Modeling of Melatonin behavior in major depression: A fuzzy logic modeling

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Abstract. According to the world health organization, major depressive disorder (MDD) is considered as the fourth main cause of death and premature weakness in the whole world. Abnormality in the hormones and neurotransmitters level is the one of the main factors which may result in this disorder. In this article melatonin is chosen among these hormones, which is the most implicated to control sleep and depression. Because the measurement of melatonin is crucial important, the fuzzy logic approach as the mathematical method is utilized to making melatonin behavior model. In this paper, two effective factors on melatonin are modeled by fuzzy logic. This model is only a part of our project which is performed for modeling of the major depression.

Introduction

Mood disorders include a large group of disorders in which pathological mood and related disturbances dominate the clinical picture [1]. The common mood disorder is major depression that affects more than 120 million of children and adults [2] and they are the cause of approximately about 850,000 deaths every year in the world [3]. However there is no way for evaluation for both diagnosis and prognosis [4]. Melatonin is a hormone that was discovered in 1958 and named because its skin-bleaching influence in melanin. Low melatonin levels have been observed in depressed subjects, unipolar or bipolar affective disorders and chronic schizophrenia. Low nocturnal melatonin has been proposed as a trait marker for major depressive disorders by Beck-Fris et al., 1985 [5].

IT professionals and biologists, including medical scientists, have a long history of working successfully together. They form large models of human behavior via a mathematical model, which attempts to find analytical solutions to problems and thereby enable the prediction of the behavior of the human being condition from a set of parameters and initial conditions. Sophisticated mathematical results have been used in and have emerged from the life sciences [6-14].

The goal of paper is to develop a model that accurately represents the complexity and fuzzy nature of the assessment of melatonin. Fuzzy logic is a popular mathematical method for approximating any nonlinear and qualitative function to arbitrary accuracy with a suitable number of fuzzy rules. So in this article fuzzy logic approach is used to model melatonin. In this paper, we outline our vision for the fuzzy modeling of melatonin.

Method

The fuzzy logic system is a kind of conclusive (inference) system which coping the human thinking and its basic form is consist of a fuzzifier, some fuzzy IF–THEN rules, a fuzzy inference engine and a defuzzifier [15-17].

In this system, singleton is chosen for fuzzifier and defuzzification is centroid. The fuzzy rules are drawn from various references. These fuzzy rules are forming by the known languages, such as fuzzy inference system (FIS) which is employed by Matlab Simulink [12].
In this article we have found two factors, which affect melatonin. The factors are serotonin and cortisol. As a first factor, serotonin (SE) is a neurotransmitter, a kind of chemical which helps relay signals from one part of the brain to another. Although serotonin is produced in the brain, where its primary functions is performed there but 90 percent of our serotonin supply is found in the digestive tract and in blood platelets. Serotonin can help the regulation of other neurotransmitter and hormone systems; decreased serotonin activity may let these systems to act in unusual and irregular ways [18].

The second factor is cortisol which is critical for maintaining energy homeostasis and modulating immune function. Melatonin and cortisol tend to run opposite to each other.

That is, cortisol becomes at its low point at bedtime, whereas melatonin reaches its highest point a few hours after cortisol bottoms out [19].

Serotonin as the first input space is divided in to five trapezoidal membership functions: very-low, low, normal, high and very-high. Because of the behavior of the brain serotonin is related to behavior of the plasma serotonin and also because plasma serotonin is measured by available laboratorial kits, so in this paper, serotonin of the plasma is modeled by Serotonin RIA kits [20] criteria instead of the brain serotonin. The range of normal membership function is 101 to 283ng/ml [21], the lowest level of plasma serotonin is 20ng/ml and the highest level of serotonin is 2000ng/ml [20].

In order to have a better view of diagram, it is plotted in rang 20 to 400 as shown in Fig. 1. The second input, cortisol space is divided into three trapezoidal membership functions: low, normal and high as illustrated in Fig. 2. The normal range of normal membership function is 0.8 to 1.5ng/ml, the lowest level of cortisol is 0.156ng/ml and the highest level of cortisol is 10ng/ml [22, 23].

![Figure 1. Fuzzy membership functions of serotonin.](image1.png)

![Figure 2. Fuzzy membership function of cortisol](image2.png)

The relationships between inputs and output are presented in the form of IF-THEN statements, based on medical literature and involving the professional opinion is used. 15 rules can be identified to describe the level of melatonin which is shown in Table 1.

Table 1. The rule base of Melatonin

<table>
<thead>
<tr>
<th>Rules</th>
<th>IF: Cortisol is ~</th>
<th>And SE is ~</th>
<th>THEN: Melatonin is ~</th>
</tr>
</thead>
<tbody>
<tr>
<td>RULE 1</td>
<td>LOW</td>
<td>VERY-LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>RULE 2</td>
<td>LOW</td>
<td>LOW</td>
<td>NORM</td>
</tr>
<tr>
<td>RULE 3</td>
<td>LOW</td>
<td>NORM</td>
<td>NORM</td>
</tr>
<tr>
<td>RULE 4</td>
<td>LOW</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>RULE 5</td>
<td>LOW</td>
<td>VERY-HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>RULE 6</td>
<td>NORM</td>
<td>VERY-LOW</td>
<td>LOW</td>
</tr>
</tbody>
</table>
The output, melatonin space is divided into three trapezoidal membership functions: low, normal and high. Because of melatonin is measured by available laboratorial kits, so in this paper melatonin is modeled according to Human Melatonin ELISA Kit from IBL International GmbH criteria. The range of normal membership function is 30 to 150pg/ml, the lowest level of plasma melatonin is 3pg/ml and the highest level of melatonin is 3550pg/ml [24, 25]. In order to have a better view of the diagram, it is plotted in range 0 to 170 as shown in Fig.3.

<table>
<thead>
<tr>
<th>RULE</th>
<th>NORM</th>
<th>LOW</th>
<th>LOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>RULE 8</td>
<td>NORM</td>
<td>NORM</td>
<td>NORM</td>
</tr>
<tr>
<td>RULE 9</td>
<td>NORM</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>RULE 10</td>
<td>NORM</td>
<td>VERY-HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>RULE 11</td>
<td>HIGH</td>
<td>VERY-LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>RULE 12</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>RULE 13</td>
<td>HIGH</td>
<td>NORM</td>
<td>NORM</td>
</tr>
<tr>
<td>RULE 14</td>
<td>HIGH</td>
<td>HIGH</td>
<td>NORM</td>
</tr>
<tr>
<td>RULE 15</td>
<td>HIGH</td>
<td>VERY-HIGH</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

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**Simulation and Results**

This section describes the simulation result of the proposed model. Melatonin level is modeled using fuzzy logic in Matlab environment, simulink section. Fig. 3 shows the melatonin level from input factors serotonin and cortisol.

As the better description, While amount of cortisol in human is 'low', the level of melatonin is 'low' for 'very-low' level of serotonin, is 'normal' for 'low' and 'normal' serotonin level and is 'high' if serotonin level is 'high' or 'very-high'. When level of cortisol is 'normal', the level of melatonin in plasma is 'low' for 'low' or 'very-low' serotonin level, is 'high' for 'high' or 'very-high' level of serotonin and is 'normal' if serotonin level is 'normal'. Finally, if cortisol on human is 'high', the melatonin plasma level is 'low', 'normal' and 'high' when the serotonin level is 'very-low' or 'low', 'normal' or 'high' and 'very-high' respectively.

Two examples of modeling are presented as follows. In the first example, all the inputs: cortisol and serotonin are considered 1 and 150 respectively; 91.6750pg/ml for the melatonin level is received as the output.

In the second example the outputs, cortisol and serotonin levels are changed into 0.5 and 70 respectively then the response will be 3pg/ml.
Conclusions

As it mentioned melatonin has the key role in the human circadian rhythms and health system. The model which is presented in this article considers some of the factors which can effect on melatonin; there may be some other factors so we can divide the future works into four main parts as follows:

- Recognizing other factors which can effect on melatonin level and adding them to list
- Modeling all the factors (which is not modeled in this article) as the separate fuzzy logic system
- Completing the rule base
- Modeling stress as which influences in depression directly and also as a factor that effect on melatonin level (because there is not enough information about this factor effect, it is not modeled).

By considering more factors influence on melatonin, there will be the model which is closer to the reality.

This model can be applied in measuring other neurotransmitters, hormones and depression symptoms as the part of major depressive disorder model.

References


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