An Approach for the Neuropsychological Diagnosis of Alzheimer's Disease: A Hybrid Model in Decision Making

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Abstract. This work presents a hybrid model, combining Influence Diagrams and the Multicriteria Method, for aiding to discover, from a battery of tests, which are the most attractive questions, in relation to the stages of Clinical Dementia Rating in decision making for the diagnosis of Alzheimer's disease. This disease is the most common dementia. Because of this and due to limitations in treatment at late stages of the disease early diagnosis is fundamental because it improves quality of life for patients and their families. Influence Diagram is implemented using GeNie tool. Next, the judgment matrixes are constructed to obtain cardinal value scales which are implemented through MACBETH Multicriteria Methodology. The modeling and evaluation processes were carried out through a battery of standardized assessments for the evaluation of cases with Alzheimer's disease developed by Consortium to Establish a Registry for Alzheimer's disease (CERAD).

Keywords: Alzheimer's disease, Diagnosis, Multicriteria Method, Bayesian Network, Influence Diagram.

1 Introduction

Alzheimer's disease is the most frequent cause of dementia and is responsible (alone or in association with other diseases) for 50% of the cases in western countries [9]. Dementias are syndromes described by a decline in memory and other neuropsychological changes especially occurring in the elderly and increasing exponentially in function of age. According to [2], despite its high incidence, doctors fail to detect dementia in 21 to 72% of their patients.

One way to identify whether a patient is having a normal aging, or are developing some form of dementia, is through a neuropsychological evaluation [2].

There are several tests available, and one of the major challenges is to find out which test would be more efficient in establishing the diagnosis of dementia.

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One factor that must be observed is the brevity of the tests, that is, the shorter the test, it will be more effective.

The main focus of this work is to develop a multicriteria model for aiding in decision making in order to find out which are the most attractive, for a given test or set of tests for the diagnosis of Alzheimer's disease. Due to be a difficult diagnosis of disease, with initial symptoms subtle, progressing slowly until it is clear and devastating. The battery of tests used in this work is from the Consortium to Establish a Registry for Alzheimer's disease (CERAD). It was necessary to construct value scales originating from semantic judgments of value with the objective of defining a ranking with the classification of the impact of issues in relation to the stages of the CDR (Clinical Dementia Rating). Finally conclusions and futures works are shown.

2 Diagnosis of Alzheimer's Disease

Diagnosis of Alzheimer's disease is carried out in several steps. For the global cognitive evaluation, the Mini-Mental State Examination was recommended; memory evaluation: delayed recall [6] or of objects presented as drawings; attention: trail-making or digit-span; language: Boston naming; executive functions: verbal fluency or clock-drawing; construction abilities.[4].

This study seeks to help in deciding the best manner to define the diagnosis. To do this, we sought to choose the most important questions in the diagnosis of Alzheimer's disease, using a battery of CERAD tests. This battery was chosen because it encompasses all the steps of diagnosis and has been used all over the world.

Therefore, the questions selected through this decision making process will be applied preferentially because, in accordance with the decision maker, these questions play a main role in diagnosis.

3 CERAD - An Overview

The original mandate of the CERAD in 1986 was to develop a battery of standardized assessments for the evaluation of cases with Alzheimer's disease who were enrolled in NIA-sponsored Alzheimer's Disease Centers (ADCs) or in other dementia research programs [7]. Despite the growing interest in clinical investigations of this illness at that time, uniform guidelines were lacking as to diagnostic criteria, testing procedures, and staging of severity.

CERAD developed the following standardized instruments to assess the various manifestations of Alzheimer's disease: Clinical Neuropsychology, Neuropathology, Behavior Rating Scale for Dementia, Family History Interviews and Assessment of Service Needs.

4 Model Construction

4.1 Definition of Problem

In studies developed by [3] and [8] the application of the multicriteria model for aiding in diagnosis of Alzheimer's disease was presented. In [8] we analyzed the

results of the implementation of a case study conducted with the battery of the CERAD neuropathological assessment.

In [3] we sought to validate the model through of neuropsychological data of patients. The data used in the analysis of the study are part of the battery of neuropsychological CERAD [7].

In the present study, we sought to validate the model in the identification of issues that have greater impact on each stage of the CDR, in deciding the diagnosis of AD, will be held from the combination of the battery of neuropsychological tests of CERAD with the scale functional CDR [5].

We selected six of the eight tests of the battery of neuropsychological CERAD for applying the model of decision support that will assess what are the issues (among all the issues that are implemented in selected tests) that have greater attraction for each stage of CDR, for the definition of the diagnosis of Alzheimer's disease. The tests selected are: Verbal Fluency (J1), Boston Naming Test (J2), Word List Memory (J4), Constructional Praxis (J5), Word List Recall (J6) and Word List Recognition (J7) [7].

The CDR was chosen to be a tool that allows the classification of the prevalence of the various degrees of dementia, on six cognitive-behavioral categories: memory, orientation, judgment and problem solving, community affairs, home and hobbies and personal care [7].

Furthermore, the CDR identifies the questionable cases, or those that are not classified as normal subjects. These cases may correspond to the so-called cognitive decline associated with aging, mild cognitive impairment or, in other epidemiological studies that are part of the group that has a higher rate of conversion to dementia.

Despite of the CDR has only five stages of dementia: none, questionable, mild, moderate and severe, the CERAD implemented a change in scale including two stages: profound and terminal. For the application of the model will be taken into account the scale of the CDR modified by CERAD [5].

Next, the application of the decision model will be presented for solving the problem of choosing the issues considered most attractive in the definition of the neuropsychological diagnosis of AD.

4.2 Phase 1: Structuring

Step 1: Identify the decision makers. Individuals classified as cases in the database of CERAD were defined as the decision makers (actors) involved in the process of building the model of defining the issues of greatest impact in defining the neuropsychological diagnosis of AD. That decision was taken, considering that, from the values (responses) issued by the cases, it was the definition of the degree of dementia.

Analyzing the data pertaining to the cases through the database of CERAD was found a negligible quantity of actors to evaluate the attractiveness of the model in multicriteria. The degrees of dementia: none, profound and terminal, are respectively 0, 1 and 2 answers, i.e. between the cases that have been assessed with dementia-type: none, profound and terminal, only 0, 1 and 2 people

Table 1. Classification of variables in the problem of decision

Problem: Define the issues of greatest impact in each stage of the CDR in the neuropsychological diagnosis of Alzheimer's disease Heading level	
Objectives	To establish between the various levels of dementia classified by CDR (questionable, mild, moderate, severe), which are the items that have the greatest impact on the decision of a test or set of tests for the definition of the diagnosis of AD
The set of the possible actions	The set of actions (alternative) is defined as (A), where the issues are that are part of the battery of neuropsychological tests of the CERAD were selected for the implementation of the decision model: Verbal Fluency (J1), Boston Naming Test (J2), Word List Memory (J4), Constructional Praxis (J5), Word List Recall (J6) and Word List Recognition (J7).
Criteria	Correspond to the CDR stages of dementia that had a significant amount of actors (questionable, mild, moderate, severe).
Restrictions (properties of criteria that are specified as desirable)	CDR stages: - CDR_QUESTIONABLE > 0 and CDR_QUESTIONABLE <= 0.5; - CDR_MILD > 0.5 and CDR_MILD <= 1; - CDR_MODERATE > 1 and CDR_MODERATE <= 2; - CDR_SEVERE > 2 and CDR_SEVERE <= 3;

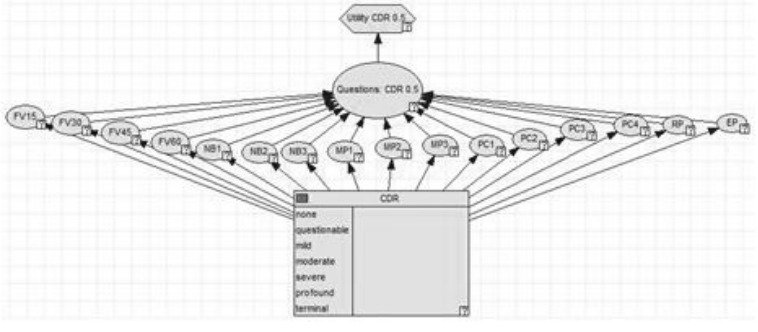

Fig. 1. Hierarchical structure of the problem of the decision to stage the CDR questionable

respectively, answered each of the issues of the CERAD battery. Therefore, these degrees of dementia have not been evaluated by the model.

Step 2: Identify the alternatives and criteria relevant to the issue of decision. Definition of the hierarchical structure of the problem. This step is related to identify the variables of interest and the determination of the interrelationship between them. The variables can be classified as: objectives, actions, criteria, restrictions and factors, as shown in Table 1.

The end result of this step is to define the hierarchical structure of the problem by creating a graphic model represented by a Directed Acyclic Graph (DAG), as shown in Fig. 1. We have identified 23 of probability, including one decision nodes and 7 utility nodes [4].

After defining the structure of the network should be carried out to quantify the probability of us, which was made from the calculation of probabilities in

the form of the influence diagram with the data obtained by the database of the CERAD.

For to define the issues more attractive, but it is necessary to examine the level of impact (or attraction) of the responses of actors in each of the stages of the CDR. This initial assessment is important because the database of the CERAD, you can discover from the responses of a particular actor, which is the stage of CDR.

The attractiveness of the responses is measured by use of the construction of judgments matrixes of value and obtains the scales of global value for each question. Table 2 shows the values of each level of impact for all FPVs in relation FV15.

Table 2. Values of each level of impact for each FPV in relation FV15

Alternatives	FPV1 – CDR: Questionable	FPV2 – CDR: Mild	FPV3 – CDR: Moderate	FPV4 – CDR: Severe
FV15_99	0.50	1.00	2.00	3.00
FV15_0	0.46	0.96	1.92	2.92
...	...	...	...	...
FV15_11	0.00	0.51	1.01	2.01

With this result, it will be possible to apply the model to discover the attractiveness of the issues involved in the battery of neuropsychological CERAD for each stage of the CDR.

Step 3: Definition of descriptors. The construction of descriptors should be made for each point of view of the fundamental problem. Thus, for this problem, have been identified two sets of descriptors with each of three phases: (i) description of each descriptor for each of the fundamental points of view (FPVs), (ii) obtain the impacts according to each key point of view, and (iii) analysis of the impacts each second fundamental point of view.

The number of states of each PVF will always be equivalent. It was defined 16 descriptors for each PVF. The states of PVFs are not equivalent, therefore, cannot be the representation of more than one state at a single level of impact. The Table 3 shows the descriptors for the FPV1. The levels of impact of each descriptor were ordered based on each issue that has relevance for each stage of the CDR, as regards the issue that has greater influence in defining the diagnosis of AD. This relevance was defined based on the sum of the result obtained in the judgment matrixes of decision in the application of the model on the answers of the questions.

Table 3. Descriptor for FPV1 - CDR: Questionable

NI	Description	Order
N16	FV15: I want you to tell me all the animals you can think (from 0-15 seconds)	1°
N15	MP2: Repeat list of 10 words - attempt 2	2°
...	...	...
N01	PC1: Draw circle	16°

Step 4: Carry out the analysis of impacts. This step is related to the definition of impact assessment according to each FPV. We defined the upper and lower values of each impact and relevant aspects of the distribution of impacts in each of them. In all the FPVs of this model, instead of scoring is attributed to the involvement of dementia in accordance with each stage of the CDR which is being evaluated.

The Table 4 presents one summary table that shows the descriptors and their values lower and higher to be considered for obtaining the basis of value for each FPV.

Table 4. Summary table of descriptors and impacts seconds each PVF

FPV	Descriptor	Upper Level	Lower Level
FPV1 – CDR: Questionable	Answers a question from the battery of neuropsychological CERAD	0	0.50
FPV2 – CDR: Mild		0.51	1
FPV3 – CDR: Moderate		1.01	2
FPV4 – CDR: Severe		2.01	3

Step 5: Definition of a function of value for each alternative. This function was obtained from the division between the sum of the results obtained through the judgment matrixes in relation to the responses to a question, by the sum of the results obtained through the judgment matrixes in relation to the issue or set of issues that are part of a battery of neuropsychological subtest of CERAD, on a stage of the CDR.

$$v(b_j) = \frac{\sum_{n}^{i} a_i}{\sum_{n}^{i} b_j}$$

This function of value was applied to all sets of issues relevant to their respective tests. In the next stage, will be the implementation of the function of value for a particular set of options.

Step 6: Construction of the judgment matrixes. In this step were performed the following steps: (i) the calculation of the difference of attractiveness in the judgment matrix, and (ii) the equivalence of the dimensions of attractiveness, and (iii) the way it was maintained the consistency of judgment matrixes.

For the evaluation of issues, all the FPVs were worked through a descriptor with 16 reference levels, and a lower limit (which was generated from the lower value, the sum obtained regarding the outcome of the evaluation of the issues), an upper limit (which was generated from the higher value, the sum obtained regarding the outcome of the evaluation of the issues) and 14 intermediate levels of reference. Shown in Fig. 2 is a matrix of assessment of value and scale of cardinal value obtained with the methodology for the FPV1 MACBETH - CDR: Questionable [1].

Following the procedure for construction of judgments matrixes of value and obtain the scales of global value for each of the FPV.

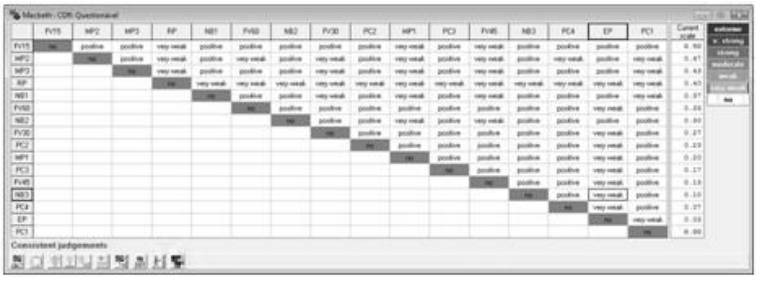

Fig. 2. Matrix of judgment of value and scale for the FPV1 - CDR: Questionable

The result of the judgment matrixes shows that the stage of the CDR was questionable that most benefited from the implementation of the model. CDR: questionable obtained the highest value in relation to other criteria, and through the accumulated weights for each option, with the CDR: questionable accumulating 50% of the total weight of the criteria.

This result is very positive, because one of the major goals of medicine in the search for a diagnosis, especially that of Alzheimer's disease, is get it in earlier stages of the disease.

5 Conclusion

The diagnosis of Alzheimer's disease is made up of many steps. The first step is to discover if the patient has dementia and then the patient is assessed to see if he has Alzheimer's.

The methodologies applied have been crucial to the analysis of the most attractive in the definition of the diagnosis of Alzheimer's disease, while the methodological design of the model, mapped the possibilities regarding the performance results for the decision.

The model in question, which applies structured assumptions in decision-making problems, provided important impacts for the research and supported in the chain of neuropsychological responses to identify the diagnostic criteria.

As a future project, this model can be extended with the inclusion of new criteria or new models which can be developed using other batteries of assessments.

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