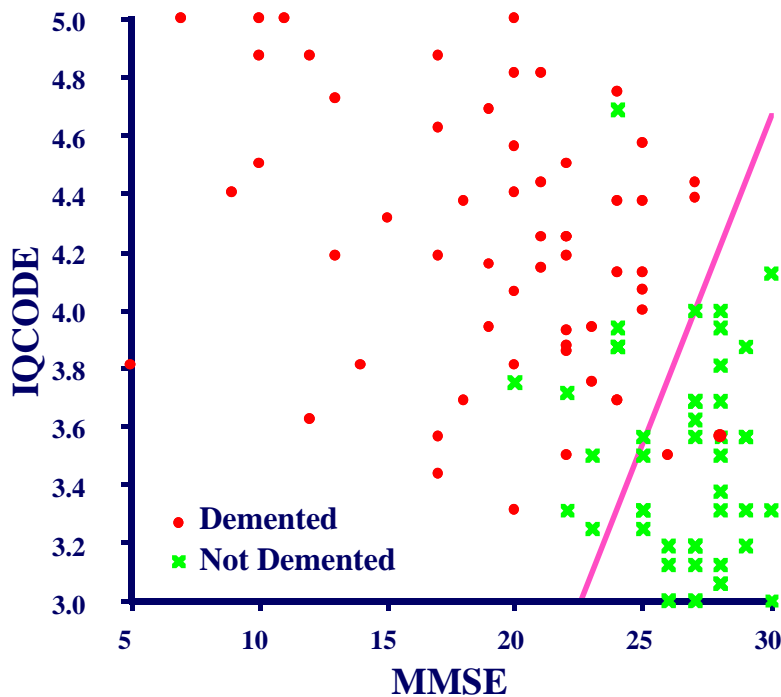
Instruments

French versions of the MMSE and the short form of the IQCODE (Jorm, 1994) were employed. Both tests have been shown to have comparable properties to the original English tests (see Gagnon et al., 1990 and Mulligan et al., 1996).

Procedure

The MMSE and IQCODE were administered by different staff in accordance with the directions given by the tests developers'. Diagnoses of dementia according to DSM-IV criteria were made by one of two senior psychiatrists using a checklist. Diagnoses were made blind to the outcome of the psychometric tests.

RESULTS



Fifty-eight patients met DSM IV criteria for dementia. MMSE scores for all patients ranged from 4 to 30 (Mean 22.5, S.D. 5.6) while IQCODE ratings ranged from 3.00 to 5.00 (Mean 3.87, S.D. 0.56). As would be expected, means of both scales differed substantially between demented and non-demented patients (MMSE 19.3 vs 26.5, IQCODE 4.22 vs. 3.49, $p < 0.0001$). A scatterplot of MMSE and IQCODE scores is shown on the left. The correlation between the tests was -0.58.

The table below shows the results of a logistic regression analysis predicting DSM IV caseness from MMSE and IQCODE scores. MMSE score alone is a strong and statistically significant predictor of caseness. The possibility of a nonlinear relationship between caseness and MMSE was assessed by adding a quadratic term to the model. This term was nonsignificant and negligible in size. Adding IQCODE to the equation resulted in a significant improvement in prediction. Adding a multiplicative term to represent interaction between the two tests was not significant. The results obtained using the IQCODE as the basis of the prediction equation mirrored those using the MMSE. There was no evidence of a nonlinear relationship for either test nor any interaction between them.

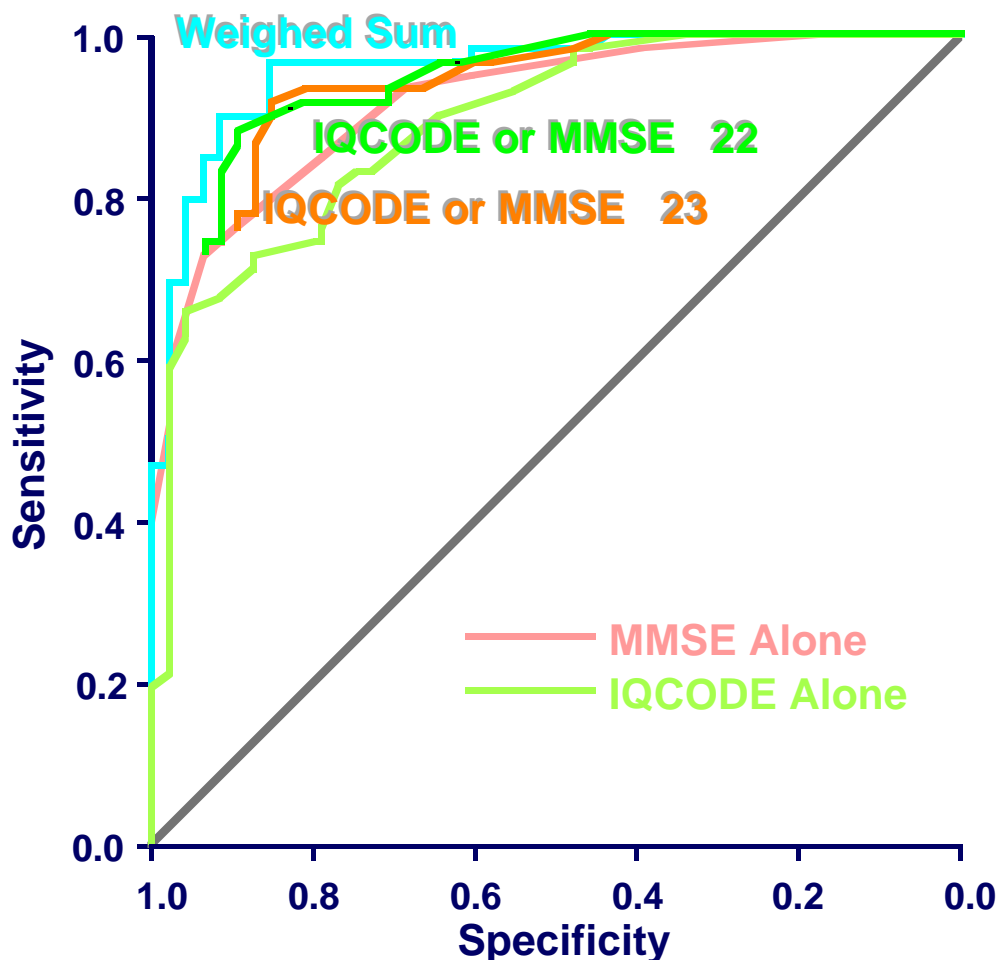
Term Added	Change in G^2	p
MMSE	70.26	<0.0001
MMSE ²	0.01	0.9203
IQCODE	20.67	<0.0001
MMSE × IQCODE	0.05	0.8231
IQCODE	58.64	<0.0001
IQCODE ²	0.42	0.5169
MMSE	32.30	<0.0001

All significance tests have 1 degree of freedom.

It was concluded that each test yields nonredundant information in the prediction of dementia. The tests could thus be combined to increase screening performance.

PERFORMANCE OF COMBINATIONS

Receiver Operating Characteristic curves were constructed for each test and the area under each curve was calculated. The area under the MMSE ROC curve was 0.92 while that for the IQCODE was 0.89.



The performance of the 'or' and 'and' rules was investigated by calculating the sensitivity and specificity across all possible cutpoints for the IQCODE while implementing the rule with fixed cutpoints of the MMSE. This was repeated for all possible MMSE cutpoints and yielded a series of ROC-like curves for each rule, one for each MMSE cutpoint. It is not possible to calculate an area under these curves. Nevertheless the curves suggested that useful improvements in test performance could be obtained by the 'or' rule using MMSE cutpoints in the range 22 to 24 in conjunction with the IQCODE. The table below shows test performance statistics for combinations using several cutpoints.

Using a cutpoint of the IQCODE of scores greater than 4.0 or an MMSE cutpoint of 23|24 increased sensitivity significantly ($p < 0.01$ two-tailed binomial test) over using the MMSE alone while not significantly reducing specificity ($p > 0.50$). No combination using an 'and' produced better results than tests used alone.

The graph also shows the ROC curve for the weighed sum of the MMSE and IQCODE derived from the logistic regression equation: The area under this curve was 0.96. This area was significantly greater than that under the curve of either test used alone. The logical cutpoint for this combination is that associated with the patient having a greater probability of being demented than not demented (i.e, greater than 0.50). Sensitivity at this point was significantly greater than that achieved using the MMSE alone at the 23|24 cutpoint ($p < 0.001$) while specificity was not significantly reduced. No statistically significant differences between the weighed sum and the 'or' rule were found.

Test	Sensitivity	Specificity	Pos Pred Value	Neg Pred Value
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DISCUSSION

The analyses presented here demonstrate that the informant report and cognitive testing are complementary approaches to the assessment of dementia. These tests can be used together and combined in a compensatory manner to improve the accuracy of screening for dementia.

On purely statistical grounds the performance of the simple logical combination cannot be distinguished from the weighed sum in this sample. The logical rule is extremely simple to use and thus would be expected to be attractive in many clinical situations. The implementation of weighed sum rule is more complex requiring either calculation or use of our template.

The advantage of the weighed sum is that the trade-off between the scales is graduated: the more evidence there is that the patient is unimpaired according to one test, the more evidence is required that he or she is impaired according to the other test. Consider a patient with a score on Test B that is marginally above the cutoff value. Because increases in screening sensitivity of the 'or' rule at the possible cost of specificity, there are a priori grounds for preferring the weighed sum rule.

There was no support for the use of a rule requiring evidence of impairment on both scales. This is despite the fact that there is some resemblance between the structure of formal classification criteria for the disorder and this type of rule.

From a clinical perspective, the combination of cognitive testing and informant report adds little to the clinician's burden. Similarly, either of the proposed methods for combining this test with the MMSE is straightforward and the role of the two tests in the decision reached is transparent. While different levels of performance might be obtained and different cutoff values might be necessary to optimize performance, it is unlikely that the mechanism by which performance is enhanced (i.e., the information collected by one test that is not available from the other) would differ in different settings.

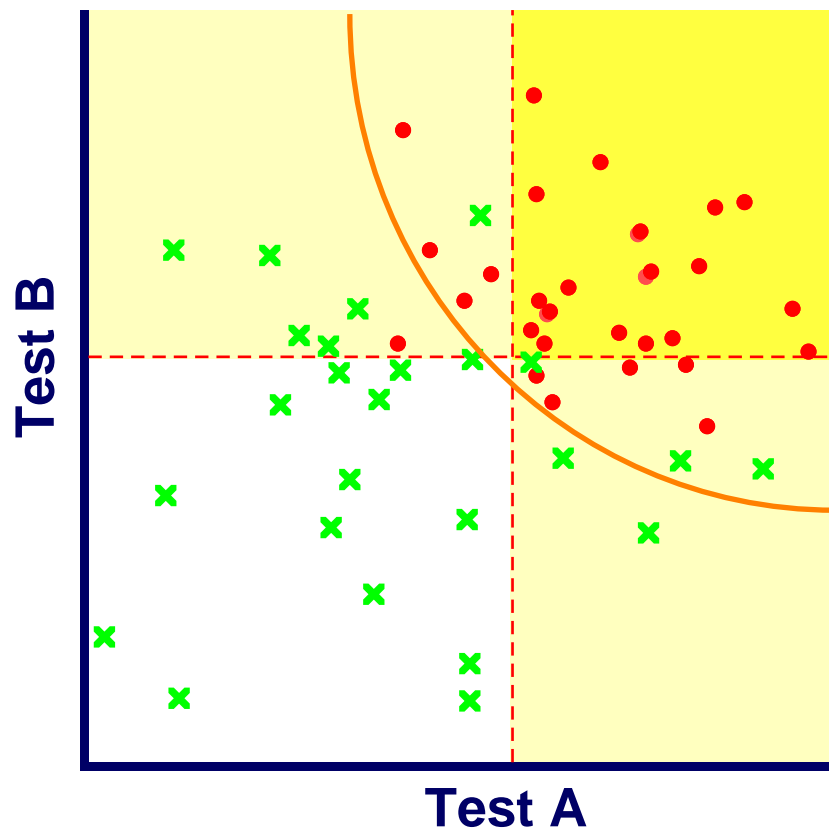
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ACKNOWLEDGMENTS

The authors would like to thank Dr. P. Giannakopoulos for his assistance in the diagnosis of patients in this study, and Dr. R. Conroy for suggesting of the possibility of a graphical implementation of test combination rule.

COMBINING TESTS



Tests can be combined in a number of ways:

Compensatory ('or') Rule

Patients are classified as cases if either test is positive. (All the shaded area.) Only patients with negative values on both tests are considered as non-cases.

Useful if one test may pick up information missed by the other

Can increase sensitivity above either test used alone.

The specificity of the combination cannot be greater than either test.

Conjunctive ('and') Rule

Only patients positive on both tests are classified as cases (Only the deeply shaded area). Patients positive on only one test or neither are classified as non-cases.

May be considered as requiring diagnostic consensus.

Can improve specificity over either test used alone.

The sensitivity of the combination can be no higher than that of either test.

Combining Test Values

A mathematical function of the two test scores that differentiates cases from noncases. (may be linear or non-linear).

Similar to the 'or' rule but uses more information.

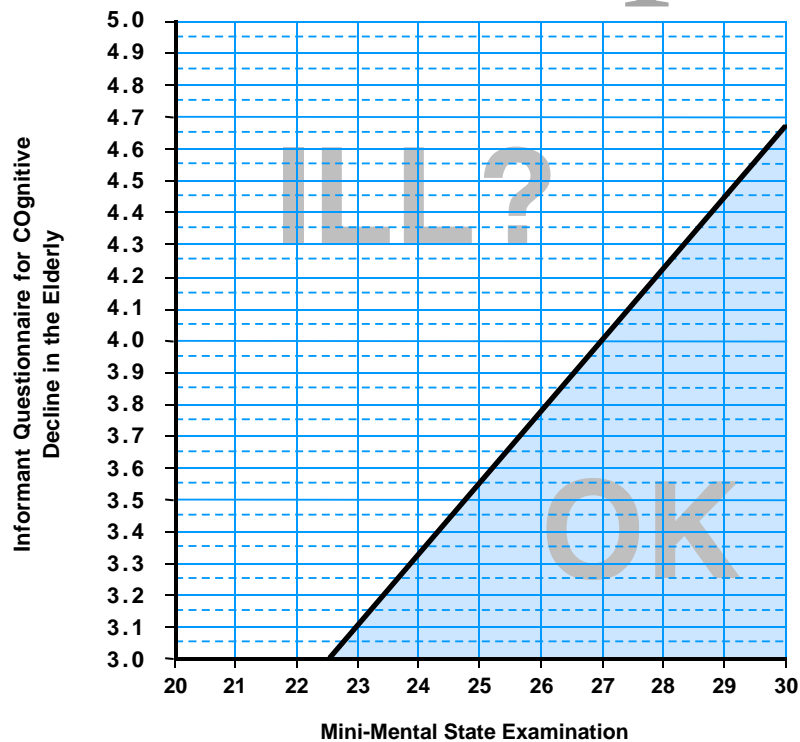
Requires some calculation to arrive at the classification score.

The calculated score is on a new, arbitrary scale.

THE DEMEGRAPH

The Demegraph is a simple graphical method implementing the weighed linear approach to combining the MMSE and the IQCODE. It requires no calculation and the impact of scores on the two tests remains transparent to the user. A copy is obtainable from the authors or from the Demegraph web site.

DemeGraph



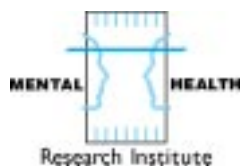
INSTRUCTIONS

- Administer the Mini-Mental State Examination (MMSE; Folstein et al., 1975) and the Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE; Jorm, 1994) according to the instructions given by the test authors.
- Calculate test scores and plot them on the above template.
- Patients whose score profile falls above the diagonal line (the unshaded portion of the graph) are likely to meet criteria for DSM-IV Dementia. Patients who fall below the line (the shaded part of the graph) are unlikely to meet the criteria for this disorder.
- This template is suggested for screening purposes only. Diagnosis of dementia requires appropriate investigation by suitably qualified personnel.

Folstein, M., Folstein, S., & McHugh, P. R. (1975). Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189-198.

Jorm, A. F. (1994). A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Development and cross-validation. *Psychological Medicine*, *24*, 145-153.

Mackinnon, A.J. & Mulligan, R. (1997) Combining cognitive testing and informant report to increase accuracy in screening for dementia, *submitted*.



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