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The Cortisol Awakening Response Using Modified Proposed Method of Forecasting Based on Fuzzy Time Series

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ABSTRACT
A growing body of data suggests that a significantly enhanced salivary cortisol response to waking may indicate an enduring tendency to abnormal cortisol regulation. More methods have been proposed to deal with forecasting problems using fuzzy time series. In this paper, our objective was to apply the response test to a population already known to have long-term hypothalamo–pituitary–adrenocortical (HPA) axis dysregulation. We hypothesized that the free cortisol response to waking, believed to be genetically influenced, would be elevated in a significant percent age of cases, regard less of the afternoon Dexamethasone Suppression Test (DST) value based on fuzzy time series and genetic algorithms. The proposed method adjusts the length of each interval in the universe of discourse for forecasting the Longitudinal Dexamethasone Suppression Test (DST) data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout the experimental results show that the proposed method gets good forecasting results.

Keywords: Fuzzy Time Series, Fuzzy Logical Relationship, Mean Square Error, glucocorticoids, salivary cortisol, bipolar disorder, lithium, Dexamethasone Suppression Test, DST.

I. INTRODUCTION

Forecasting activities play an important role in our daily life. In order to solve the forecasting problems, many researchers have proposed many different forecasting methods [1], [2], [3], [5]. In [21], Song et al. proposed the definition of fuzzy time series. They also proposed the time-invariant model [22] and the time-variant model [23] of fuzzy time series to forecast enrollments of the University of Alabama. Both the time-invariant model and time-variant model used Max-Min Composition operations. Huarng [15] in another work is used a heuristic function to present a method for forecasting the enrollments of the university of Alabama based on chen's method [2]. Hurang and yu [16] presented a method for dealing with forecasting problems using ratio-based lengths of intervals to improve the forecasting accuracy rate. Chen et-al.[8] presented a method for forecasting enrollments using automatic clustering technique and fuzzy logical relationships. Kuo et al. [17] presented a method for forecasting enrollments using fuzzy time series and particles warm optimization techniques. Chen and chen [10] presented online fuzzy time series analysis based on entropy discretization and fast fourier transform. Erolegrioglu [12] presented a method in fuzzy time series which is based on particle swarm optimization technique to handle the high order fuzzy time series model. A growing body of literature points to hypothalamo–pituitary–adrenocortical (HPA) axis dysregulation as a critical factor in the development of mood disorders. Long-term enhanced cortisol secretion may have important health ramifications in addition to its contribution to mood syndromes. The free cortisol response to waking is a promising series of salivary tests that may provide a useful and non-invasive measure of HPA functioning in high-risk studies. The small sample size limits generalizability of our findings. Because interrupted sleep may interfere with the waking cortisol rise, we may have underestimated the proportion of our population with enhanced cortisol secretion. Highly cooperative participants are required [11].

II. FUZZY TIME SERIES

In this session, we brief review the concept of fuzzy time series from [21], [22], [23]. The main difference of fuzzy time series and traditional time series is that the values of fuzzy time series are represented by fuzzy sets [27] rather than real values.

Let D be the universe of discourse, where $D = \{d_i\}_{i=1}^{n}$. A fuzzy set A_i in the universe of discourse D is defined as follows:

$$A_i = \sum_{i=1}^{n} \frac{f_{A_i}(d_i)}{d_i}$$, Where f_{A_i} is the membership function of the fuzzy set A_i, $f_{A_i}: D \to [0,1]$,

$f_{A_i}(d_j)$ is the degree of membership of d_j in the fuzzy set A_i, $f_{A_i}(d_j) \in [0,1]$ and $1 \le j \le n$.

Recently, interest has turned to more refined testing and the probability that HPA dysregulation may even predate the onset of clinical illness [9]. Preliminary data suggest that this dysregulation may be concentrated within the families of individuals with mood disorders [10], suggesting the hypothesis that early abnormalities in cortisol regulation may confer a risk for the future development of mood disorders. To understand the temporal relation between HPA dysregulation and the onset of bipolar disorder (BD), it is essential to have a reliable and non-invasive test that can be repeatedly administered prospectively and is acceptable to high-risk populations. Promising candidates for such a test include the salivary free cortisol response to waking and the short day time profile, a test that adds afternoon and evening measurements to the waking values[9].

Let $Y(t)\,(t = \ldots,0,1,2\ldots)$ be the universe of discourse in which fuzzy sets $f_i(t)\,(i = 1,2\ldots\ldots)$ are defined in the universe of discourse $Y(t)$. Assume that $F(t)$ is a collection of $f_i(t)\,(i = 1,2\ldots\ldots)$, then $F(t)$ is called a fuzzy time series of $Y(t)\,(t = \ldots,0,1,2\ldots)$.

Assume that there is a fuzzy relationship $R(t-1,t)$, such that $F(t) = F(t-1)\, o\, R(t-1,t)$, where the symbol "$o$" represents the max-min composition operator, then $F(t)$ is called caused by $F(t-1)$.

Let $F(t-1) = A_i$ and let $F(t) = A_j$, where A_i and A_j are fuzzy sets, then the fuzzy logical relationship (FLR) between $F(t-1)$ and $F(t)$ can be denoted by $A_i \to A_j$, where A_i and A_j are called the left-hand side(LHS) and the right hand side (RHS) of the fuzzy logical relationship, respectively.

Fuzzy logical relationships having the same left-hand side can be grouped into a fuzzy logical relationship group(FLRG). For example, assume that the following fuzzy logical relationships exist:

$A_i \to A_{ja}, A_i \to A_{jb}, A_i \to A_{jc}, \ldots A_i \to A_{jm}$,

III. A MODOFIED PROPOSED METHOD FOR FUZZY TIME SERIES FORECASTING

In this session, we present a new method to forecast the Longitudinal Dexamethasone Suppression Test (DST) [10] data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout, based on fuzzy time series and genetic algorithms.

Step 1: In many of the exiting algorithms, the universe of discourse is considered as $D = [B_{\min} - B_1, B_{\max} + B_2]$ into intervals of equal length, where $B_{\min}$ and $B_{\max}$ are the minimum value and the maximum value of the historical data, respectively, and B_1 and B_2 are two proper positive real values to divide the universe of discourse D into n intervals $d_1, d_2, \ldots\ldots, d_n$ of equal length. Here we considered the universe of discourse using normal distribution range based definition, i.e., D = [μ - 3σ, μ + 3σ] where μ and σ are mean and standard deviation values of the data, respectively. Also, in the exiting method [9], the forecasted variable is calculated by taking into account all the values including the repeated values are considered as single value. We call the forecasted value is modified forecasted variable, because of these modifications, the root mean square error of the modified method is minimum composed to the existing method.

Step 2: Here μ = 216.61, σ = 89.03, μ - 3σ = -50.48 and μ + 3σ = 483.7 the universe of discourse D = [-50.48, 483.7] ≃ [-50, 480]. But $A_1, A_2, \ldots\ldots and A_8$ are linguistic terms represented by fuzzy sets. Therefore, the universe of the discourse D = [50, 450]. Firstly, divide the universe of discourse D into Eight intervals d_1, d_2, d_3, d_4, d_5, d_6, d_7 and d_8, where d_1 = [50, x_1], d_2 = [x_1, x_2], d_3 = [x_2, x_3], d_4 = [x_3, x_4], d_5 = [x_4, x_5], d_6 = [x_5, x_6], d_7 = [x_6, x_7] and d_8 = [x_7; 450]; x_1, x_2, x_3, x_4, x_5, x_6 and x_7 are integer variables and $x_1 < x_2 < x_3 < x_4 < x_5 < x_6 < x_7$. We can see that the universe discourse D = [50, 450] into Eight intervals d_1, d_2, d_3, d_4, d_5, d_6, d_7 and u_8, where d_1 = [50, 100], d_2 = [100, 150], d_3 = [150, 200], d_4 = [200, 250], d_5 = [250, 300], d_6 = [300, 350], d_7 = [350, 400] and d_8 = [400; 450];

Step 3: Define the linguistic terms A_i represented by fuzzy sets, shown as follows

$$A_1 = \frac{1}{d_1} + \frac{0.5}{d_2} + \frac{0}{d_3} + \frac{0}{d_4} + \frac{0}{d_5} + \frac{0}{d_6} + \frac{0}{d_7} + \frac{0}{d_8},$$

$$A_2 = \frac{0.5}{d_1} + \frac{1}{d_2} + \frac{0.5}{d_3} + \frac{0}{d_4} + \frac{0}{d_5} + \frac{0}{d_6} + \frac{0}{d_7} + \frac{0}{d_8},$$

$$A_3 = \frac{0}{d_1} + \frac{0.5}{d_2} + \frac{1}{d_3} + \frac{0.5}{d_4} + \frac{0}{d_5} + \frac{0}{d_6} + \frac{0}{d_7} + \frac{0}{d_8},$$

$$A_4 = \frac{0}{d_1} + \frac{0}{d_2} + \frac{0.5}{d_3} + \frac{1}{d_4} + \frac{0.5}{d_5} + \frac{0}{d_6} + \frac{0}{d_7} + \frac{0}{d_8},$$

$$A_5 = \frac{0}{d_1} + \frac{0}{d_2} + \frac{0}{d_3} + \frac{0.5}{d_4} + \frac{1}{d_5} + \frac{0.5}{d_6} + \frac{0}{d_7} + \frac{0}{d_8}$$

$$A_6 = \frac{0}{d_1} + \frac{0}{d_2} + \frac{0}{d_3} + \frac{0}{d_4} + \frac{0.5}{d_5} + \frac{1}{d_6} + \frac{0.5}{d_7} + \frac{0}{d_8},$$

$$A_7 = \frac{0}{d_1} + \frac{0}{d_2} + \frac{0}{d_3} + \frac{0}{d_4} + \frac{0}{d_5} + \frac{0.5}{d_6} + \frac{1}{d_7} + \frac{0.5}{d_8},$$

$$A_8 = \frac{0}{d_1} + \frac{0}{d_2} + \frac{0}{d_3} + \frac{0}{d_4} + \frac{0}{d_5} + \frac{0}{d_6} + \frac{0.5}{d_7} + \frac{1}{d_8},$$

Where $A_1, A_2, ... and A_n$ are linguistic terms represented by fuzzy sets. Then, we can fuzzify the Longitudinal Dexamethasone Suppression Test (DST)[10] data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout, shown in Table 1, as shown in Table 3. Furthermore, we can get the fuzzy logical relationship groups as shown in Table 4, where the ith fuzzy logical relationship group contains fuzzy logical relationships whose current state is A_i, where $1 \leq i \leq 8$. Then, apply the following forecasting method to forecast the data [1]:

Step 4: Assume that the fuzzified data of the ith year is A_j and assume that there is only one fuzzy logical relationship in the fuzzy logical relationship groups in which the current state of the fuzzy logical relationship is A_j , shown as follows:

"$A_j \rightarrow A_k$"

where A_j and A_k are fuzzy sets and the maximum membership value of A_k occurs at interval d_k, then the forecasted data of the i + 1th year is the midpoint m_k of the interval d_k.

Step 5: Rules For Forecasting

LV_j – lower value of the interval d_j
UV_j – upper value of the interval d_j
L_j – length of the interval d_j
The midpoint m_k of the interval d_k
The fuzzified data of the j^{th} year is A_j in which the current state of the fuzzy logical relationship is A_k , shown as follows:

"$A_j \rightarrow A_k$"

G_n – Given value of state 'n'
G_{n-1} – Given value of state 'n'
G_{n-2} – Given value of state 'n'
F_j – forecasted value of the current state 'j'

Computational Algorithms

For i = 3, 4, 5, ...(end of time series data)
Obtained fuzzy logical relation for "$A_j \rightarrow A_k$"
V = 0 and x =0
1.$D_n = |(G_n - 2G_{n-1} + G_{n-2})|$
2. a) if $m_j + D_n/4 \geq LV_k$ & $m_j + D_n/4 \leq UV_k$
then $V = V + m_j + D_n/4$, $x = x + 1$
b) if $m_j - D_n/4 \geq LV_k$ & $m_j - D_n/4 \leq UV_k$
then $V = V + m_j - D_n/4$, $x = x + 1$
c) if $m_j + D_n/2 \geq LV_k$ & $m_j + D_n/2 \leq UV_k$
then $V = V + m_j + D_n/2$, $x = x + 1$
d) if $m_j - D_n/2 \geq LV_k$ & $m_j - D_n/2 \leq UV_k$
then $V = V + m_j - D_n/2$, $x = x + 1$
e) if $m_j + D_n \geq LV_k$ & $m_j + D_n \leq UV_k$
then $V = V + m_j + D_n$, $x = x + 1$
f) if $m_j - D_n \geq LV_k$ & $m_j - D_n \leq UV_k$
then $V = V + m_j - D_n$, $x = x + 1$
g) if $m_j + D_n \geq LV_k$ & $m_j + D_n \leq UV_k$
then $V = V + m_j + D_n$, $x = x + 1$
h) if $m_j - 2D_n \geq LV_k$ & $m_j - 2D_n \leq UV_k$
then $V = V + m_j - 2D_n$, $x = x + 1$
3. $F_k = (V + m_k) / (x + 1)$
Next i

Example

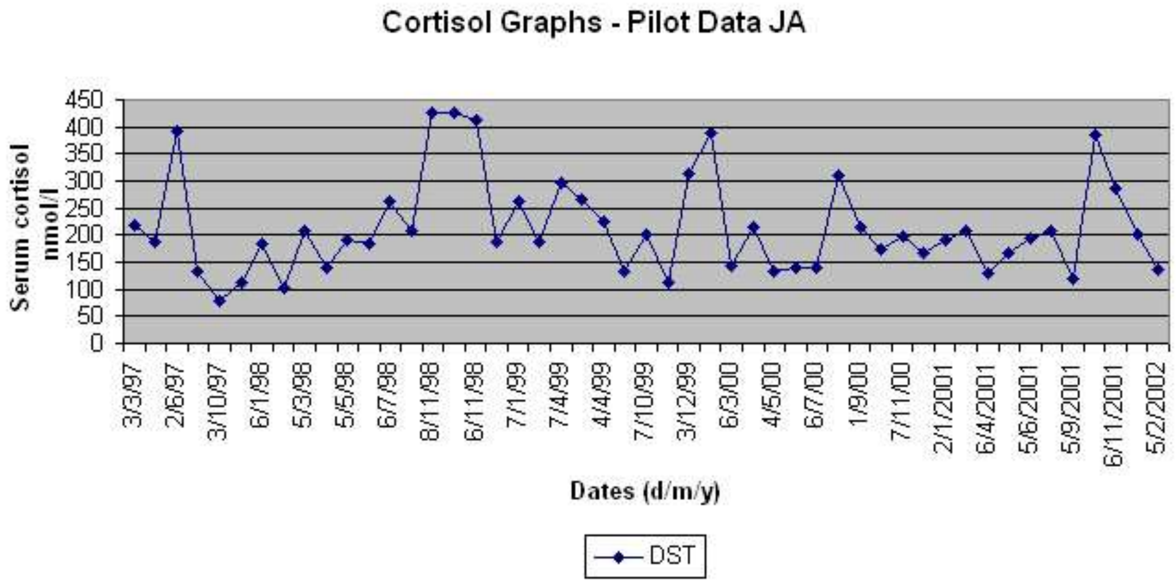

Figure 1: The Longitudinal Dexamethasone Suppression Test (DST) data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout.

Table 1: Fuzzified value and Fuzzy logical relationships for Medical data

S. No	Actual Value	Fuzzy set	Fuzzy logical relationships
1	225	A_4	-
2	190	A_3	$A_4 \rightarrow A_3$
3	395	A_7	$A_3 \rightarrow A_7$
4	140	A_2	$A_7 \rightarrow A_2$
5	90	A_1	$A_2 \rightarrow A_1$
6	120	A_2	$A_1 \rightarrow A_2$
7	180	A_3	$A_2 \rightarrow A_3$
8	110	A_2	$A_3 \rightarrow A_2$
9	210	A_4	$A_2 \rightarrow A_4$
10	145	A_2	$A_4 \rightarrow A_2$
11	190	A_3	$A_2 \rightarrow A_3$
12	185	A_3	$A_3 \rightarrow A_3$
13	260	A_5	$A_3 \rightarrow A_5$
14	210	A_4	$A_5 \rightarrow A_4$
15	430	A_8	$A_4 \rightarrow A_8$
16	430	A_8	$A_8 \rightarrow A_8$
17	420	A_8	$A_8 \rightarrow A_8$
18	190	A_3	$A_8 \rightarrow A_3$
19	260	A_5	$A_3 \rightarrow A_5$
20	190	A_3	$A_5 \rightarrow A_3$
21	295	A_5	$A_3 \rightarrow A_5$
22	270	A_5	$A_5 \rightarrow A_5$
23	230	A_4	$A_5 \rightarrow A_4$
24	140	A_2	$A_4 \rightarrow A_2$
25	199	A_2	$A_2 \rightarrow A_2$
26	120	A_2	$A_2 \rightarrow A_2$

27	315	A_6	$A_2 \rightarrow A_6$
28	390	A_7	$A_6 \rightarrow A_7$
29	145	A_2	$A_7 \rightarrow A_2$
30	210	A_4	$A_2 \rightarrow A_4$
31	135	A_2	$A_4 \rightarrow A_2$
32	140	A_2	$A_2 \rightarrow A_2$
33	140	A_2	$A_2 \rightarrow A_2$
34	310	A_6	$A_2 \rightarrow A_6$
35	210	A_4	$A_6 \rightarrow A_4$
36	180	A_3	$A_4 \rightarrow A_3$
37	195	A_3	$A_3 \rightarrow A_3$
38	175	A_3	$A_3 \rightarrow A_3$
39	190	A_3	$A_3 \rightarrow A_3$
40	210	A_4	$A_3 \rightarrow A_4$
41	135	A_2	$A_4 \rightarrow A_2$
42	175	A_3	$A_2 \rightarrow A_3$
43	195	A_3	$A_3 \rightarrow A_3$
44	210	A_4	$A_3 \rightarrow A_4$
45	120	A_2	$A_4 \rightarrow A_2$
46	385	A_7	$A_2 \rightarrow A_7$
47	290	A_5	$A_7 \rightarrow A_5$
48	195	A_3	$A_5 \rightarrow A_3$
49	140	A_2	$A_3 \rightarrow A_2$

Mean square error = $\mathrm{MSE} = \dfrac{\sum_{i=1}^{n} |\,\mathrm{forecastedvalue}_i - acutualvalue_i\,|^2}{n}$

Forecasted Error = |Forecasted value – Actual value|/Actual value

Average Forecasting Error = sum of forecasting error / number of errors

Table 2: Forecasted Value and MSE

S. No	Actual Value	Forecasted Value	Forecasted Error
1	225	-	-
2	190	-	-
3	395	335	0.151899
4	140	135	0.035714
5	90	74.38	0.173556
6	120	120	0
7	180	375	1.083333
8	110	120	0.090909
9	210	217.5	0.035714
10	145	133.75	0.077586
11	190	169.17	0.109632
12	185	175	0.054054
13	260	265	0.019231
14	210	227.08	0.081333
15	430	425	0.011628
16	430	425	0.011628

17	420	425	0.011905
18	190	175	0.078947
19	260	262.5	0.009615
20	190	175	0.078947
21	295	268.75	0.088983
22	270	275	0.018519
23	230	235	0.021739
24	140	125	0.107143
25	199	125	0.371859
26	120	125	0.041667
27	315	325	0.031746
28	390	371.67	0.047
29	145	163.75	0.12931
30	210	225	0.071429
31	135	125	0.074074
32	140	125	0.107143
33	140	125	0.107143
34	310	325	0.048387
35	210	225	0.071429
36	180	173.33	0.037056
37	195	175	0.102564
38	175	175	0
39	190	175	0.078947
40	210	225	0.071429
41	135	127.5	0.055556
42	175	170.42	0.026171
43	195	175	0.102564
44	210	225	0.071429
45	120	122.5	0.020833
46	385	375	0.025974
47	290	280	0.034483
48	195	175	0.102564
49	140	130	0.071429

Mean square error = 1108.9
Average forecasted error = 8.6%

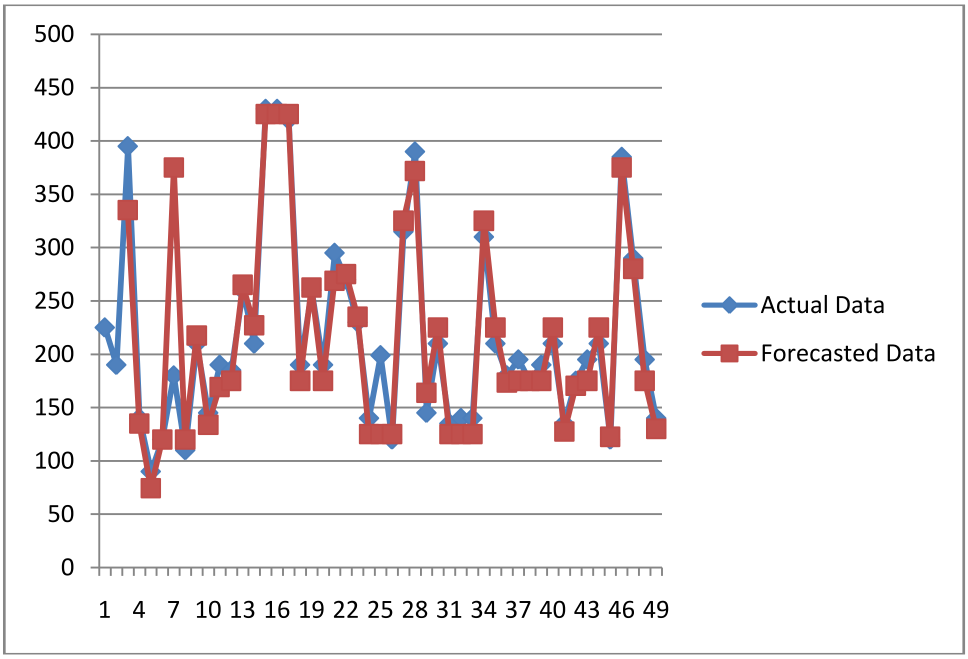

Figure 2: Comparison of actual data forecasted value

IV. Experimental Results

There was a significant difference between BD patients and our control subjects in the maximum percentage rise of salivary cortisol response to awakening. Those showing a waking response also had significantly higher mean cortisol values at 30 minutes after waking, compared with 509 normal subjects described in Wust's and others study. Base line values at time zero, immediately upon waking, did not differ significantly between our sample and Wust's control subjects. Patients and our 5 control subjects did not differ significantly in the percent age decline from the peak morning value to the evening values. In this section we apply the proposed for forecasting the Longitudinal Dexamethasone Suppression Test (DST) data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout.

It means that the modified proposed method gets a higher average forecasting accuracy rate than other existing methods to forecast the maximum percentage rise of salivary cortisol response to awakening. We can see that the modified proposed method get the smallest Mean square error.

V. CONCLUSION

In this paper, Our dysregulation, even when lithium-responsive BD patients are clinically well and their DSTs are observations support the hypothesis that the free cortisol response to waking can reflect relatively enduring HPA normal. Because the test is easy to administer, the free cortisol response to waking may hold promise as a marker in studies of high-risk families predisposed to, or at risk for, mood disorders, we have presented a new method for forecasting the Longitudinal Dexamethasone Suppression Test (DST) data on a fully remitted lithium responder for past 5 years who was asymptomatic and treated with lithium throughout based on fuzzy time series and genetic algorithms. We also make a comparison of the MSE of the forecasted medical data for different methods. In this paper, we use the MSE to compare the performance of prediction of students' enrollment. However, how to narrow the maximum deviation of predicted value from the actual one is more important than the MSE. Therefore, in the future, we will develop a new method to deal with a more accurate prediction by narrowing the maximum deviation of predicted value from the actual one.

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