Alzheimer Dementia Detection Based on Time-series Instability of Heart Rate

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Abstract— **Towards early detection of Alzheimer dementia (AD), this paper focuses on time-series instability of heart rate of AD patient, and proposes the AD detection method based on heart rate acquired by an unconstrained mattress sensor for daily life use. Through the human subject experiments on 124 days of heart rate of one AD patient and 39 days of heart rate of 21 healthy subjects, the following implication have been revealed: (1) an accuracy of the proposed AD detection method based on the time-series features of heart rate is approximately 98%; and (2) the time-series instability of heart rate is found in the rapid oscillation of heart rate (i.e., an increase/decrease of heart rate over 2 seconds).**

I. Introduction

Alzheimer dementia (AD), which is an approximately half of all dementia, is caused by an atrophy of brain. To detect AD, Mini-Mental State Examination (MMSE) [1] is widely used as medical examination by interview. However, suspicious questions on dementia in MMSE psychologically burdens to patients especially in the early stage of dementia because the patients in this stage do not tend to accept to be dementia. For this issue, Hanai et al. proposed the screening method that automatically classifies AD, frontotemporal lobar degeneration (FTLD), and healthy subjects by the voice features [2]. However, it is difficult to handle the voice from a privacy perspective and also difficult to classify the voice of the target subject in the conversation among multiple persons. As another approach, Nikamalfard et al. focused on a sleep disorder of dementia, and estimated the sleep duration and the number of awakenings from a mattress sensor to check a sleep disorder [3]. However, such a sleep disorder is also found in non-AD elderly persons, which makes it difficult to classify AD with non-AD elderly persons.

To overcome these problems, our previous research proposed the AD detection method based on the circadian rhythm of heart rate during sleep, which data can be easily measured by an unconstrained mattress sensor placed under the mattress [4][5]. This approach detects AD when the unstable circadian rhythm of heart rate is found, which is based on the fact that (a) melatonin secretion follows circadian rhythm in healthy persons but not in AD [6] and (b) heart rate follows the circadian rhythm [7]. (Note that the heart rate variability of Lewy body dementia was well studied such as [8] but the circadian rhythm of heart rate of dementia was not focused on except for our research.) From the feature of our proposed method, (1) the privacy problem and (2) the sleep disorder problem, described above, can be solved as follows: For (1) problem, patients are not asked the private issue from medical doctors; and For (2) problem, the circadian rhythm disorder of heart rate has a high possibility of being only found in AD. However, an AD detection accuracy of our previous method depends on a sleep duration, because the circadian rhythm may be differently estimated by the slightly larger/smaller amount of data (*i.e.*, the heart rate).

To tackle this issue, this paper focuses on the "time-series instability" of heart rate from a *micro* perspective instead of the "circadian rhythms disorder" of heart rate from a *macro* perspective. This is because it is difficult to acquire the detailed transitions of heart rate specific to AD from the circadian rhythms. To investigate an effectiveness of the time-series instability of heart rate, this paper explores what kinds of time-series features of heart rate are related to AD and proposes the AD detection method based on the founded time-series features. Note that it is quite difficult to define the instability of heart rate because of many kinds of its instability, and thus its feature is clarified in this paper.

The rest of this paper is organized as follows. Section II analyzes the time-series features of heart rate. Section III proposes the AD detection method based on the time-series features of heart rate. Section IV compares the accuracy of the AD detection method between AD and non-AD. Finally, our conclusion is given in Section V.

II. Analyzing Time-series Features of Heart Rate

A. Data Set Obtained From Human Subject Experiment

To analyze the heart rate of humans, the experimental procedures involving human subjects were approved by the ethics community of St.Marianna University and the University of Electro Communications. Our experiment obtained the data set composed of 124 days of the heart rate during sleep of one AD patient in the care house ($n = 124$), while 39 days of the heart rate during sleep of 21 healthy

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subjects ($n = 39$). In the healthy subjects, in particular, 39 days of the heart rate is composed of several days of three elderly people (60s∼70s) ($n = 7$), ten middle-aged people (40s∼50s) ($n = 18$) and eight young people (20s∼30s) ($n = 14$). The data of the heart rate and body movement were obtained from the EMFIT mattress sensor by EMFIT Ltd., and the heart rate during sleep was extracted from the sleeping time to waking up time, determined by the body movement.

B. Statistical Analysis of 780 Time-series Features

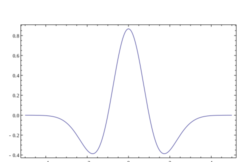
To find the time-series features of heart rate specific to AD, the heart rate data is extracted in the 10 minutes window to calculate its time-series features by shifting its window by one minute. For these data, our experiment employed the "Tsfresh" python library composed of 780 time-series features and conducted the statistical analysis of 780 time-series features in terms of classifying between AD and non-AD. Concretely, Mann-Whitney U-test was conducted after checking that the sample of features did not match the normal distribution by ShapiroWilk test.

From the statistical analysis, "the partial auto-correlation coefficient of lag 2" x_{pac} and "the peak count of the continuous wavelet transform (CWT)" x_{ncp} showed the smallest and the second smallest p-values among 780 time-series features. This result determined to employ them as the time-series features of heart rate to detect AD. Concretely, x_{pac} is the auto-correlation between time-series data (x_t) and their lag 2 data (x_{t-2}) from which their lag 1 data (x_{t-1}) is excluded as shown in Eq. (1). In general, a_k is calculated as the auto-correlation between x_t and its lag k value x_{t-k} from which the middle variable $\{x_{t-1}, \ldots, x_{t-k+1}\}$ are excluded as shown in Eq. (2) [9].

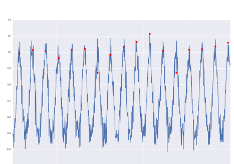
$$x_{pac} = \alpha_2 = \frac{Cov(x_t, x_{t-2}|x_{t-1})}{\sqrt{Var(x_t|x_{t-1})Var(x_{t-2}|x_{t-1})}} \tag{1}$$

$$\alpha_k = \frac{Cov(x_t, x_{t-k}|x_{t-1}, \ldots, x_{t-k+1})}{\sqrt{Var(x_t|x_{t-1}, \ldots, x_{t-k+1})Var(x_{t-k}|x_{t-1}, \ldots, x_{t-k+1})}} \tag{2}$$

On the other hand, x_{ncp} is the number of peaks found by CWT (Continuous Wavelet Transform) which detects the temporal changes in frequency and power spectrum (scalogram) [10]. In CWT, the Mexican hat function (ricker) represented by Fig. 1(a) is generally employed as the mother wavelet function. The founded peaks of the time-series data are shown in the red marks of Fig. 1(b), where x_{ncp} is 17.



(a) Mexican hat (ricker) function used in the mother wavelet function of CWT



(b) Examples of peaks in time-series data found by CWT

Fig. 1. The peak count of the continuous wavelet transform (CWT)

C. Statistical Analysis of x_{pac} and x_{ncp}

Fig. 2 shows the results of the U-test for $\overline{x_{pac}}$ and $\overline{x_{ncp}}$. The upper and lower graphs respectively show $\overline{x_{pac}}$ and $\overline{x_{ncp}}$, with the data plots (dots) and the box-and-whisker plots for the AD patient (in blue) and the healthy subjects (in orange). The results show that both $\overline{x_{pac}}$ and $\overline{x_{ncp}}$ have significant differences between the AD patient and the human subjects at $p < 0.0001$. Since the large differences in the distribution between the AD patient and the healthy subjects are found, this paper applies the logistic regression to these data and the heart rate of the AD patient and that of the healthy subjects can be classified by $\overline{x_{pac}} = -0.06$ and $\overline{x_{ncp}} = 47.0$, respectively.

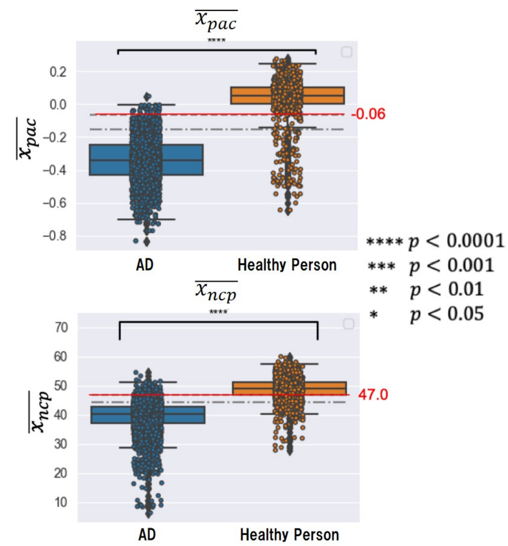


Fig. 2. Statistical comparison results of the partial auto-correlation coefficient $\overline{x_{pac}}$ and the peak count $\overline{x_{ncp}}$.

III. AD Detection Method with Time-series Features of Heart Rate

A. Delimited Range of Heart Rate

Although the significant difference of the time-series features of x_{pac} and x_{ncp} between AD and non-AD are found as described in the previous section, x_{pac} and x_{ncp} are overlapped between AD and non-AD. To find the time period that x_{pac} and x_{ncp} are largely difference between AD and non-AD, the time-series data are delimited within a certain range according to "the correlation with the Benford distribution" x_{bec}. The Benford distribution is the distribution of the numerical values that appear in nature, *i.e.*, the distribution of the first digits (from 1 to 9) follows Newcomb-Benford's law. From this definition, x_{bec} is calculated by the correlation between the distribution of the first digit of the input time-series data and the Benford distribution. Fig. 3 shows that a high relation that x_{bec} increases when the heart rate is relatively stable, where the blue and orange lines represent the heart rate and x_{bec}, respectively. Since x_{pac} and x_{ncp} are correctly calculated as the heart rate becomes stable, the stable time-series data are extracted according to x_{bec}. However, the stability of the heart rate has individual differences, which makes it difficult to determine an appropriate threshold of x_{bec}. To tackle this issue, the multiple thresholds (*e.g.*, the four thresholds in this experiment) are employed to extract heart rate in the range of various lengths, and x_{pac} and x_{ncp} are calculated in each region. Such regions are represented in a light orange area in Fig. 3. Concretely, the region of heart rate is set within the range of $\alpha\%(= 90.0, 70.0, 50.0, 30.0)$ of the difference between the maximum and minimum of x_{bec}.

B. AD Detection Based on Delimited Range of Heart Rate

To detect AD, the average of the partial auto-correlation coefficient and the peak count ($\overline{x_{pac}}$ and $\overline{x_{ncp}}$) are calculated in each delimited range of heart rate, and Random Forest (RF) [11] as one of the machine learning methods learns the multiple decision trees using $\overline{x_{pac}}$ and $\overline{x_{ncp}}$ to judge AD in each range. Since the multiple AD judgments are done by RF because of the multiple range, our method decides to detect AD when the judgment ratio of all ranges ($RFR(\overline{\boldsymbol{x}_{pac}}, \overline{\boldsymbol{x}_{pac}})$) is larger than the threshold value r as shown in Fig. 4.

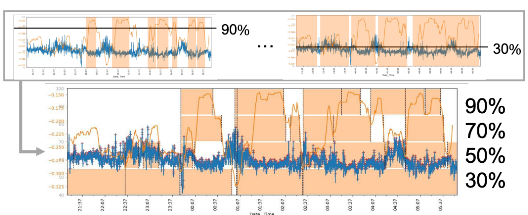


Fig. 3. Correlation between heart rate and Benford distribution

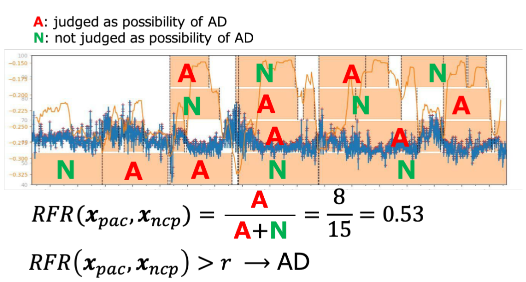


Fig. 4. AD detection with the possibility judgments of the cropped intervals of heart rate

IV. Subject Experiment

A. Experimental Setup

To investigate the effectiveness of the proposed AD detection method, this paper compares it with our previous proposed AD detection methods, *i.e.*, ADDCRARaH [4] and ADDUCRRaH [5]. As the evaluation criteria, this paper calculates the accuracy, precision, recall, and F_1-score of all three methods that classifies the data of the AD patient ($n = 124$) with that of the healthy subjects ($n = 39$). The depth and the number of RF decision trees were respectively set to 5 and 100, and five cross-validation is performed. To balance the class between the AD patient and the healthy subjects, the weight of the AD patient class was $(124 + 39)/(2 \times 124) = 0.657$ and that of healthy subjects class was $(124 + 39)/(2 \times 39) = 2.090$. The threshold r of $RFR(\overline{\boldsymbol{x}_{pac}}, \overline{\boldsymbol{x}_{pac}})$ to the AD classification was set to 0.6, determined by the cross-validation.

B. Result and Discussion

TABLE I shows the accuracy, precision, recall, and F_1-score of all three methods. From this table, all values of the proposed AD detection method is the highest among the three methods and all of them exceeds 97%. Fig. 5 shows the heart rate, x_{pac}, and x_{ncp}, where the horizontal axis indicates a time of 500 seconds and the vertical right and left axes indicate x_{pac} and x_{ncp}, respectively. The blue, green and red lines indicate the heart rate, x_{pac}, and x_{ncp}, respectively. The upper and lower graphs show the results of the AD patient and the healthy subjects, respectively. The baselines as the scale reference of each graph ($x_{pac} = -0.06$ and $x_{ncp} = 47$) indicates the green and red dotted lines, respectively. Note that x_{pac} in this experiment means x_{pac} with lag 2 described in Subsection II-B. From this figure, the time-series features of the AD patient and the healthy subjects are summarized as follows:

TABLE I
COMPARISON BETWEEN THE PROPOSED AND CONVENTIONAL METHODS

	Acc.	Precision	Recall	F_1
Proposed method	98.1	97.9	99.1	98.8
ADDCRARaH	73.5	95.9	65.3	77.6
ADDUCRRaH	78.4	89.1	79.2	83.8

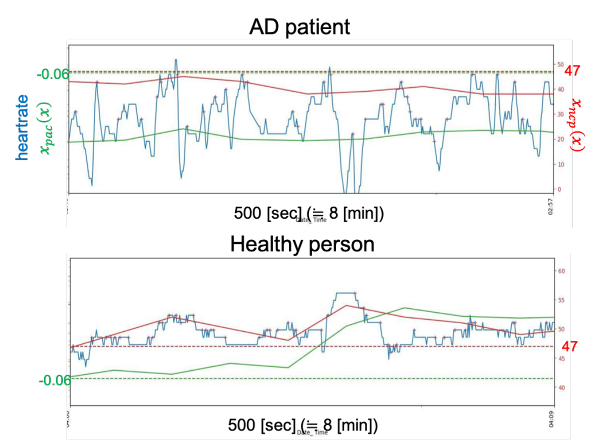


Fig. 5. Partial auto-correlation $\overline{x_{pac}}$ and peak number $\overline{x_{ncp}}$

- Partial auto-correlation (x_{pac}) of the AD patient is negative (which is smaller than the baseline (-0.06)), while that of the healthy subjects is close to 0 or positive (which is larger than -0.06). Since x_{pac} of the AD patient is negatively correlated with the heart rate between t and $t - 2$, the heart rate of the AD patient decreases/increases in a unit of 2 and more seconds.

Since x_{pac} of the healthy subjects is "not" negatively correlated with the heart rate between t and $t-2$, the heart rate of the healthy subjects tends to keep it as the same rate or quickly put back into the former rate due to homeostasis. Such a decrease/increase of heart rate in an unit of 2 and more seconds is called as "2-second oscillation" in this paper.

- Peak count (x_{ncp}) of the AD patient is smaller than the baseline (47), while that of the healthy subjects is larger than 47. This result means that the number of peaks of the heart rate of the AD patient is smaller than the healthy subjects because of the 2-second oscillation (*i.e.*, the peak of the heart rate of the AD patient is found in an unit of more than 2 seconds but not in every 1 second like in healthy subjects caused by homeostasis).

The above analyses suggest that the partial auto-correlation ($\overline{x_{pac}}$) and the peak count ($\overline{x_{ncp}}$) of heart rate have a potential of being new features of AD as time-series instability of heart rate. In order words, the instability of heart rate of AD can be represented by $\overline{x_{pac}}$ and $\overline{x_{ncp}}$. What should be noted, however, is that "only" $\overline{x_{pac}}$ or $\overline{x_{ncp}}$ does not always show the features of AD in all days, *i.e.*, it may show the features of non-AD. For this issue, this paper analyzes how the proposed method solves it from Fig. 6. The lower of this figure shows one of the decision trees of the learned RF by the proposed method. In this RF, a certain healthy subjects was misjudged (judged as AD) by $\overline{x_{pac}}$ but correctly judged (as the healthy subjects) by $\overline{x_{ncp}}$. The misjudgment of $\overline{x_{pac}}$ occurs because the 2-second oscillation of the heart rate (marked with the green oval) occurs even in the healthy subjects as shown in the upper of this figure. However, the number of such oscillation of the healthy subjects is not small like the AD patient, which contributes to keeping $\overline{x_{ncp}}$ as close to $\overline{x_{ncp}}$ of other healthy subjects. Utilizing this tendency, the proposed method successfully classifies the AD patient from the healthy subjects, *i.e.*, the two-stage judgment prevents from the one-stage misjudgment of either on $\overline{x_{pac}}$ or $\overline{x_{ncp}}$.

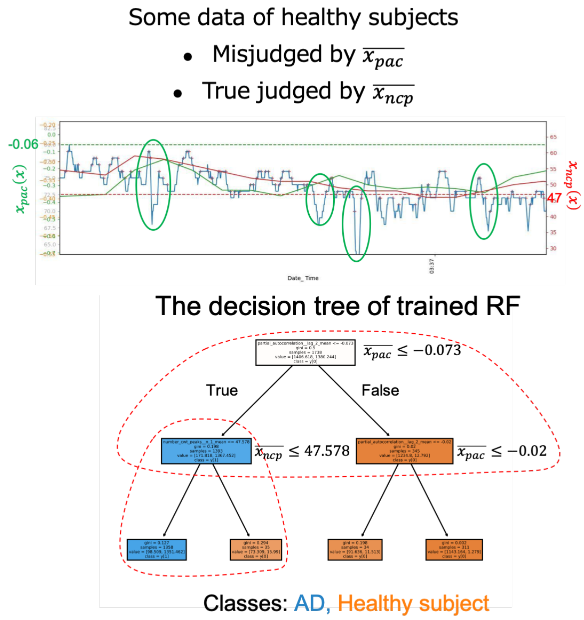


Fig. 6. Mutual assistance of $\overline{x_{pac}}$ and $\overline{x_{ncp}}$.

V. Conclusions

This paper proposed the AD detection method based on time-series feature values from the viewpoint of the instability of heart rate. The comparison experiments between the AD patient and healthy subjects revealed that the proposed method had an accuracy of approximately 98%. This result suggests that ($\overline{x_{pac}}$ and $\overline{x_{ncp}}$) of the heart rate have a potential of being new features of AD as time-series instability of heart rate and clearly show the different values between the AD patient and the healthy subjects.

What should be noted here is that the above implications were found from the one AD patient, which needs to generalize the implications by increasing the number of the AD patients. In addition to this future direction, the following research must be done in the near future. (1) Exploring the AD detection method by combining the circadian rhythm with the time-series features; (2) Applying the proposed method for early stage AD detection; and (3) Investigating an effect of the proposed method for the other types of dementia.

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