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Comparison between Conventional Statistic Approach and Modelling Based on Artificial Neural Network in Differentiating Fronto-Temporal Dementia from Alzheimer's Disease with the Tower of London Test

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Introduction

Purpose of this brief commentary was to underline the usefulness of well know neuropsychological tests when their results were analysed by new statistical methods which, at variance with the classical statistical tests, can manage complexity even with relatively small samples and to the subsequent unbalanced ratio between variables and records.

Scores of Tower of London task analysed by Artificial Neural Networks (ANNs) are able to reliably differentiate Alzheimer's disease (AD) and Frontotemporal Dementia (FTD).

An early differentiation between AD and FTD may help choosing a therapeutic approach with cholinesterases inhibitors, which are restricted to AD, while for FTD there is no symptomatic or disease-modifying therapy. Furthermore, both AD and FTD have significant implications for family members and a correct genetic counselling is largely dependent on a correct diagnosis. Lastly, AD and FTD have different natural histories and prognostic features that patients and their caregivers have to face with, Besides current clinical criteria [1,2], mostly descriptive particularly for FTD, several behavioural, neuroimaging, biochemical and functional tools have been proposed to achieve an early and reliable differentiation.

There is a general agreement that neuropsychological tests measuring executive functions are valid instruments to differentiate AD from FTD [3]. However, executive deficits traditionally linked to the prefrontal dysfunction are heterogeneous and difficult to measure with a single test.

The Tower of London (ToL) has been derived from the more complex Tower of Hanoi, which is one of the classic puzzles created by French mathematician Eduardo Lucas in 1883 and originally proposed as a valid tool to study visuospatial planning abilities and problem solving.

In a previous study [4] using the simplified version of ToL by Krikorian, et al. [5], we found a reduced planning ability of AD patients compared to normal controls.

Recently the use of Krikorian's ToL has been recommended in clinical practice [5] and as good method to diagnose AD [6] in comparison with non-demented elderly subjects [7].

Patients and Methods

Twenty two Italian Dementia Centers recruited consecutively 94 FTD patients (frontal/dysexecutive variant) and 160 AD patients to administer Krikorian's ToL along with standard neuropsychological tests. The diagnoses were done according to current research criteria [1,2] 6 to 24 months earlier and the dementia was of mild-to moderate severity without clinical evidence of aphasia. AD patients were significantly older (p<0.005) and less educated (p<0.05) than FTD patients. In the FTD group there were significantly more men (p<0.001) and the duration of disease was longer (p<0.005).

Statistical Analysis

The statistical analysis of the results was performed using standard procedures (discriminant validity of ToL scores between FTD and AD patients has been checked by ROC curve analysis) and by A NNs.

Decision-support systems, based on conventional statistical methods made their entry into medicine several years ago and efforts to improve predictive and prognostic performance of these systems have led to the application of ANNs as tools for clinical decision-making. ANNs are highly flexible computerized mathematical models for understanding and predicting complex and chaotic dynamics in complex biological systems, and have been effectively used to solve non-linear problems related to diagnostic or prognostic queries. Thus, ANNs would appear to be a promising tool for clinical decision-making and have been applied in various areas of Alzheimer research.

Classical statistical analysis

ToL global score was significantly better in AD than in FTD group (p=0.051).

The ability of ToL scores to discriminate FTD from AD was poor, as suggested with ROC analysis (AUC 0.57), although among other neuropsychological tests, only phonological fluency was slightly better (AUC 0.69), namely for women (AUC 0.74).

Neural networks analysis

The global predictive accuracy obtained with standard ANNs ranged from 70.04% to 80.73%; the corresponding area under the ROC curve was 0.82.

Conclusion

An impairment in ToL performance could occur either because of the inability to successfully inhibit inappropriate move selections at a specific point of the decisional pathway, or because of a deficit of visuospatial working memory or a planning deficit.

In the present work, using classical statistical methods we were unable to accurately differentiate AD from FTD in single case study, whereas as a group, AD patients performed better in ToL scores.

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However, when ANNs methodology was used, the overall accuracy of ToL to discriminate AD from FTD becomes more accurate reaching a diagnostic accuracy rarely obtained by other diagnostic tools, much more expensive and less patient-friendly, such as functional neuroimaging techniques.

A limitation of this study is the lack of any pathological or genetic confirmation of the clinical diagnoses. Even though mistakes are not uncommon in the clinical differentiation of AD from FTD, in our sample the diagnoses were made by experienced Dementia Centers, routinely involved in the follow-up of the patients and consequently in the clinical confirmation of the diagnostic process.

Strengths of our study are the size of the sample studied and the accurate training of the neuropsychologists involved in the test administration.

The final consideration resides on the suggestion to pursue alternative ways to the conventional statistical methodological approach, i.e., by using ANNs analysis which seem to increase the diagnostic accuracy between different types of dementia.

First of all, the comparison of results obtained with two different analytical approaches (classical statistics and ANNs), points out the need to employ systems that are really able to handle the disease complexity instead of treating the data with reductive approaches that are unable to detect multiple interactions among variables.

Second point, ANNs at variance with the classical statistical tests, can manage complexity even with relatively small samples and to the subsequent unbalanced ratio between variables and records.

In conclusion, we think that the Krikorian's version of ToL might be included in the neuropsychological battery for the early diagnosis of AD vs. FTD also in single case study, along with new unconventional statistical methods, able to consider complexity of the test and to solve non-linear problems related to diagnostic or prognostic queries.

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