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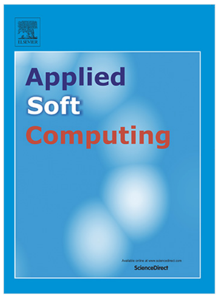

Using Multilayer Fuzzy Cognitive Maps to diagnose Autism Spectrum Disorder

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***Highlights (for review)**

A Multilayer Fuzzy Cognitive Maps to diagnose the Autism Spectrum Disorder

Multilayer Fuzzy Cognitive Maps carries out the diagnosis using two autism knowledge

Autism knowledge sources are based on the current standards for autism diagnosis

Fuzzy model of diagnosis integrates a parent questionnaire and a patient interview

The model carries out the same diagnosis of the experts that use these standards

Using Multilayer Fuzzy Cognitive Maps to Diagnose Autism Spectrum Disorder

E. Puerto[a], J. Aguilar[b,d], C. López[c], D. Chávez[d,*]

Abstract

Autism Spectrum Disorder (ASD) is comprised of a group of heterogeneous neurodevelopmental conditions, typically characterized by a triad of symptoms consisting of (1) impaired communication, (2) restricted interests, and (3) repetitive and stereotypical behavior pattern. An accurate and early diagnosis of autism can provide the basis for an appropriate educational and treatment program. In this work, we propose a computational model using a Multilayer Fuzzy Cognitive Map (hereafter referred to as MFCM) based on standardized behavioral assessments diagnosing the ASD (MFCM-ASD). The two standards used in the model are: the Autism Diagnostic Observation Schedule, Second Edition (ADOS2), and the Autism Diagnostic Interview Revised (ADIR). The MFCM's are a soft computing technique characterized by robust properties that make it an effective technique for medical decision support systems. For the evaluation of the MFCM-ASD model, we have used real datasets of diagnosed cases, so as to compare against other method/approaches. Initial experiments demonstrated that the proposed model outperforms conventional Fuzzy Cognitive Maps (FCMs) for ASD diagnosis. Our MFCM-ASD model serves as a diagnostic tool required to support the medical decisions when determining the correct diagnosis of Autism in children with different cognitive characteristics.

Keywords: Autism Spectrum Disorder, Multilayer Fuzzy Cognitive Map, Medical Decision Support Systems, Autism Diagnostic Observation Schedule, Autism Diagnostic Interview Revised.

1. INTRODUCTION

ASD is comprised of a group of heterogeneous neurodevelopmental conditions typically characterized by a triad of symptoms consisting of (1) impaired communication, (2) restricted

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interests, and (3) repetitive and stereotypical behavior patterns [1]–[3]. The medical decision process of predicting autism is extremely complicated; the diagnostic criteria are complex and change with the development [4]. The large number of elements/parameters/data (such as symptoms, qualitative/quantitative information, etc.) involved in its process needs to be elicited and analyzed as a means of diagnosing the severity of the condition [5]. A high percentage of medical errors, committed due to physician's lack of experience, huge volume of data to be analyzed, and inaccessibility of previous patient's medical records, can be reduced using computer-aided techniques. Therefore, designing more efficient medical decision-support systems (MDSSs) to assist physicians in decision-making is crucial. According to Groumpos et al. [6], [7], through combining the properties of fuzzy logic and neural networks, FCMs are among the latest, most efficient and strongest artificial intelligence techniques, for the development of MDSSs and complex systems. FCMs are a tool to represent knowledge from a qualitative perspective, allowing us to create models of complex systems where an exact mathematical model cannot be used owing to the complexity of the system [8]–[12]. Recently, significant results have been obtained in modeling medical decision-making using FCMs [13]–[18]. Mythili and Shanavas [15] have proposed a MDDS for the early prediction of the occurrence of cognitive disorders among children, which are presented in Autism, Dyslexia or Delirium, has been proposed. Attributes linked to learning, social interaction, behavior, object understanding, amongst others, have been considered. The proposed prediction method involves an approach based on a Meta-Heuristic and FCMs, called MEHECOM. The primary aim of MEHECOM is to identify the disorders among children in order to define a set of mechanisms to alleviate them. Also, Al Farsi et al. [14] have defined a fuzzy method for evaluating the weights between causal and decision concepts of an FCM applied to the ASD diagnostic is proposed, and Papageorgiou and Salmeron [19] have proposed a decision system for autism diagnosis based on the human knowledge and experience, and a trained FCM using an unsupervised non-linear Hebbian-learning algorithm. In this work, the Hebbian algorithm is used to train FCMs for the autistic disorder prediction problem. Subbaraju et al. [20] have carried out a study on ASD detection in females, applying the ABIDE dataset, where classifiers based on different techniques, such as the Radial Basis Artificial Neural Networks, are used.

Previous ASD diagnostic models are based on the Modified Checklist for Autism in Toddlers (MCHAT) standard. Some other studies on ASD prediction use intelligent techniques, such as those mentioned in section 2.2. Some of the previous works are interesting because they have proposed FCMs for the computational modeled of different aspects around autism: prediction, identification, classification, etc. But in general, said works only use a single level of knowledge (i.e., monolayer FCM), such that they are limited to a single window of observation of the autistic phenomenon.

In our work, we look at ASD from a multilayer perspective, based on previous works, including MCFM [25], [26] and FCM Designer Tool [26], [27]. To accomplish this, it was necessary to modify the MCFM model's component responsible for calculating the relationship values in accordance with the ADIR and ADOS instruments, so that autistic disorder in real ASD cases can be predicted (see section 3.1 for more details).

The modelling capability of a MFCM is much higher, allowing the characterization of different aspects of the Autism [28], [29]. Our model carries out the diagnosis using two levels of autism knowledge: a questionnaire for parents and an interview, as well as standardized observational measures, all based on the diagnostic instruments ADIR and ADOS2, respectively [30]–[37]. These instruments were selected for being standards, generally applied in conjunction, for the ASD assessment [38]. ADIR is a semi-structured interview, designed to assess the three core aspects of ASD [32], [36]: social communication, repetitive behavior, and restricted interests. The Autism Diagnostic Observation Schedule, Second Edition (ADOS2) [32], [39], is an observational measure designed to assess reciprocal social interaction, communication, and the use of imagination. [40]–[43] are some important previous works based on ADOS and ADIR. Some of these jobs have validated ADIR and ADOS in preschool children with developmental delays, others in the assessment of possible pervasive developmental disorders (PDD). According to these results, it is important to combine the usage of ADOS and ADIR in young children with unclear developmental problems, including the suspicion of ASD. Real datasets from different autistic disorders belonging to real clinical cases are used to demonstrate the quality of our model, resulting in a better approximation of ASD predictions, compared to FCMs used in previous works (see section 5 for more details).

This work is organized as follows. Section 2 provides the main aspects of the phenomenon known as ASD, Fuzzy Cognitive Maps and a review of the computational models used to predict ASD. Section 3 presents our MFCM-ASD model. Section 4 presents simulations and results. Section 5 compares our work with previous works, and finally, some conclusions, future works and ethical standards are given.

2. THEORETICAL FRAMEWORK

This section presents the two base models of behavioral assessment (ADIR, ADOS2), and the computational method for the diagnosis of autism (the MFCM), used in this work.

2.1 Autism.

The past 30 years have been a very active period for ASD diagnostic instrument development, addressing a need in both research and clinical domains [4], [44]. Diagnostic measures have been designed to capture behaviors in the areas of communication, social interaction, and restricted and repetitive conducts, which characterize ASD. These measures attempt to quantify behaviors associated with ASD by assigning numerical scores. These behavior scores are then translated into summary scores allowing classification of the individual as having ASD or not [4]. Current diagnostic instruments include parental questionnaires and interviews, as well as standardized observational measures [5], [13], [30], [35], [38], [39], [42], [45]. Two of these instruments are ADIR and ADOS2.

The ADIR is a clinical interview allowing an in-depth evaluation of subjects suspected to have autism. The original version was developed in English in [36]. The instrument, through 93 questions, explores the three large subscales altered by autism: the quality of the social interaction (e.g., emotionally sharing, comfort offering and seeking, socially smiling, and responding to other children); communication and language (e.g., stereotypical utterances, pronoun reversal, social usage of language); and repetitive, restricted and stereotypical interests and behavior (e.g., unusual preoccupations, hand and finger mannerisms, unusual sensory interests) [31], [32]. This instrument applies to children whose mental ages are over 2 years.

These 93 items are synthesized in two algorithms: Diagnostic and Current Behavior Algorithms. These then use scores in each of the three areas (i.e., communication and language, social interaction, and restricted and repetitive behaviors). The algorithms specify a minimum score in each area to determine a diagnosis of autism. The total cutoff score for the communication and language domain is 8 for verbal subjects and 7 for nonverbal subjects. For all subjects, the cutoff for the social interaction domain is 10, and 3 for restricted and repetitive behavior. Elevated scores indicate problematic behaviors in a particular area. According to experts, a classification as autism is given when the scores in at least two of the three areas (communication, social interaction, and behavior patterns) meet or exceed these cutoffs. Finally, the onset of the disorder is usually evident by 36 months of age [36].

Regarding ADOS2, the original version (Module 1-4) was developed in English by researchers of the Western Psychological Service [32], and a second version (Module T) in [33]. The ADOS2 is an observational assessment of the ASD. The ADOS2 includes five modules, each module involves the evaluation of a series of activities using interactive stimulus materials. An individual is evaluated in only one module, selected on the basis of his or her expressive language level and chronological age:

- Toddler Module—for children between 12 and 30 months of age with no consistent use of speech
- Module 1—for children 31 months and older with no consistent use of speech
- Module 2—for children of any age who use the speech, but are not verbally fluent
- Module 3—for verbally fluent children and young adolescents
- Module 4—for verbally fluent older adolescents and adults

In Modules 1 through 4, algorithm scores are compared with cutoff scores to yield one of the three classifications: autism, autism spectrum, or non-spectrum. The difference between autism and autism spectrum is the severity, the former indicating a more pronounced symptom. In the Toddler Module, algorithms yield "ranges of concern" rather than more specific classification scores [31], [32]. Recently, Zander et al. [43] have validated the quality of ADIR and ADOS in a clinical sample of children with ages of 18 to 47 months. This validation was carried out for each instrument separately, and then combined, against a diagnosis with clinical consensus. This work is similar to ours, but a computational tool is not used.

2.2 Computational models to predict ASD.

There are different approaches to computationally predicting ASD: methods based on behavioral assessment [21]-[24], [48]-[53], methods based on data neuroscientists (structural and functional) [54],[55] and methods combining both features [56]. Some proposed methods based on behavioral assessment are: Cohen et al. [57] have proposed an Artificial Neural Network (ANN) to discriminate between Autism and Mental retardation, based on the Autism Behavior Interview (ABI). The ANN used in this work was the Backpropagation ANN. Arthi and Tamilarasi [58] have proposed a neuro-fuzzy system that converts parent's answers into a questionnaire using fuzzy values. Those values are then evaluated with "if-then" rules, and the fuzzy output becomes the input for the previous ANN Backpropagation. Another approach is the Knowledge Based Screener (KBS), an expert system with factual and heuristic knowledge to analyze children development and identify developmental disorders [50]. Also, Wall et al. [59], [60] have proposed a decision tree (ADTree) tool that works as a classifier based on the 8 questions from the Module 1 of the ADOS instrument. There is another version of this ADTree that detects autism rapidly through 7 questions from the ADIR instrument [60]. Tarantino et al. [61] have developed an ICT-based tool to support the imagination of behaviors necessary for role-play in predictable environments that includes diagnosis and gamification. Ojeda [51] has defined a method based on genetic algorithms to support ASD diagnosis. Bone et al. [24], [52] have studied the use of machine learning in autism detection. They conclude that machine learning can be applied in the diagnosis of ASD when a large dataset is present. Most of these methods must use a large sample size in order to train their models, and all treat the problem of autism from a single perspective.

On the other hand, Subbaraju et al. [54] have proposed an ASD detection method from structural MRI, using an Extended Metacognitive Radial Basis Function Neural Classifier (EMcRBFN). Zhang et al. [55] have designed an automated white matter connectivity analysis method for ASD detection based on diffusion MRI tractography. Moreover, Anirudh et al. [56] have defined a method combining different types of features (behavioral, structural and functional information) that act as biomarkers in a predictive model for different neuro-pathological conditions. In particular, they develop a version of the graph convolutional neural networks (G-CNNs) for ASD classification based on such ideas. Finally, recently, Abbas et al. [70] have proposed a tool for the early autism detection by applying Machine Learning algorithms. This tool combines two screening methods into a single assessment, one based on short, structured parent-reported questionnaires, and the other based on tagging key behaviors from short, semi-structured home videos of children. Additionally, a generalized framework for using machine learning algorithms to simultaneously search for the presence of many different conditions in the context was proposed.

Our approach is based on behavioral assessment, using the MFCM technique for modeling the ADIR and ADOS2 decision-making process. It was implemented using the FCM Designer Tool [27]. The FCM Designer Tool allows defining FCMs with concepts and relationships that can change during the execution time and has been extended to allow the creation of MFCM [25]. With this extension, it is possible to have several FCMs for the same problem, where each one expresses a different domain of knowledge of the system under study, but with relationships between them [25].

2.3 Fuzzy Cognitive Maps (FCM)

FCM theory uses a symbolic representation for the description and modeling of a phenomenon or system. It utilizes concepts to illustrate different aspects of a system's behavior, and these concepts interact with each other to describe system dynamics. A FCM integrates the accumulated experience and knowledge on system operations using human experts who know the system and its behaviors in different circumstances. They are modeling methods based on knowledge and experience, to describe particular domains using concepts (variables, states, inputs, outputs), and the relationships between them [6], [9], [12], [46],[47],[62],[63]. FCM can describe any system using a causality-based model (that indicates positive or negative relationships), which takes fuzzy values and is dynamic (i.e., the effect of a change in one concept/node affects other nodes, which in turn may affect further nodes). The fuzzy part allows us degrees of causality, represented as links between the nodes of these models, also known as concepts. This structure establishes the forward and backward propagation of causality [64].

Cognitive maps may be graphically represented, where concepts are connected by arcs through a connection matrix. In the connection matrix, the i-nth line represents the weight of the arc connections directed outside of the C_i concept, i.e., toward those concepts C_j affected by C_i. The i-nth column lists the arcs directed toward C_i, i.e., those affecting C_i [47], [62].

$$w_{i,j} = M(C_i, C_j) \tag{1}$$

Where M represents the causal function of the arc that has concept C_i with the preceding concept, C_j is the consequent concept, and $w_{i,j}$ is the weight of the relationship between these two concepts. In general, concept C_i increases C_j causally if $w_{i,j}$= 1, decreases it causally if $w_{i,j}$= −1, and does not affect it if $w_{i,j}$= 0.

With respect to the FCMs, they were initially presented as fuzzy mechanisms, where concepts and relationships could be represented as fuzzy variables (expressed in linguistic terms) [9]. In a FCM, the level of representation of each concept depends on the level of its predecessors in the previous iteration, and is calculated by means of a normalized sum of products, where the relationship between a concept and its predecessors is modeled by a simple weight, according to the following equation [9]:

$$C_m(i+1) = s\left[\sum_{k=1}^{N} w_{m,k} \cdot C_k(i)\right] \tag{2}$$

Where $C_m(i+1)$ indicates the value of the concept in the following iteration, N indicates the number of concepts, $w_{m,k}$ indicates the value of the causal relationship between the concept C_k and the concept C_m, and $S(.)$ is a function to normalize the value of the concept. The initialization of each concept, $C_m(0)$ is done by setting specific values based either on expert opinions or on a specific scenario that we would want FCM to predict. On the other hand, an extension of the FCM is the MCFM.

2.3.1 Multilayer Fuzzy Cognitive Map (MFCM)

To construct the MFCM, the Eq (2) for calculating the current status of the concepts of a FCM had to be modified, in order to integrate the function generated by the interface from the rules describing the relationships between different maps (layers). In that sense, the new mathematical equation is defined in [25], [26] as:

$$C_m(i+1) = s\left[\sum_{k=1}^{N} w_{m,k} \cdot C_k(i)\right] + F(mp) \tag{3}$$

Where $C_m(i+1)$ indicates the value of the concept in the next iteration, N indicates the number of concepts, $w_{m,k}$ indicates the value of the causal relationship between C_k concept and C_m concept, $s[.]$ is a function used to normalize the value of the concept, and $F(mp)$ is the input function generated by the interface of the multilayer map.

Thus, the update function of the concepts has two parts. The first part is the classic, which calculates the value of the concept in iteration $i+1$ based on the values of concepts in iteration i. All these concepts belong to the same layer to which the "m" concept belongs. The second part is the calculation of the causal relationship between the concepts in different FCMs (see [25] for more details). This formalism has been included in the FCM Designer Tool [25], [27]. For more detail about the FCM Designer Tool see [27].

With this extension, it is possible to have several FCMs for the same problem, where each one expresses a different level of knowledge of the system under study, but remain interlinked [25], [26]. Thus, one can have a first level of detailed system abstraction with specific information, and then more general levels. In addition, the variables of one level depend on those of other levels. That is, the multilayer approach enriches the modeled systems with a flow of information between layers, to derive information about the concepts involved in a layer, from the concepts in other layers. In the multilayer approach used in this work [26], relationships between the cognitive maps in different layers can be carried out in various ways [25], [26]: with fuzzy rules, connections with weights, or with mathematical equations.

Other work about MFCM can be seen in [65]. This work introduces a framework and a series of steps to gather both static and dynamic information, in order to build MFCM models. Other advances in FCM theory can be found in [8].

3. The MFCM-ASD model

In general, upon diagnosing ASD, our MFCM-ASD model follows the ADIR and ADOS2 decision-making process. In this section, firstly, we give a description of our MFCM-ASD model components, which are its concepts and relationships. Then, the set of rules that the MFCM-ASD model follows in order to update the relationship between the concepts is defined.

Specifically, the MFCM-ASD model is multilayer for expressing the different dimensions of knowledge required by the instrument used for the ASD diagnosis. One dimension is based on the information about the children, and the other in parental information. In this way, MFCM-ASD model cover naturally the different knowledge dimensions of the autism diagnosis of the ADIR/ADOS2 instrument.

3.1 Model Bases

In this subsection are specified the concepts and the relationships between the concepts of the ADIR and ADOS2 layers.

3.1.1 Description of the MFCM-ASD model concepts

In this study, the concepts used to model our MFCM-ASD are extracted from both, expert observations and the ADIR and ADOS2 diagnostic Instruments. Extracted concepts are listed in Tables 1 and 2. Input concepts represent the symptoms and signs of ASD. Output concepts represent severity levels of the symptoms.

Table 1

ADIR concepts used in the first layer of the MFCM

CONCEPT	DESCRIPTION
A1	Inability to use nonverbal behaviors in the regulation of social interaction
A2	Inability to develop relationships with peers
A3	Lack of shared joy or pleasure
A4	Lack of social or emotional reciprocity
TOTALA	Total of qualitative alterations of the reciprocal social interaction
B1	Lack or delayed spoken language and inability to make up for this lack by gestures, in verbal subjects.
B4	Lack of imaginative play or spontaneous and varied imitative social play, in verbal subjects
B2(V)	Relative inability to initiate and sustain a conversational exchange, in verbal subjects
B3(V)	Stereotyped, repetitive and idiosyncratic speech, in verbal subjects
TOTALBV	Total of qualitative alterations of the communication, in verbal subjects. These concepts only are active in verbal subjects
B1NV	Lack or delayed spoken language and inability to make up for this lack by gestures, in nonverbal subjects
B4NV	Lack of imaginative play or spontaneous and varied imitative social play, in nonverbal subjects. This concepts only are active in nonverbal subjects
TOTALBNV	Total of qualitative alterations of the communication in nonverbal subjects
C1	A forbidding preoccupation or circumscribed interest pattern
C2	Apparently compulsive adherence to non-functional routines or rituals
C3	Stereotypical and repetitive mannerisms
C4	Preoccupation with parts of objects or non-functional elements of materials
TOTALC	Total restricted, repetitive and stereotypical behavior patterns
OUTADIR	A classification of Autism or No autism is given when the scores in at least two of the three areas of communication, social interaction, and patterns of behavior, meet or exceed the specified cutoffs.

The A1, A2, A3, and A4 concepts are input concepts and represent the qualitative alterations of reciprocal social interaction. The TOTALA concept is an output concept and defines the severity level of the symptoms of qualitative alterations from reciprocal social interaction. The B1, B4, B2(V) and B3(V) concepts are input concepts and represent the qualitative alterations in the communication in verbal subjects. The TOTALBV concept is an output concept and defines the level of severity in the communication in verbal subjects. The B1NV and B4NV concepts are input concepts and represent the qualitative alterations in the communication in nonverbal subjects. The TOTALBNV concept is an output concept and defines the level of severity in the communication in nonverbal subjects. The C1, C2, C3, and C4 concepts are input concepts and represent restricted, repetitive and stereotypical behavior patterns. The TOTALC concept is an output concept and defines the level of severity of the restricted, repetitive and stereotypical behavior patterns. Finally, the OUTADIR concept is an output concept that represents the presence (or absence) of Autism. This classification is given when scores in at least two of the three output concepts (TOTALA, TOTALBV/TOTALBNV or TOTALC) meet or exceed their specified cutoffs.

Table 2

ADOS2 concepts used in the second layer of the MFCM

CONCEPT	DESCRIPTION
C-ADOSMX	Communication problems, evaluated with the algorithms of the module X (X refers to the module T, 1, 2 or 3).
ISR-ADOSMX	Reciprocal social interaction problems, evaluated with the algorithms of the module X.
CRR-ADOSMX	Restricted and repetitive behavior problems, evaluated with the algorithms of the module X.
OUT-MX	Level of social impairment and restricted and repetitive behaviors, evaluated with the algorithms of the module X.
C-ADOSM4	Communication problems, evaluated with the algorithms of the module 4.
ISR-ADOSM4	Reciprocal social interaction problems, evaluated with the algorithms of the module 4.
CRR-ADOSM4	Restricted and repetitive behavior problems, evaluated with the algorithms of the module 4.
IC-ADOSM4	Imagination and creativity problems, evaluated with the algorithms of the module 4
OUT-M4	Level of social impairment and restricted and repetitive behaviors, evaluated with the algorithms of the module 4
OUT-ADOS2	It is the final output value of the diagnostic according to ADOS2
OUT-TEA	It is the final output value of the concepts OUTADIR and OUT-ADOS2

In ADOS2, each module evaluates three elements that describe the main problems related to autism in specific chronological ages. These elements are: communication problems, reciprocal social interaction problems and restricted and repetitive behavior problems (with the exception of module 4, which include a fourth element: imagination and creativity).

The C-ADOSMX, ISR-ADOSMX, and CRR-ADOSMX concepts represent the input information from the Toddler Module, Module 1, Module 2 or Module 3. The first concept (C-ADOSMX) represents communication problems; the second concept (ISR-ADOSMX) represents reciprocal social interaction problems, and the third concept (CRR-ADOSMX) represents restricted and repetitive behavior problems. OUT-MX is an output concept, which determines the level of social impairment and restricted and repetitive behaviors, evaluated with the algorithms of the module X. The C-ADOSM4, ISR-ADOSM4 and CRR-ADOSM4 concepts measure the same problems mentioned above. IC-ADOSM4 represents the particular problems of imagination and creativity. OUT-M4 is an output concept, which determines the level of social impairment and restricted and repetitive behaviors, evaluated by the algorithms from module 4. OUT-ADOS2 is the final output value of the diagnostics according to ADOS2. Finally, OUT-TEA represents a measure that combines the degree of autism assessment of both, ADIR and ADOS2.

In total, 30 concepts were considered in the model: divided into two layers: 19 concepts model the knowledge around ADIR, and 10 around ADOS2. Finally, a general output conjugates the simultaneous application of both instruments. We considered all these concepts when designing our MFCM-ASD model. Figure 1 shows the general model of our MFCM-ASD for predicting ASD.

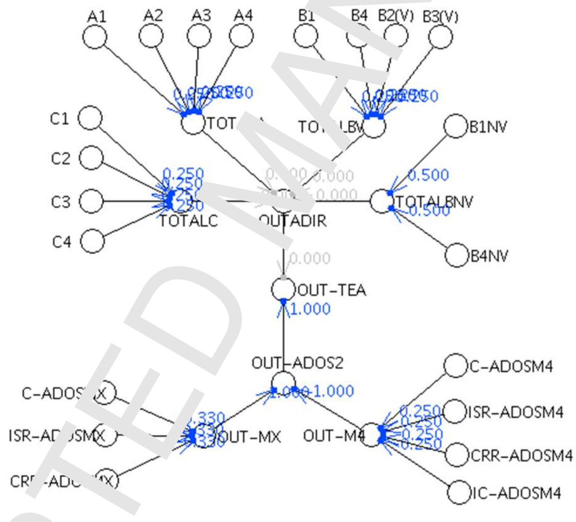

Fig. 1. MFCM-ASD for predicting ASD.

3.1.2 Description of the relationships between the concepts of the ADIR layer.

According to Aguilar [28], there are three ways to establish causal relationships between the concepts: 1) based on the expert opinion (each expert provides their individual FCM matrix according to personal experience); 2) through augmented FCMs (several FCMs are combined to form a new FCM); and 3) based on historical data (system performance data is used as input pattern). The first option is used in this work, based on ASD diagnostic instruments.

The weights are defined based on the expert opinions regarding relationships between concepts defined in the previous section according to the ADIR and ADOS2 diagnostic instruments. According to their opinions, each concept involved in the evaluated domain (quality of social interaction, communication and language, etc.) contributes in the diagnosis in the same way. So, the weight of each relationship is 1 divided by the number of input concepts of the domain.

On the other hand, the value of each input concept is assigned by the expert according to the used ADIR or ADOS2 instrument (more specifically, the diagnostic algorithm employed). Concepts values given by the experts, are normalized to [0, 1].

Description of the relationships of the TOTALA layer.

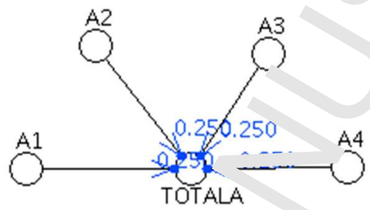

Fig. 2. Concepts and relationships of the qualitative alterations of the reciprocal social interaction.

This domain has four input concepts and each relationship has a weight of 1/4 = 0.25 (see Figure 2). The expert, according to ADIR, gives the value of the A1, A2, A3 and A4 concepts. The TOTALA concept is activated when the cut-off point for this domain is surpassed. The normalized cut-off for this case is 0.33.

Description of the relationships of the TOTALBV layer.

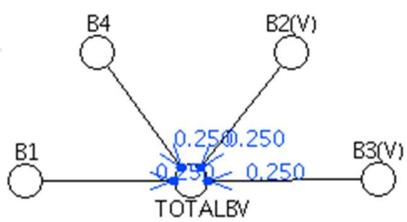

Fig. 3. Concepts and relationships of the qualitative alterations of Communication (Verbal Subjects).

This domain has four input concepts and each relationship has a weight of 1/4 = 0.25 (see Figure 3). The expert, according to ADIR, gives the value of the B1, B4, B2(V) and B3(V) concepts. The TOTALBV concept is activated when the cut-off point for this domain is surpassed. The normalized cut-off for this case is of 0.30.

Description of the relationships of the TOTALBNV layer.

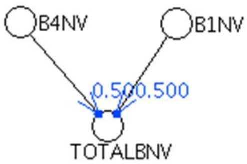

Fig. 4. Concepts and relationships of the qualitative alterations of Communication (Nonverbal Subjects)

This domain has two input concepts and each relationship has a weight of 1/2 = 0.50 (see Figure 4). The expert, according to ADIR, gives the value of the B4NV and B1NV concepts. The TOTALBNV concept is activated when the cut-off point for this domain is surpassed. The normalized cut-off for this case is of 0.27.

Description of the relationships of the TOTALC layer.

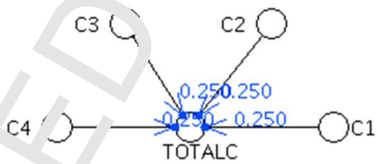

Fig. 5. Concepts and relationships of the repetitive and stereotypical behavior pattern.

This domain has four input concepts and each relationship has a weight of 1/4 = 0.25 (see Figure 5). The expert, according to ADIR, gives the value of the C1, C2, C3 and C4 concepts. The TOTALC concept is activated when the cut-off point for this domain is surpassed. The normalized cut-off for this case is of 0.25.

Description of the relationships of the OUTADIR layer.

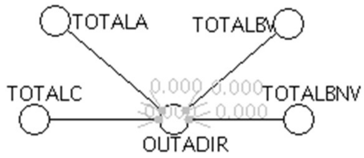

Fig. 6. Concepts and relationships of the causativeness of autism based on ADIR

As we can see in the figure 6, the weights of all relations are 0. Relationship weights are activated dynamically when the value of the previous concepts (TOTALA, TOTALBV, etc.) has exceeded the cutoff point. If two of the three concepts reach or exceed the cut-off point, then the OUTADIR concept is activated. In this domain, the TOTALBV and TOTALBNV concepts are exclusive. They cannot be activated simultaneously; when one is active the other one goes out. So, each relationship has a weight of 1/3 = 0.33. Based on the above, an activation threshold (Δ=0.66) has been defined for the OUTADIR concept. When a concept exceeds the cut-off, then its value becomes 1 and the weight of the relationship is set to 0.33. The possible activation combinations of the OUTADIR concept are shown in Table 3.

Table 3

Activation combinations of the OUTADIR concept

CONCEPTS	TOTALA	TOTALBV-BNV	TOTALC	OUTADIR
ACTIVATION	On	Off	Off	Off
	Off	On	Off	Off
	Off	Off	On	Off
	On	On	Off	On
	On	Off	On	On
	Off	On	On	On
	On	On	On	On

“On” means that the cut-off point or threshold is exceeded and “Off” that is not.

3.1.3 Description of the relationships between ADOS2 *layer concepts*

Description of OUT-MX layer relationships

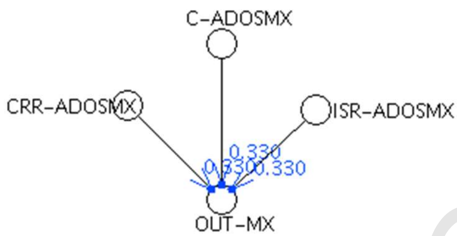

Fig. 7. Concepts and relationships of the OUT-MX layer.

This layer is comprised of four modules (Module T, Module 1, Module 2, and Module 3). The four modules are grouped into one because they all evaluate the same elements (Communication, Interaction Social Reciprocal, and repetitive and stereotypical behavior pattern), only that for different age range and language constraints. Thus, this domain has three concepts: C-ADOSMX, CRR-ADOSMX and ISR-ADOSMX. Each relationship has a weight of 1/3 = 0.33 (see Figure 7). The values of the concepts recorded by the expert on the observation instrument are normalized in [0,1].

Description of OUT-M4 layer relationships

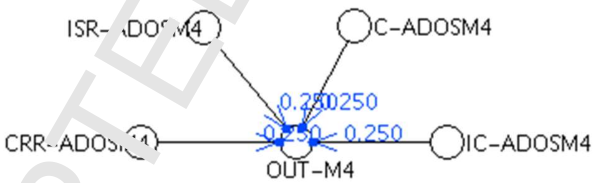

Fig. 8. Concepts and relationships of the OUT-M4 layer.

This layer corresponds to Module 4. This domain has four concepts: C-ADOSM4, CRR-ADOSM4, ISR-ADOSM4 and IC-ADOSM4. Each relationship has a weight of 1/4 = 0.25 (see Figure 8).

Description of the relationships of the OUT-ADOS2 layer

Fig. 9. Concepts and relationships of the OUT-ADOS2 layer

Regardless of the ADOS2 observation model used (OUT-MX or OUT-M4), its contribution to the general OUT-ADOS2 output is the same (they have an equal weight in the relationship (1.0)), and its value passes to OUT-ADOS2 (see Figure 9).

Description of OUT-TEA layer relationships

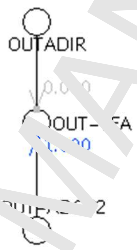

Fig. 10. OUT-TEA

The connection of the two maps (ADIR and ADOS2) is done through direct connection rules in which the concept of origin, the concept of destination, and the weight of the connection are defined. Specifically, the OUT-TEA output is derived from one of the two instruments used, predominating the AUT-ADOS2 output for when the two instruments are simultaneously applied (see Figure 10).

3.2, Rules followed by the MCFD-ASD model to map the ADIR and ADOS2 decision-making process

MFCM-ASD is based on MFCM (see Section 2.3.1). In designing the MCFD-ASD, a certain part of the MCFM method had to be modified. The main change was in the concept relationship value calculation mechanism. This mechanism consists of a set of rules from which each value is calculated. Some of the rules defined for the MCFD-ASD model to calculate concept relationship values are shown below:

Rule 1:

1. IF the initial relationship concept is equal to "OUTADIR" and the final concept of the relation is equal to "OUT-TEA" THEN

   1.1 IF cutoff point of ADIR is exceeded THEN the relationship value is 1.0.

   1.2. ELSE the relationship value is 0.0.

Line 1 of the rule determines the relation to be treated; in line 1.1 determines whether the value of the general cut for the diagnosis with ADIR has been exceeded. If so, then it assigns a value of 1.0 (showing signs of autism) to the weight of the relation, otherwise, in line 1.2 is assigned a value of 0.0 to the relation (that shows no signs of autism).

Rule 2:

2. IF the initial relationship concept is equal to "TOTAL_A" and the final concept of the relationship is equal to "OUTADIR" THEN

   2.1 we get the relationship value.

   2.2. IF cutoff point of A is exceeded THEN the relationship value is 0.33.

   2.3. ELSE the relationship value is 0.0

Line 2 of the rule determines the relationship to be treated. Line 2.1 gets the current value of the relationship. If the value exceeded the cutoff point of A, then it assigns a value of 0.33 (a symptom of autism is present) to the weight of the relationship; otherwise, line 2.3 assigns a value of 0.0.

In total, 26 rules representing the diagnostic logic underlying of the ADIR and ADOS2 instruments were defined.

4. Simulations and Results

This section presents the different experiments carried out with the MCFM-ASD model. The experiments are classified into three groups: firstly, autism cases were analyzed with ADIR, then analyzed with ADOS, and finally using both instruments.

4.1. Experimental data

In this subsection, the dataset used for testing the MCFM-ASD model is described.

Participants. The study sample was 300 children: 150 from the clinical group (diagnosed with autism or Asperger syndrome) and another 150 neurotypical children, i.e., free of these conditions. In the clinical group, 30.2% were diagnosed with Autism and 14.3% with Autistic Spectrum. The children were between 2 and 12 years of age, and comprised of 76 girls and 224 boys. The children are a sample from the Ecuadorean coastal and sierra regions, ethnically defined as "mestizos" and chosen from different social classes. This data has been provided by the Association of Parents and Friends for the Support and Defense of the rights of people with Autism (APADA, for its acronym in English) from Ecuador (see section 7 for ethical standards).

Sampling procedure. The diagnosis was carried out through the application of the ADIR test with the parents, and the observation of the children through ADOS2 and other specialized studies, such as CT scans, resonances, and clinical studies. The tests were applied in appropriate scenarios to provide cozy, distraction-free, well-lit environments, with adequate furniture and privacy for the convenience of both interviewees and researchers, and original test materials were used for each test. In this study, the instruments were applied by three well certified professionals.

4.2. Experiments with ADIR cases

In this section, the test experiments carried out are presented. In our system, the experts give the values of the input concepts by analyzing the different options of ADIR. For the input concepts of ADIR the following input vector is defined:

ADI^0 ={A1, A2, A3, A4, TOTALA, B1, B4, B2(V), B3(V), TOTALBV, B1NV, B4NV, TOTALBNV, C1, C2, C3, C4, TOTALC, OUTADIR}

OUTADIR has been considered by the experts as a decision output concept (DOC), and could be categorized as No evidence of symptoms (NES), Moderate Evidence of Symptoms (MES) and Definite Evidence of Symptoms (DES), which take the values NES=0, MES=0.66 and DES= 0.99, respectively. MES occurs when two of the three diagnostic elements exceeded the cut-off. DES occurs when the three diagnostic elements exceeded the cut-off, and NES when none or at most one has achieved the cut-off point. When only one diagnostic element exceeded the cut-off, it tells us that a person has a specific abnormal behavior, which is likely to occur due to other developmental, neurological, or psychiatric disorders, so it is treated as NES.

Now, we describe different autism diagnostic cases with ADIR. ADIR uses two algorithms: *one for current behavior and a second diagnostic algorithm*. Each one considers different elements of autism, according to the chronological age. Our model covers both algorithms.

ADIR-1 Case. CA1 is a subject with a chronological age of 3 years and a half, and to whom the diagnostic algorithm of ADIR was applied. In this case, the initial values of each concept are: A1=2, A2=4, A3=6, A4=7, TOTALA=18, B1=0, B4=0, B2(V)=0, B3(V)=0, TOTALBV=0, B1NV=8, B4NV=5, TOTALBNV=13, C1=2, C2=0, C3=2, C4=2, TOTALC=6 and OUTADIR=DES. The diagnostic vector given by the expert is: ADI^1 ={2, 4, 6, 7, 19, 0, 0, 0, 0, 0, 8, 5, 13, 2, 0, 2, 2, 6, Definite Evidence of Symptoms}. Then the normalized initial numerical values used for the simulation process are S^1 = {0.33, 1, 1, 0.7, 0, 0, 0, 0, 0, 0, 1, 0.83, 0, 0.5, 0, 1, 1, 0, 0}. The values corresponding to the output TOTALA, TOTALBV, TOTALBNV, TOTALC, and OUTADIR=DES concepts are assigned by default in 0. The MFCM infers these values. Making use of the FCM Designer Tool, we load the input concept values into our model (see Figure 11).

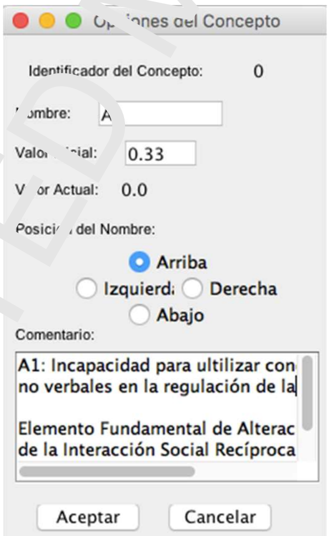

Fig. 11. Initialization of the concept A1 in 0.33.

Once all the values have been loaded, the model is executed. The results are presented in Table 4.

Table 4

Concept values at each interaction of our MFCM for the ADIR-1 Case.

[0.31, 1.0, 1.0, 0.75, 1.0, 0.98, 0.81, 1.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.5, 0.0, 1.0, 1.0, 1.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0,0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.98, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.98**, 0.0, 0.0, 0.0, 0.0, 0.0]

Each row in the table 4 has 30 values, each of which corresponds to our model's concept vector: [A1 A2 A3 A4 TOTALA B1NV B4NV TOTALBNV B1 B4 B2(V) B3(V) TOTALBV C1 C2 C3 C4 TOTALC OUTADIR C-ADOSMX ISR-ADOSMX CRR-ADOSMX IC-ADOSM4 OUT-ADOS2 OUT-TEA OUT-MX C-ADOSM4 ISR-ADOSM4 CRR-ADOSM4 OUT-M4]. In the first iteration, the concept values TOTALA, TOTALBNV and TOTALC have changed from 0 (inactive) to 1 (active). That means that they reached the cutoff point. In the second iteration, the value of OUTADIR = 0.98 means that the three previous elements are present, giving the result of *Definite Evidence of Symptoms*, as has been specified by the experts. The value in the fourth iteration corresponds to the concept of output OUT-TEA (0,98).

ADIR-2 Case. CA2 is a subject with a chronological age of 9 years, and to whom the *diagnostic algorithm* of ADIR was applied. In this case, the initial values of each concept are: A1=6, A2=8, A3=5, A4=7, TOTALA=26, B1=7, B4=5, B2(V)=4, B3(V)=2, TOTALBV=18, B1NV=0, B4NV=0, TOTALBNV=0, C1=0, C2=0, C3=0, C4=1, TOTALC=1 and OUTADIR=PES. The diagnostic vector given by the expert is: ADI^2={6, 8, 5, 7, 27, 7, 5, 4, 2, 18, 0, 0, 0, 0, 0, 0, 1, 1, Probable Evidence of Symptoms}. Then, the normalized initial numerical values used for the simulation process are S^2 = {0.96, 1, 0.8, 0.7, 0, 0.87, 0.8, 1, 0.25, 0, 0, 0, 0, 0, 0, 0, 1, 0,0}. Once all the values have been loaded, the model is executed. The results are presented in Table 5.

Table 5

Concept values at each interaction of our MFCM for the ADIR-2 Case.

[0.9, 1.0, 0.8, 0.73, 1.0, 0.0, 0.0, 0.0, 0.84, 0.95, 0.21, 0.8, 1.0, 0.0, 0.0, 0.0, 0.25, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.05, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0625, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.68, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.68**, 0.0, 0.0, 0.0, 0.0, 0.0]

In the first iteration, concept values TOTALA and TOTALBV have changed from 0 (inactive) to 1 (active). This means that they reached the cutoff point. In the second iteration, the value of TOTALC = 0.0625 means that it does not pass the cut-off point and it is not active. In the third iteration, the value of OUTADIR = 0.68 means that only two concepts passed the cutoff point, giving the result of *Moderate Evidence of Symptoms*, as has been specified by the experts. The value in the fourth iteration corresponds to the concept of output OUT-TEA (0.68).

ADIR-3 Case. CA3 is a subject with a chronological age of 12, and to whom the *diagnostic algorithm* of ADIR was applied. In this case, the diagnostic vector given by the expert is: ADI^3 ={6, 8, 4, 9, 27, 2, 3, 5, 3, 13, 0, 0, 0, 3, 3, 4, 4, 14, Definitive Evidence of Symptoms}. Subsequently, a data normalization process is performed, and the initial numerical values used for the simulation process are S^3 = {0.96, 1, 0.64, 0.9, 0, 0.75, 0.75, 0.62, 0.48, 0, 0, 0, 0, 0.75, 0.75, 0.5, 1, 0, 0}. Once all the values have been loaded, the model is executed. The results are presented in Table 6.

Table 6

Concept values at each interaction of our MFCM for the ADIR-3 Case.

[0.94, 1.0, 0.58, 0.86, 1.0, 0.0, 0.0, 0.0, 0.25, 0.75, 0.65, 0.46, 1.0, 0.7, 0.72, 0.5, 1.0, 1.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0,0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.99, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.99**, 0.0, 0.0, 0.0, 0.0, 0.0].

In the first iteration, concept values TOTALA, TOTALBV and TOTALBV have changed from 0 (inactive) to 1 (active). This means that they reached the cutoff point. In the second iteration, the value of OUTADIR = 0.99 means that the three previous elements are present, giving the result of Definitive Evidence of Symptoms, as has been specified by the expert.

4.3. Experiments with ADOS2 cases

Similar to the previous section, in our system experts give input concept values by analyzing the different ADOS2 options.

Now, we describe different scenarios of autism diagnostic cases with ADOS2. It uses distinct algorithms: the module T uses the algorithms for younger/older children with little or no words and older children with some words. Module 1 uses the algorithms of few or no words and with some words. Module 2 uses the algorithms of children under 5 and over 5 years. Modules 3 and 4 have a single algorithm. For the input concepts of ADOS2 the following input vector is defined: ADO^0 ={C-ADOSMX, ISR-ADOSMX, CRR-ADOSMX, OUT-MX, IC-ADOSM4, ISR-ADOSM4, CRR-ADOSM4, IC-ADOSM4, OUT-M4, OUT-ADOS2}. The OUT-ADOS2 concept determines the severity score according to the ADOS2 module . Table 7 shows the cut-off and the classification for the module 1, according to the Michigan State Department of Health and Human Services [69].

Table 7

Module 1 Case

MODULE 1 TOTAL CUTOFF SCORE		
	FEW NO WORDS	SOME WORDS
AUTISM	16	12
AUTISM SPECTRUM	11	8
ASSIGN THE ADOS2 CLASSIFICATION		
AUTISM	Total is equal to or greater than the autism cutoff • Little or No Words- Total is 16 or higher • Some Words- Total is 12 or higher	
AUTISM SPECTRUM	Total is equal to or greater than the autism spectrum cutoff, but less than the autism cutoff. • Little or Words- Total is 11 to 15 • Some Words- Total is 8 to 11	
NON-SPECTRUM	Total is less than the autism spectrum cutoff. • Little or No Words- Total is 10 or lower • Some Words- Total is 7 or lower	

According to table 7, a child with little or no words is diagnosed as autistic, when the total is greater than the autism cutoff (16 or higher). Whereas a child with little or no words is diagnosed with autism or outside the spectrum, when the total is less than the autism spectrum cutoff (10 or lower). Similar tables are defined for the other modules [69]. Experts have considered OUT-ADOS2 as a decision output concept and could be categorized as Non-Spectrum (NS), Autism Spectrum (ASD) and Autism (AUT). Our system uses a normalized scale in the range [0,1] to infer its response. A more detailed description of the values range related to age used in our system is shown in the table 8 (similar tables are defined for the other modules).

Table 8

Calibrated Severity Score, Module 1, No Words.

ADOS Classification	Calibrated Severity Score	Module 1, No Words 2 yrs	3 yrs	4–5 yrs	6–14 yrs
NS	1	0–6	0–6	0–3	0–3
	2	7–8	7–8	4–6	4–6
	3	9–10	9–10	7–10	7–10
ASD	4	11–13	11–14	11–12	11–13
	5	14–15	15	13–15	14–15
AUT	6	16–19	16–20	16–19	16–19
	7	20–21	21–22	20–21	20–22
	8	22	23	22–23	23–24
	9	23–24	24	24–25	25
	10	25–28	25–28	26–28	26–28

ADOS2-Module 1 Case. In this case, we have a 7-year old non-verbal child, to whom the module 1 diagnostic algorithm was applied. The diagnostic vector given by the expert is: $ADO^1 = \{4, 15, 7, 26, 0, 0, 0, 0, 0, AUT\}$. The patient is on the autistic spectrum, with a high level of symptoms (AUT). Subsequently, a data normalization process is performed, and the initial values of the simulation process are $S^1 = \{1, 0.93, 0.87, 0, 0, 0, 0, 0, 0, 0\}$. Once all the values have been loaded, the model is executed. The results are shown in Table 9.

Table 9

Concepts values at each interaction of our MFCM for the ADOS2-Module 1 Case.

[0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 1.0, 0.91, 0.79, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.95, 0.0, 0.0,0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.95, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.95,** 0.0, 0.0, 0.0, 0.0, 0.0, 0.0]

In the second iteration, we have the value calculated for the OUT-MX concepts, which in this case corresponds to the output of model 1. 0.95 in the classification of Table 8 gives a calibrated severity score of 10, i.e., OUT with a high level of symptoms, as has been specified by experts. In interaction 3, we have the output for the OUT-ADOS2 concept, and finally, in iteration 4 we have the output of the OUT-TEA concept.

ADOS2-Modulo 2 Case. In this case, we have a child of 11-year and verbal, to whom the module 2 diagnostic algorithm was applied. The input vector given by the expert is: ADO^2 ={0, 5, 5, 10, 0,0,0,0,0, ASD}. The patient is on the autistic spectrum, with moderate levels of symptoms (ASD). After the normalization process, the initial values of the simulation process are: S^2 = {1, 0.93, 0.87, 0, 0, 0, 0, 0, 0, 0}. Once all the values have been loaded and the model executed, the results are shown in Table 10.

Table 10

Concept values at each interaction of our MFCM for the ADOS2-Module 2 Case.

[0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.29, 0.61, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.315, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.315, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.315**, 0.0, 0.0, 0.0, 0.0, 0.0]

In the second iteration, we have the value calculated for the OUT-MX concept, which in this case corresponds to the output of the model 2. 0.315 in the classification table of module 2 gives a calibrated severity score of 6, i.e., autism with a moderate level of symptoms, as has been specified by the experts.

ADOS2- Module 3 Case. In this case, we have a child of 12-year and verbal, to whom the module 3 diagnostic algorithm was applied. The input vector given by the expert is: ADO^3 ={5, 10, 5, 20, 0,0,0,0,0, AUT}. The patient is on the autistic spectrum, with high levels of symptoms (AUT). After to the normalization process, the initial values of the simulation are: S^3 = {0.830, 0.714, 0.625, 0, 0, 0, 0, 0, 0, 0}. Once all the values have been loaded and the model executed, the results are given in Table 11.

Table 11

Concept values at each interaction of our MFCM for the ADOS2-Module 3 Case.

[0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.8, 0.73, 0.65, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.725, 0.0, 0.0, 0.0, 0.0],[0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.725, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0], [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, **0.725**, 0.0, 0.0, 0.0, 0.0, 0.0]

In the second iteration, we have the calculated value of the OUT-MX concept, which corresponds in this case to the output of model 3. 0.725 in the classification table of module 3 gives a calibrated severity score of 10; i.e., autism with high levels of symptoms, as has been specified by the experts.

4.4 Experiments with ADIR and ADOS2

Now, we test our MFCM in a dataset composed of 43 cases of ADIR with Definite Evidence of Symptoms, 10 case of ADIR with Moderate Evidence of Symptoms, and 8 cases of ADIR with no Evidence of Symptoms. The dataset also has 3 cases of ADOS2-Module T with a Moderate level of symptoms, 2 cases of ADOS2-Module T with a high level of symptoms, 7 cases of ADOS2-Module 1 with a Moderate level of symptoms, 5 cases of ADOS2-Module 1 with a high level of symptoms, 8 cases of ADOS2-Module 1 with a Low level of symptoms, 3 cases of ADOS2-Module 2 with a high level of symptoms, 4 cases of ADOS2-Module 2 with a Low level of symptoms, 3 cases ADOS2-Module 2 with a Moderate level of symptoms, 8 cases of ADOS2-Module 3 with a Moderate level of symptoms, 5 cases of ADOS2-Module 3 with a high level of symptoms, 5 cases of ADOS2-Module 3 with a low level of symptoms, 3 cases of ADOS2-Module 4 with a Moderate level of symptoms, and 3 cases of ADOS2-Module 4 with a high level of symptoms.

We analyze MCFM-ASD model performance using the accuracy metric in the previous dataset. The following accuracy was achieved (see tables 12 and 13, respectively).

Table 12

Classification results of our MCFM model for ADIR.

	NES	MES	DES
ADIR	8/7	10/8	43/43

The diagnostic accuracy is calculated as: Accuracy Percentage = (8/7+10/8+43/43)/3 =89.2%. MCFM-ASD is very accurate in cases where there is Definite Evidence of Symptoms (DES =

43/43). Though it is not true for cases with Moderate Evidence of Symptoms (MES = 10/8 or those with No evidence of symptoms (NES = 8/7). Hence, its general accuracy is 89.2%.

Table 13

Classification results of our MCFM model for ADOS2

	NS	ASD	AUT
ADOS2-MODULE T	No dataset available	3/3	2/2
ADOS2-MODULE 1	8/8	7/7	5/5
ADOS2-MODULE 2	4/4	3/3	3/3
ADOS2-MODULE 3	5/5	8/7	5/5
ADOS2-MODULE 4	No dataset available	3/3	3/3

The diagnostic accuracy is calculated as: Accuracy Percentage = (3/3+2/2+8/8+7/7+5/5+4/4+3/3+3/3+5/5+8/7+5/5+3/3+3/3)/13 =99%. Unlike the previous simulations of ADIR, which yielded some cases where it failed to detect cases of light autism or without autism, the ADOS2 simulations were very successful, reaching 99% accuracy. The accuracy of the instruments evaluated separately are consistent with the fact that ADOS provides a better diagnostic than ADIR [43].

5. Comparisons with other methods

In this section are carried out quantitative and qualitative comparisons. A first quantitative comparison is with a similar computational model (FCM) that use another instrument for the ASD diagnostic, proposed in Kannappan et al. [50]. The qualitative comparison is based on the quality of the instrument for the ASD diagnosis. Finally, the last comparison is with machine learning algorithms used for the ASD diagnosis.

5.1 Quantitative comparison

Kannappan et al. [50] have proposed a diagnostic ASD model using a FCM based on the MCHAT (F-MCHAT) standard. This model focuses on the soft computing technique of FCM with the NHL (Nonlinear Hebbian Learning) training algorithm for the estimation of ASD. The 24 FCM model concepts proposed in Kannappan et al. [50] are shown in the second column of the Table 14. The third column is its equivalent in our model. This equivalence was made in order to use the same data and to carry out the same tests, to compare them. This comparison is important because they use the same computational paradigm that our approach.

Table 14

FCM model concepts proposed in [50] and their equivalents in our model.

#	MCHAT	ADOS2
C1	Enjoy being swung	CRR-ADOSMX
C2	Take an interest in other children	ISR-ADOSMX
C3	Climbing on things	CRR-ADOSMX
C4	Enjoy playing	ISR-ADOSMX
C5	Pretend other things	C-ADOSMX
C6	Pointing index finger	C-ADOSMX
C7	Indication of interest	ISR-ADOSMX
C8	Playing with small toys	CRR-ADOSMX
C9	Bringing objects to parents	ISR-ADOSMX
C10	Eye contact	C-ADOSMX
C11	Oversensitive to noise	CRR-ADOSMX
C12	Smile in response to parents face	ISR-ADOSMX
C13	Imitate	C-ADOSMX
C14	Responding to the name	ISR-ADOSMX
C15	Looking at a toy when pointing	C-ADOSMX
C16	Walking	CRR-ADOSMX
C17	Look at things	CRR-ADOSMX
C18	Unusual finger movements near his/her face	CRR-ADOSMX
C19	Attract the attention	ISR-ADOSMX
C20	Deafness	CRR-ADOSMX
C21	Understanding what others say	C-ADOSMX
C22	Stare at nothing	CRR-ADOSMX
C23	Look at the face to check the reaction	ISR-ADOSMX
OUTC1	Autism (High, Probable autism and No autism)	OUT-MX

Thus, following the same input vector notation defined in section 4.2. A general input vector to the model proposed in [50] is: V= {C1 C2 C3 C4 C5 C6 C7 C8 C9 C10 C11 C12 C13 C14 C15 C16 C17 C18 C19 C20 C21 C22 C23 OUTC1} where the first 23 values correspond to the 23 input concepts evaluated by the expert, and the last value corresponds to the Decision Output Concept (DOC=OUTC1). Kannappan et al. [50] have used as Calibrated Severity Score for classification: 0.41 <= DA (definite Autism) <= 1.00, which is also the diagnosis given by the expert 0.26 <= PA (probable autism) <= 0.40, and 0 <= NA (no autism) <= 0.25, respectively.

To compare the results of this model with our model, we have carried out an equivalence process between MCHAT and ADOS2. The equivalence is shown in the columns 2 and 3 of the Table 14. In our model, the input vector is reduced to three values ADO^0 ={C-ADOSMX, ISR-ADOSMX, CRR-ADOSMX…}, where the value of each concept in our vector is the average value of the equivalent concepts of [50], that is

CRR-ADOSMX= (C1+C3+C8+C11+C16+C18+C20+C22)/8

ISR-ADMX= (C2+C4+C7+C9+C12+C14+C17+C19+C23)/9

C-ADOSMX= (C5+C6+C10+C13+C15+C21)/6

Specifically, we use the ADOS2 Model 1 diagnostic algorithm. Applying our model to the three base cases described in [50], we have obtained the following results (Table 15 shows the comparison of the results):

Case 1: Vector given by the expert V^1= {0.3 0.55 0.6 0.65 0.2 0.6[illegible] 0.73 0.77 0.86 0.1 0.57 0.4 0.5 0.62 0.6 0.71 0.9 0.15 0.25 0.45 0.49 0.34 0.62 **0.51**} Diagnostic: Definitive Autism (**0.51=DA**). Equivalent input vector for our model ADO^1={0.430, 0.620, 0.486, 0,0,0,0,0,0,0}. Applying our model, the result is **OUT-MX=0.50**, Diagnostic: Autism (AUT).

Case 2: Vector given by the expert V^2= {0.17 0.3[illegible] [illegible].32 0.43 0.2 0.1 0.01 0.32 0.41 0.13 0.15 0.44 0.28 0.5 0.64 0.15 0.25 0.3 0.29 0.27 0.[illegible]1 [illegible]4 0.42 **0.41**}. Diagnostic: Probable Autism (**0.41=PA**). Equivalent input vector for our model ADO^1={0.277, 0.339, 0.260, 0,0,0,0,0,0,0}. Applying our model, the result is **OUT-MX=0.28**, Diagnostic: Autism (ASD).

Case 3: Vector given by the expert V^3= {0.56 0.72 0.53 0.64 0.75 0.66 0.87 0.76 0.95 0.45 0.76 0.52 0.73 0.44 0.75 0.67 0.57 0.48 0.4[illegible] 0.4 0.41 0.42 0.43 **0.87**}. Diagnostic: Probable Autism (**0.87=DA**). Equivalent input vector for our model ADO^1={0.625, 0.626, 0.573, 0,0,0,0,0,0,0}. Applying our model, the result is **OUT-MX=0.60**, Diagnostic: Autism (AUT).

Table 15
Comparison of the diagnostic results

EXPERT	MFCM-ASD	FCM [50]
0.51=DA	0.50=AUT	0.73=DA
0.41=PA	0.28=ASD	0.37=PA
0.87=DA	0.60=AUT	0.659=DA

Our MCFM model follows the three expert diagnoses and the model proposed in [50] very well. Now, we use the same dataset used in [50], with 40 diagnosed cases. They obtained the following results: 20 out of 23 cases were diagnosed as definite Autism (DA), 10 out of 13 as probable autism (PA), and 3/4 as no autism (NA). Using our MFCM, we have obtained the next results: 23 out of 23, 11 out of 13, and 3/4, giving an accuracy rate of 92.5%, which is higher when compared to the 82.5% accuracy achieved by the FCM used in [50].

Now, we show the ROC (Receiver Operating Characteristic) curve for these two models, so as to analyze their sensitivity and specificity in the ASD diagnostics process (see Fig. 12). In general, diagnostic methods with high sensitivity are required since most ASD patients must give positive results during the diagnostic test. Diagnostic methods with high specificity are also required because we are interested in seeing negative results from those without ASD. In the ROC curve, we can calculate an area under that curve, called the AUC (Area under curve), with a value that goes from 0 to 1. In the ROC curve, the ideal value is close to the point (0, 1), that is its upper left vertex, which at the same time represents a lot of sensitivity and specificity (a very good diagnostic method). That, in the case of UAC means that the closer to 1 the value the better diagnostic method, representing a diagnostic method with more possibilities of discerning this disease and no disease. In Figure 12, the AUC value reached by the MCFM model is of 0.889, indicating that it is close to the left-hand and top border of the ROC curve, therefore giving very precise results. On the other hand, the AUC reached by [50] is of 0.761, indicating less precise results than our model.

MCFM-ASD [50]

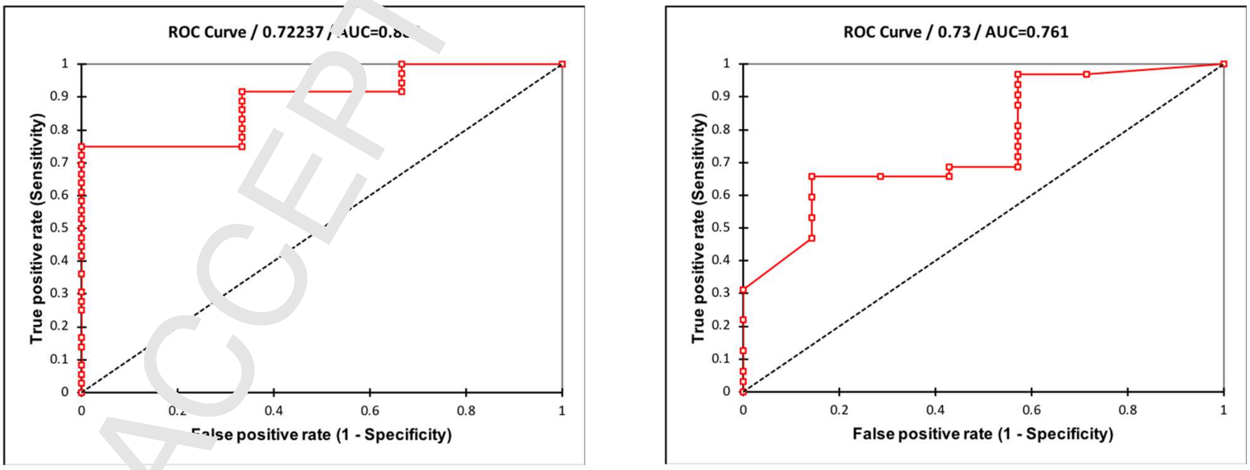

Fig. 12. Comparison of sensitivity and specificity

5.2 Qualitative comparison

At the 2008 International Meeting for Autism Research (IMFAR) in London, ADIR and ADOS were defined as the gold standard for autism research [35]. ADOS is an observational instrument that can be applied from the age of 18 months, allowing early diagnosis and to know the degree of severity of the autism. Studies showed that ADOS has a sensitivity of 0.9, a specificity of 0.8, an internal consistency of 0.47-0.94, reliability of 0.65-0.82 and temporal stability of 0.59-0.82. Excellent inter-rater reliability within each module (0.65-0.78) and a good test-retest reliability (0.59-0.82) [35]. ADIR is an interview directed at parents with the aim of diagnosing autism, it can be applied from 2 years of age and evaluates 4 domains: social; restricted and repetitive behaviors, verbal and communication. Instrument sensitivity is between 0.86 and 1.0, specificity between 0.75-0.96, internal consistency between 69-95 and temporal stability of 91%. For each domain, a range of sensitivity (.86-1.0) and specificity (.75-.96) values are indicated for various combinations of scoring and the individual's linguistic ability evaluated [35].

CHAT is a questionnaire containing parents' responses and observations of the subjects assessed quickly, it can be applied in children from 18 months of age. Based on parents' responses on the MCHAT, the physician follows subsequent evaluation flow charts to reach a decision on diagnosis. This decision can be imprecise and intuitive, depending on the perception and expertise of the physician. These procedures can also be time consuming, with a high degree of information loss in the assessment procedure, due to its dependence on crisp inputs. It has a specificity of 0.97, a sensitivity of 0.18 and a predictive value of 0.58 [68]. In 2001, this instrument was modified through a screening program, taking the name of MCHAT, an instrument solely diagnosing through the parents' and caregiver's responses. Its sensitivity is of 0.87, specificity of 0.99 and has a predictive power of 0.80 [68]. A further modification has been made, called the M-CHAT-R/F, allowing better detection and reduces the rate of false positives.

As can be seen, MCHAT can have a high sensitivity and specificity, but not a good internal consistency or a predictive value to be placed at the same diagnostic level as ADIR and ADOS, since MCHAT does not take the complexity of the diagnosis process into account. And worse still, only takes the parent's or caregiver's impression into account, when it has been proven in the scientific practice that rather often parents, in the despair of a diagnosis, have not objectivity in their answers [51].

Our diagnosis model integrates ADOS2 and ADIR, and provides a comprehensive understanding of the ASD structure. The use of ADOS2 and ADIR make the tool more robust with respect to previous works based on other standards (e.g., MCHAT) that the psycho-social community considers worse. Furthermore, our MFCM allows consideration of these instruments in an isolated way, simply turning these concepts off during the diagnosis, i.e., our model allows us to consider different application situations of both instruments (ADIR, ADOS2). Zander et al. [43] have shown the utility of considering using these instruments separately. In addition, we can add or remove new layers to or from the model, in order to consider other aspects during the diagnosis, such as the social situation, neurophysiological properties, amongst others.

5.3 Comparison with other Machine Learning algorithms

In this section, we have used the NSCH dataset to compare our model with classical machine learning algorithms for classification tasks [71]. More specifically, we have used three of the most popular algorithms [72]: Naive Bayes, Random Forest and Support Vector Machine. The NSCH dataset has 95577 records of children with 367 variables. Because only a small percentage of the dataset represent children with ASD, we have selected a random sample with roughly 50% of children with ASD and 50% of children without ASD. We calculate performance metrics of F-measure (a combination of precision and recall metrics) and accuracy to compare our MCFM-ASD model with these machine learning algorithms. We have also carried out an equivalence process between the 367 variables of the dataset with the concepts of our model to introduce these variables in the concepts of our model. In the test, we use the k-fold cross validation technique, with k = 10, such that 90% of the dataset samples are used for training. We have tested 2 classes (no ASD or ASD) with the data set. The results are shown in the Table16.

Table 16

Comparison with other Machine Learning algorithms [72]

	F-MEASURE	ACCURACY
MCFM-ASD	0.843	0.842
SVM	0.833	0.833
RANDOM FOREST	0.852	0.851
NB	0.865	0.865

These results show that our MCFM-ASD model can predict ASD in this dataset, with a rough value of 83%. The main problem is in the definition of equivalences of the data set attributes with the concepts of our model, since certain attributes can be linked to different concepts in our model. The weight of certain attributes in the dataset to diagnoses ASD could also be exploited. For example, what is the importance of Developmental delays, Learning disabilities or other problems for ASD? This type of information could be considered in our model, when concept equivalence is established. Future studies could be easily made with psychologists, to analyze such aspects with our model.

Our goal with this test was to determine the quality of our model in predicting ASD. Its performance is very close with respect to the machine learning algorithms. In addition, our MCFM-ASD model has the virtue of allowing the expert (e.g. psychologist) to interpret its results in an easy and intuitive way. This is the main contribution, which compensates to a large extent their tenuous difference of precision with respect to the other techniques, whose results are good, but they do not help much in contextualizing the results, which is very important for psychologists in their diagnostic processes.

6. Conclusion and Future Works

The knowledge-based approach used in this work focuses on the MFCM for the ASD prediction process. This is the first work proposing MFCM-ASD to support ASD identification and classification. Our approach observes the autistic phenomenon using two levels of knowledge, defined by ADIR and ADOS2. The utilization of multiple layers makes our approach more robust because at each level, we can introduce different aspects to be considered for the diagnosis. Specifically, in our case, we have very easily integrated ADOS and ADIR, and our model can be expanded with more aspects. For example, in our model can be defined new layers to consider neuroimages. This extension will allow comparing our approach with previous studies using ABIDE dataset [73].

In the proposed model, the MFCM models a fuzzy inference by means of fuzzy IF-THEN rules, which describe naturally the ASD diagnostic instrument used in this paper (ADIR/ADOS2), facilitating its utilization and interpretation for the psychologists; an important aspect in order to give it usability to this tool. Our approach has obtained the same results as the experts, on the datasets of diagnosed cases, applying ADOS and ADIR standards. Additionally, results obtained by our approach in the MCHAT standard, with respect to previous works, are better showing versatility. A disadvantage of the model is that it does not explain its reasoning, this being an important quality as a support system in decision making.

Our model implicitly has the own limitations with the interview based clinical diagnostic methods being unable to point out any biological basis behind observed behavioral symptoms. But we have compared the predictive capability of our models in different contexts and datasets, obtaining very good performance. The main problem is the dataset variable equivalence definition with the concepts of our model (see sections 5.1 and 5.3).

Future works will address improvement of our MFCM-ASD through the introduction of new layers to evaluate ASD, which represents new dimensions of symptoms to be included in the diagnostic process, as for example, the social context of the subject, demographic variables, other cognitive scores such as verbal ability, and neuroimaging characteristics. A future study with psychologists must also study the sensibility of our model to different aspects/variables that can be observed to diagnose ASD. Also, next works must study the quality of our approach with respect to other models based on other loss functions and SoftMax functions. Finally, future works must analyze the utilization of the deep learning paradigm in the context of our study at different levels, to extend the MFCM used in our work with this type of learning; and to study its application for the Autism diagnosis, particularly, to discover new features that can be used in the construction of diagnosis rules. These new rules must be previously interpreted by Autism experts, in order to be used during the diagnostic process.

7. Ethical standards

This work has been carried out in accordance with the World Medical Association Code of Ethics (Declaration of Helsinki) for experiments involving humans. The data obtained and used in this work were taken with consent of members (parents) of the Association of Parents and Friends for Supporting and Defending the Rights of Persons with Autism, APADA. Even the work has the informed knowledge of each of the children who participated in the study, so not only of APADA. APADA is a non-profit NGO created on March 27, 2013 through Agreement # 0080 of the Ministry of Social Inclusion and Economy made up of parents and people within this spectrum (https://goo.gl/weXhZK). APADA has allowed the use of data under their confidentiality policy, for this reason, the names have been changed to protect identities https://goo.gl/Mzoiia.

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