

A Hybrid Case-Based System in Clinical Diagnosis and Treatment

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Abstract — Computer-aided decision support systems play an increasingly important role in clinical diagnosis and treatment. However, they are difficult to build for domains where the domain theory is weak and where different experts differ in diagnosis. Stress diagnosis and treatment is an example of such a domain. This paper explores several artificial intelligence methods and techniques and in particular case-based reasoning, textual information retrieval, rule-based reasoning, and fuzzy logic to enable a more reliable diagnosis and treatment of stress. The proposed hybrid case-based approach has been validated by implementing a prototype in close collaboration with leading experts in stress diagnosis. The obtained sensitivity, specificity and overall accuracy compared to an expert are 92%, 86% and 88% respectively.

Index Terms— Artificial intelligence, Biofeedback, Case based reasoning, Diagnosis, Information retrieval, Rule based reasoning, Stress measurement.

I. INTRODUCTION

TODAY medical knowledge is expanding rapidly to the extent that even experts have difficulties in following all the new results, changes and new treatments. Decision support systems (DSS) that bear more similarities with human reasoning are often easily accepted by physicians in the medical domain [2], [3], [4], [5]. Today many clinical DSS are developed to be multi-purposed and often combine more than one AI method and technique [3], [6], [7], [8].

Many of the early AI systems attempted to apply rule-based reasoning (RBR) for decision support. However, for broad and complex domains with a weak domain theory, i.e. the domain is not so well understood, rule-based systems encountered several problems. For instance, knowledge acquisition bottleneck (since the medical knowledge evolves rapidly, updating large rule-based systems and providing their consistency is expensive), transparency (rules become increasingly complex in medical applications) and reliability (one faulty rule makes the whole system unreliable) [1]. Case-based reasoning (CBR) is inspired by a cognitive model on how humans solve a certain class of problems e.g. solve a new problem by identifying a similar previously solved problem and adapting the solution to the current problem [9], [10]. Aamodt and Plaza have introduced a CBR life cycle with four RE-s: Retrieve, Reuse, Revise and Retain [9]. The advantages of CBR in the medical domain have been identified in several research works i.e. in [2], [3], [6], [11], [12], [13], [14], [15]. Cases including textual features or textual cases with ontology are explored in [4]. The authors in [16], [17], [18] introduce Fuzzy logic with CBR in similarity measurements. The integration of CBR and RBR is explored in systems like CASEY [19] and FLORENCE [20].

This paper presents a hybrid clinical DSS for stress diagnosis and treatment based on a novel combination of several techniques from artificial intelligence. In this proposed approach, CBR is used as the core technique. By using textual information retrieval (IR) with ontology the system is able to handle patient's contextual information such as lifestyle and habits better. Fuzzy rule-based classification scheme handle the so called boot strap problem where only a limited number of cases are available in the beginning of the system. The Fuzzy similarity technique incorporated into the CBR system can handle vagueness, uncertainty inherently existing in clinicians' reasoning better than other similarity techniques. The system was evaluated using 68 reference cases classified by one of the expert who has more than 20 years of experience in the domain. Besides, one senior clinician with more than 8 years of experience and a number of trainee clinicians under close supervision of the senior clinicians were involved in the evaluation process. A survey of trends and advancements of recent medical CBR systems is presented in our previous work [8]. In [5] and [21] a stress diagnosis system is outlined. In [22] we look on how a CBR system can support biofeedback treatment for stress management. In this publication we build our previous work and address a combination of diagnosis, classification and treatment of stress integrating several AI techniques in a novel hybrid CBR system. We also extended our case library to 68 cases captured from 46 subjects. Furthermore, the reliability of the system is explored in comparison with the number of clinicians through sensitivity and specificity analysis and a confusion matrix.

II. HYBRID CASE-BASED STRESS MANAGEMENT SYSTEM

Figure 1 presents the construction steps of the system. These steps use a variety of methods and techniques in diagnosis and treatment of stress-related disorders.

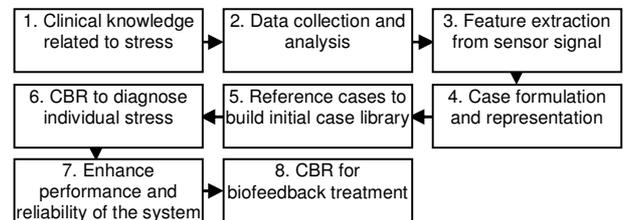


Fig. 1. Schematic diagram of the hybrid case-based stress management system

Step 1: The finger temperature (FT), which is one of the psychophysiological parameters clinically used to determine stress-related disorders, is employed in this research. It is a known clinical fact that in general FT decreases with stress. *Steps 2 and 3:* The measurement is collected from 46 subjects

using a temperature sensor. 12 women and 34 men between the ages 23 to 51 participated in this experimental study. The role of the subjects is to participate in stress profiling and to build up an initial case library. In this study, we have collected the measurements from the individual subjects following a six-step protocol (i.e. Baseline, Deep-breath, Verbal-stress, Relax with positive thinking, Math-stress and Relax) [5]. *Steps 4 and 5*: A new problem case is formulated with the features where 19 features are extracted from the sensor signal, five are selected features which reflect a subject’s perception and 1 is a textual feature which describes a subject’s contextual information. The problem description part of a case contains a vector of the extracted features and the solution part provides a level of stress. The levels of stress are denoted as *Very Relaxed, Relaxed, Normal/Stable, Stressed* and *Very Stressed*. We have used two types of cases, reference cases that are classified by an expert and artificial cases generated using the fuzzy rule-based approach. *Step 6*: To diagnose individual stress level [5], a new problem case is inserted into the CBR cycle. The new case is then matched using three different local similarity matching functions: 1) *modified distance* function 2) *similarity matrix* and 3) *fuzzy similarity* matching. The nearest neighbor (NN) algorithm is applied as a global similarity function to retrieve similar cases. Finally, the top most case or the clinician’s selected case is provided as a solution to the new problem case. A detailed description about stress diagnosis is presented in section “A”. *Step 7*: A fuzzy rule-based classification scheme and textual information retrieval are introduced to enhance performance and reliability in stress diagnosis tasks. The fuzzy rule-based classification and textual information retrieval is described in section “B” and “C”. *Step 8*: The last step in Figure 1 focuses on the biofeedback treatment. It is a three-phased CBR framework [22] deployed to classify a patient, to estimate initial parameters and to make recommendations for biofeedback training. Section “D” describes this final part.

A. CBR to diagnose individual stress

A calibration phase [5], [21], is a standard protocol that helps to establish an individual stress profile. The proposed system performs several steps to diagnose individual sensitivity to stress as shown in Figure 2. It senses the FT measurement as an input and identifies essential features to formulate a new problem case.

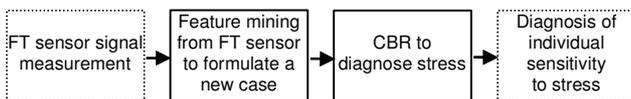


Fig. 2. Schematic diagram of the steps in stress diagnosis

The features are determined from 15 minutes of measurements (time, temperature) in 3600 samples, together with other numeric (age, room-temperature, hours since meal, etc) and symbolic (gender, food and drink taken, sleep at night, etc) parameters. The derivative of each of the steps of FT measurement is used to introduce “degree of changes” as an indication of FT changes [5]. The entire signal, except the baseline, is divided into 12 parts with one minute time interval

and 12 features are extracted (i.e. Step2_Part1, Step2_Part2, Step3_Part1, ..., Step6_Part1, Step6_Part2). The system thereafter formulates a new problem case combining these extracted features and other features namely start temperature, end temperature, minimum temperature, maximum temperature and the difference between the ceiling and floor temperature. This new problem case is then supplied into the CBR cycle to retrieve the most similar cases. The problem case is then matched using three different local similarities matching functions i.e. two cases are compared using modified distance function, similarity matrix and fuzzy similarity matching presented in [5]. The system shows a sorted list of best matching cases based on their similarity values. The solution of a retrieved old case, i.e., diagnosis and treatment suggestions, is also presented by the system.

B. Fuzzy rule-based reasoning for artificial cases

The success of the stress diagnosis system discussed in the earlier section depends on the case library since the composition of the case library is one of the key factors that decide the ultimate performance of the CBR system. The cases stored in a case library should be both representative and comprehensive in order to cover a wide spectrum of situations.

The reference cases employed in the diagnosis system are more reliable to use in a CBR cycle since they are classified by the expert. However, artificial cases are generated to initialize the case library. Initially, it is difficult to collect reference cases for the clinical deployment of many systems and the limited number of cases can impair the performance of a CBR system. For example, in our case library only 3 cases are *VeryRelaxed*. So, given a new problem case similar to *VeryRelaxed*, the system may not find any classification. Here, the artificial cases in the “*VeryRelaxed*” class could propose a classification. So, our system uses artificial cases along with the reference cases in the initial stage. However, Excremental works (A, C and D) have been conducted only using reference cases.

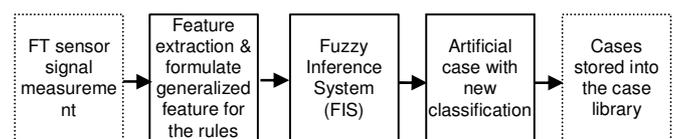


Fig. 3. The steps to create artificial cases

A fuzzy rule-based reasoning algorithm that automatically classifies new cases is introduced into the CBR system to initiate the case library with artificial cases. The steps of the approach is presented in Figure 3 and the algorithm works as follows: a) the FT sensor signal is measured through the calibration phase b) the number of features are extracted from a sensor reading and formulates a generalized feature from the extracted features c) the fuzzy inference system (FIS) is then applied together with the generalized feature to classify a new case d) the output from the FIS provides the new classification along with the feature vector e) finally, this case is saved into the case library as an artificial case (see Figure 3). The details information is presented in [26].

C. Textual information retrieval

Unlike the measurement-based experiences as we have used in our diagnostics system, human perceptions are usually expressed in an informal and natural language format, and they have proven to be important for diagnosis. Clinicians in this domain are also considering other factors such as patient's feelings, behavior, social facts, working environments, lifestyle etc. Such information can be presented by a patient using natural text format and Visual Analogue Scale (VAS). Therefore, the system added textual features into the case vector. The textual information retrieval does not contribute directly in the classification accuracy of the system, but, as a supporting system, it provides the history about feelings, behavior, social facts, working environments and lifestyle of previous patients as additional information. This information provided by the system is very useful for the clinician to use as a basis for decisions of individual treatment procedures. In addition, it helps to better interpret and understand the sensor readings and transferring valuable experiences between clinicians [21]. To enable similarity matching on less structured text cases, the combination of cosine similarity, including synonyms and ontology, is used. A vector space model [23] with the *tf-idf* (term frequency-inverse document frequency) [24] weighting scheme and cosine similarity is applied to determine similarities between two textual cases. The different steps of retrieval of similar case(s) are described in Figure 4.

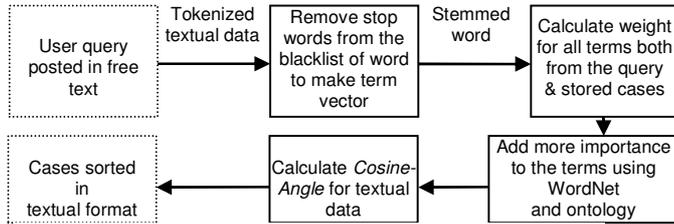


Fig. 4. The different steps for the case retrieval

The text tokenize algorithm decomposes the whole textual information into sentences, and then into individual words. Due to the huge amount of words a filtering step is required to improve the efficiency of the retrieval. The following three steps are applied to extract important textual features:

- 1) Remove blacklisted stop-words and special characters from both the users' query and the patients' record.
- 2) A list of synonyms is used to reduce the number of terms. The Porter stemming algorithm helps in stemming the words that provide ways of finding morphological variants of a search term. After calculating importance for each word, these words are represented as terms in a vector space.
- 3) Before measuring the cosine similarity value of the textual information between stored cases and a user's query case, the important assessments of candidate terms are improved using the domain specific ontology.

The similarity between a stored case vector and new case as a query vector is calculated using the cosine similarity function

[24] [25]. This ratio is defined as the cosine of the angle between the vectors, within the values between 0 and 1.

D. Biofeedback treatment

Biofeedback training is an effective method for controlling stress. The basic purpose of biofeedback is that the patient can alter their physiological or psychological state while observing measurement changes, e.g. the changes in skin temperature on a graph. For instance, if a patient is classified as 'Very Stressed' by the diagnosis system (see section 'A') from the prior education s/he is able to see how a positive or negative psycho-physiological change is represented on the graph and can train the body and/or mind to change the biological response to improve the condition.

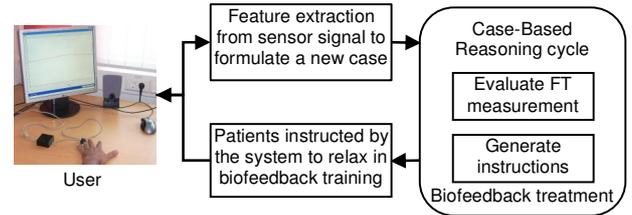


Fig. 5. Schematic diagram of the steps in the biofeedback treatment cycle

Clinical practice shows that most of the sensor based biofeedback applications comprise of three phases, a) analyze and classify a patient and make a risk assessment, b) determine individual levels and parameters, and finally c) adapt and start biofeedback training. The intention of developing a biofeedback system is to enable a patient to train himself/herself without particular supervision. A cyclic procedure as illustrated in Figure 5 is considered for the biofeedback treatment system. In this cycle, a user (patient/subject) connects a sensor to a finger and can observe changes in FT during several instructions in relaxation training. The FT measurements are collected in real time and every two minutes it evaluates the measurements of the previous two-minute period and, if necessary, generates instructions for a patient. A CBR cycle is used for the computer-based biofeedback treatment system. The biofeedback cases are formulated with a feature vector from the biomedical signal (i.e. with 2 minutes FT measurement) in the conditional part and the suggestion of relaxation in the solution part. The feedback presents evaluation of FT measurement and a recommendation for the next training. It could provide feedback with appropriate suggestions every two minutes if necessary. The training time is flexible, i.e. the patient can decide the duration of their training between 6 (as minimum) and 20 minutes (as maximum).

III. EXPERIMENTAL WORK

The contribution of this experimental work is four-fold. a) Similarity matching in CBR - it investigates the best local similarity matching function (presented in the previous chapter section "A"). b) Fuzzy rule-based classification into the CBR - it evaluates the improvement of the CBR system by adding artificial cases into the case library. c) Confusion matrix,

sensitivity and specificity analysis - shows how CBR supports in the classification of a subject. d) System performance vs. clinicians - it evaluates how the system performs compared to clinicians with different levels of expertise.

During the experiments, the performance of the system in terms of accuracy has been compared with experts in the domain where the overall goal is to see how close the system works compare to the experts. The reference cases, in their conditional or problem description part, contain a vector of the extracted features and the solution part comprised of expert's defined classification as diagnosis. In this study, the clinician who performed the classification task has been working both as a clinician and a researcher in the field of psychophysiology for more than twenty (20) years. Note that for the evaluation purpose; the measurements have been collected using different parameters (e.g., heart rate, skin conductance, respiration rate, CO₂/ETCO₂) together with finger temperature (FT).

A. Similarity matching in CBR

This evaluation uses a statistics i.e. square of the correlation coefficient or *Goodness-of-fit* (R^2) to find the best local similarity function. In [5], this experiment has been conducted considering 24 subjects, in this paper it is further extended with 46 subjects. In addition, seven test data sets in which the cases are chosen randomly are considered for the investigation.

Table I presents Set C with case id 28 as an example; the 1st column describes the identification of the two matching cases. The "Rank" columns represent the position of each case ranked by the expert and the three algorithms. The "Sim" columns display the similarity value of each case defined by both the expert and system using the three algorithms. The last row of the table shows the value of the goodness-of-fit (R^2), calculated on the basis of the ranking and similarity values identified by the expert and the system.

TABLE I
SIMILARITY MATCHING FOR THE SET C WITH CASE ID 28 IN COMPARISON WITH A CLINICAL EXPERT.

Matching (Query, Set C)	By Expert		Modified Distance		Similarity Matrix		Fuzzy Similarity	
	Rank	Sim (%)	Rank	Sim (%)	Rank	Sim (%)	Rank	Sim (%)
28, 12	1	90	1	92	1	80	1	70
28, 35	2	85	2	91	3	72	2	69
28, 31	3	82	4	89	4	69	3	68
28, 24	4	80	5	87	5	68	4	65
28, 8	5	70	6	86	2	78	5	66
28, 13	6	65	3	90	6	67	6	60
R^2 in ranking & similarity			0.44	0.27	0.43	0.13	0.89	0.80

Rank = ranking order; Sim = similarity value

Likewise, all the test sets have been sorted according to the similarity with a query case decided by a domain expert (human reasoning). The sorted cases are then converted to the rank numbers, i.e., the position of a case in the ranking. According to the expert's ranking, top six cases from each set is used as a standard for the evaluation process. The R^2 results of all the test sets are presented in Figure 6.

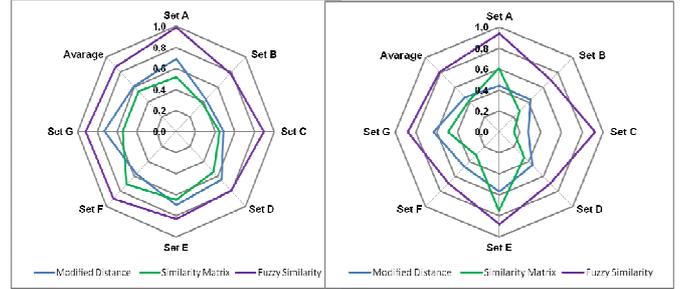


Fig. 6. R^2 both in ranking and similarity to compare the three algorithms

B. Fuzzy rule-based classification to CBR

This experiment has been done defining two different case libraries: LibraryA, with reference cases only, classified by the expert and LibraryB being twice as big as LibraryA with hybrid cases, classified by the expert and the fuzzy rule-based classification.

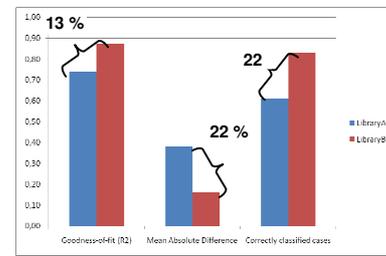


Fig. 7. Comparison results between the case libraries A and B

In Figure 7, for the two tests (test1 and test2) on an average LibraryB indicates a classification accuracy of 87% while the LibraryA reaches 74% of fitness compare to the expert's classification. So, there is 13% increase in the R^2 value and 22% (Mean absolute difference) decrease in the error rate when the system uses the LibraryB (hybrid cases). Furthermore, the CBR system can correctly classify 83% using LibraryB whereas using LibraryA the system can only correctly classify 61% of the cases.

C. Confusion matrix, sensitivity and specificity analysis

Here, the stress levels are classified by the expert into five classes ranging from 1 to 5 where 1=VeryStressed, 2=Stressed, 3=Normal/Stable, 4=Relaxed and 5=VeryRelaxed. A confusion matrix with all the cases classified in 5 classes is presented in Table II. The table shows the distribution of predicted classes in each row and the actual classes in each column.

However, the sensitivity and specificity analysis is often carried out with binary classification i.e. absence and presence of a disease. For this analysis, all the cases are divided into two groups. That is all Stressed and VeryStressed cases are in *stressed* group and all Normal/Stable, Relaxed and VeryRelaxed cases are in *healthy* group. One case is taken out from the case library at a time and the case is matched against the remaining cases. Here, the system uses the fuzzy similarity matching function as a local similarity and kNN (k=1) is applied to retrieve the similar cases. For the evaluation

purposes, the top most similar case is considered. Several indices are used to evaluate the system performance and presented in Table III.

TABLE II
CONFUSION MATRIX ON ALL CASES IN 5 CLASSES

Predicted	Actual				
	VSt	St	No/St	Re	VRe
VSt	12	1	2	0	0
St	1	10	2	2	0
No/St	0	1	13	4	0
Re	0	1	4	10	2
VRe	0	0	0	2	1
Total	13	13	21	18	3

VSt=VeryStressed; St=Stressed; No/St = Normal/Stable;
Re=Relaxed; VRe=VeryRelaxed

TABLE III
STATISTICAL ANALYSIS OF THE SYSTEM'S CLASSIFICATION

Criteria/Indices	Values
Total cases	68
Cases belong to <i>Stressed</i> group (P)	26
Cases belong to <i>Healthy</i> group (N)	42
True positive (TP):	24
False positive (FP):	6
True negative (TN):	36
False negative (FN):	2
Sensitivity = TP / (TP + FN)	≈ 0.92
Specificity = TN / (FP + TN)	≈ 0.86
Accuracy = (TP+TN)/(P+N)	≈ 0.88

From Table III, among the 26 *stressed* cases, 24 are correctly diagnosed as *stressed* (i.e. true positive) and only 2 are incorrectly identified as *healthy* (i.e. false negative) by the system. The sensitivity obtains 92% that measures the percentage of *stressed* cases those are identified as having the stress condition. Similarly, among the 42 *healthy* cases, 36 are correctly classified as *healthy* (i.e. true negative) and 6 are incorrectly classified as *stressed* (i.e. false positive) by the system. The specificity obtains 86% of *healthy* cases are correctly classified as they don't have any stress condition.

TABLE IV
THE TOTAL DISTRIBUTION OF THE CORRECTLY CLASSIFIED CASES

Classification criteria	Values
Correctly classified in <i>VeryStressed</i> class	≈ 92%
Correctly classified in <i>Stressed</i> class	≈ 77%
Correctly classified in <i>Total</i>	85%
Low false positive	≈3.8%
Low false negative	≈7.4%
Serious false negative	≈3.8%

Next, considering only the *stressed* group and pursuing the similar experiment, the obtained results are presented in Table IV. Note that, the other 42 cases in Normal/Stable, Relaxed and VeryRelaxed classes are still remained in the case library and do participation in the matching process during retrieval. As can be seen from Table IV, the system classifies 92% correctly for the class *VeryStressed* and for the *Stressed* classes it classifies with an accuracy of 77% compare to the expert's classification. In total, 85% stress-related cases are correctly classified and 15% are misclassified by the system compare to the expert.

D. System performance vs. clinicians

The system performance is compared in two manners, 1st the experiment is done by considering two trainee clinicians and 2nd the system performance is again compared with one senior clinician. One of the goals is to see how good the

system can classify compared to trainee clinicians i.e. whether the system can be useful to assist the trainee clinicians in the classification/diagnosis task. For the experiment with trainee clinician, an expert and two trainee clinicians (*TC1* and *TC2*) are participated. Both the trainee clinicians are informed and instructed by the expert about the classification task before the test is started. Two subsets of the cases (*setA* and *setB*) are created randomly with 29 and 14 expert approved cases.

TABLE V
COMPARISON RESULTS BETWEEN THE SYSTEM AND TRAINEE CLINICIANS

Evaluation Method	Test setA			Test setB		
	TC1	TC2	The System	TC1	TC2	The System
Correctly Classified Cases	62%	69%	83%	57%	65%	86%
Goodness-of-fit (R ²)	0.76	0.72	0.87	0.80	0.82	0.86
Absolute Mean Difference	0.48	0.45	0.20	0.43	0.35	0.21

The cases for the both subsets are classified by the two trainee clinicians who have less experienced in this domain and the results are presented in Table V. For the test group *SetA*, the system classifies 83% correctly and the trainee clinicians classify 69% and 62% correctly. The number of the correctly classified cases is 86% for *setB* by the system and the trainee clinicians have succeeded to classify 57% and 65% correctly.

Next, the experiment is conducted by introducing one senior clinician. For this experiment, fifteen (15) cases are selected randomly to make the test set and all the cases are classified by both the expert and the senior clinician. The comparison results are presented in Table VI. Here, the percentage of the correctly classified cases is 80% by the system and 73% by the senior clinician.

TABLE VI
COMPARISON RESULTS BETWEEN THE SYSTEM AND SENIOR CLINICIAN

Evaluation Method	Senior clinician	The System
Correctly Classified Cases	73%	80%
Goodness-of-fit (R ²)	0.82	0.88
Absolute Mean Difference	0.27	0.20

IV. DISCUSSION

Our previous works [5], [21], [22] concern the different parts of the stress management system. In this paper we combined our work into a hybrid system. We investigate the reliability of the computer-based stress management system, which is important in clinical applications and several evaluations have been conducted in this regard. As can be seen both in the "ranking number" and "similarity value" criteria (see Figure 6) which uses an increased number of subjects compared to our previous work [5], the fuzzy similarity algorithm shows more reliability than the other algorithms (i.e. it performs better in all of the seven test subsets). Figure 7, show that the system improves its performance with 22% in the criteria of correctly classified case using combined case library (i.e. both artificial cases and reference cases). So, it shows that it is possible to increase accuracy in the classification task by extending the case library with artificial cases if the case library contains a limited number of reference cases. From the sensitivity and specificity analysis in Table

III, the false positive rate and false negative rate obtained by the system are 14% and 8% respectively. The percentage of the total correctly classified cases in terms of system's accuracy is 88% and only 12% of the total cases are misclassified. From Table IV, it can be seen that among the 15% misclassified cases there are 4% low false positive i.e. cases are one step over misclassified; 8% are low false negative i.e. cases are one step under misclassified and 4% are serious false negative i.e. cases are two step under misclassified. This also reveals the reliability of the system when it comes to diagnosis. Furthermore, in Table V the Goodness-of-fit (R^2) value for both the test groups (setA and setB) are 87% and 86% by the system, whereas the R^2 values by the trainee clinicians are 76% and 72% for the set setA, and for the set setB are 80% and 82%. The absolute mean differences or error rates in the classification for both the test groups are comparatively lower (0.20 and 0.21) than the trainee clinicians. It explains that the system using the fuzzy similarity matching algorithm can classify correctly better than all the trainee clinicians. While for the senior clinician as shown in Table VI, the R^2 value is almost same for both the senior clinician and the system i.e. 82% and 88%. From these experiments, it can be observed, using different test data sets and considering both the trainee and the senior clinicians, the system can perform same as the senior clinician and better than the less-experienced clinicians. Thus, according to experimental work, the system can be used for senior clinician as a second opinion and as an expert for trainee clinicians. Moreover, since the reliability of clinical systems could certainly be increased by providing contextual information, it considers additional information in textual format which supports the reasoning tasks.

V.CONCLUSION

Clinical systems have proven able to extend the capability of clinicians in their decision making tasks. This paper presents a hybrid case-based system that supports a clinician in a number of complex tasks in stress management. It combines more than one AI techniques where CBR is applied as the core technique. The experimental work investigates the reliability of the system and shows a reliable performance close to a level of human experts. Today the system is based on one physiological parameter, i.e. FT sensor signal. The system can be extended with other parameters such as heart rate variability, breathing rate etc. and an increased number of relevant parameters will improve the performance further.

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