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Suggestions for Weather Index to Discriminate Risks of Cerebral and Myocardial Infarction

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Abstract

Many studies have demonstrated a significant relationship between weather and the incidence of stroke and myocardial infarction. It is expected that design of strategies aimed at minimizing the risk of these diseases will include observation of weather. However, attempts to forecast these diseases from meteorological factors have not generally been successful. Cold exposure was regarded as a trigger of these diseases, but risk increases even when the temperature rises. Weather itself is complex and is difficult to treat simply as numerical data. This study was designed to convert the variability of weather into a series of numerals and to integrate weather and meteorological factors and to clarify any link between disease and weather by introducing a new index, a “weather index”. We proposed a notion of a weather index and applied it to data of hospitalized patients at Nagoya City in Japan. The use of this weather index enabled us to introduce a variety of methods such as naive Bayes, which helped us to distinguish high-risk cases from low-risk cases. It also enabled us to discriminate risky patterns of weather which were known hitherto so far simply as “cold exposure”. Our findings of discrimination of weather patterns for high-risk cases suggest various mechanisms leading to the onset of diseases for different patterns of weather.

Keywords: Weather, Stroke, Heart disease, Bayes, Discrimination, Gene expression

Introduction

Many studies suggest that weather influence the incidences of stroke and ischemic heart disease [1]. Daily meteorological factors have been used to investigate the links between weather and these diseases. The onset of these diseases was reported to be related to temperature, atmospheric pressure and humidity [2]. However, an attempt to forecast these diseases from meteorological factors have not been productive. Cold exposure may be a trigger for these diseases, but there is a case of high risk even when temperatures are rising. In addition, weather itself is complicated and difficult to treat as numerical data.

We aimed to express daily data of weathers in numerical form and incorporate these data with meteorological factors. Thus we defined a “weather index” using self-organized mappings (SOMs). In our previous work, we had identified a pattern of “cool and rewarming” (CR) among high-risk cases of cerebral infarction during relatively warm days in winter seasons. Therefore, in the present study, we focused mainly on cold days in winter seasons, and distinguished differences among high-risk cases on cold days, which have been known so far simply as “cold exposure”.

Further, the use of this weather index enabled us to distinguish high-risk cases from low-risk cases, using Bayes analysis such as naive Bayes. It also enabled us to discriminate among risky weather patterns. Discrimination of weather patterns of high-risk cases suggests that there will be different mechanisms according to different patterns of high-risk cases leading to the onset of diseases. A possible mechanism will be discussed from a viewpoint of gene expression.

Method

Our study was based on four types of data: the daily numbers of hospitalized patients (of cerebral infarction or ischemic heart disease), meteorological information (such as mean temperature), our previous results of weather patterns (such as cold pattern of low atmospheric pressure [3,4] and gene expression profiles.

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The data of patients of cerebral infarction or ischemic heart disease were the daily data of the number of patients during two periods, 2002 - 2005 and 2009 - 2012, obtained from the city of Nagoya, located on the Pacific coast. Nagoya has a humid subtropical climate featuring four characteristic annual seasons. The data included the number of patients of all ages who were first transported by ambulance to a hospital and then diagnosed at the hospital with cerebral infarction or ischemic heart disease. The meteorological data were extracted from the Japan Meteorological Agency. The data comprised a selection of daily data, including temperature (mean, maximum and minimum temperatures) and the hours of sunshine and so on.

A weather index was defined in this article (in the results section), based on weather patterns [3,4]. This classification was established by using self-organized mappings (SOM), one of several well recognized techniques of data mining. SOM is a kind of "cluster mapping", and was first introduced by Kohonen [5]. It was intended to overview multivariate data sets (called the input layer), and to visualize them on graphical map displays (called the target layer). It gives us an overview of multivariate data sets (called the input layer), and supplies visualization on graphical map displays (called the target layer). Using artificial neural networks, the SOM algorithm aims to find prototype vectors that represent the input data set and at the same time realize a continuous mapping from input space to a lattice. This lattice consists of a defined number of "neurons" and forms a two-dimensional lattice that is easily visualized. The basic principle behind the SOM algorithm is that the "weight" vectors of neurons which are first initialized randomly, come to represent several original measurement vectors during an iterative data input process.

Each item in the data set was regarded as a point in n-dimensional space. These points in lattices in plane were also called "units". The map was realized by neural networks so that as much as possible of the original structure of the measurement vectors in the n-dimensional space is conserved in the lattice structure in plane. As a result, if the points in original data are "near" ("distant"), then they were mapped to "near" ("distant") units in plane. In this article, the results of SOM were applied to convert the variability of weathers to numerals and to give the definition of "weather index".

We will make use of the conditional rule of probability based on the principle of Bayesian inference, especially a naive Bayes classifier [6]. Bayesian analysis uses the rules of probability of unobserved quantities. The algorithm of a naive Bayes classifier continues to be used for data mining applications due to its simplicity and linear run-time. It is a method of classification, suitable for prediction. Naive Bayesian classification is a probabilistic method based on applying Bayes' theorem. Let C be the random variable denoting the class of an instance and X be a vector of random variables denoting the observed attribute values. Let c be a particular class label and x represent a particular observed attribute value. According to the independence assumption, attributes $X_1,...,X_n$ are all conditionally independent of one another, given C. The value of this assumption is that it simplifies the representation of the conditional probability $P(X_j \mid C)$, and the problem of estimating it from the training data.

Results

In previous works [7-9] we identified highly risky cases of cerebral infarction and ischemic heart disease in winter seasons. It was found that even when the temperature was high, there were many cases of high-risk cases for these diseases. In these cases, the temperature was once low, and then increased. Therefore, these cases were called "cool and rewarming". These warm cases had been neglected by usual method such as regression models. If we exclude these warm cases, will the remaining cold cases be very simple cases of cold exposure? The answer is critical, because there are still complex cases of high-risk with a variety of meteorological conditions. To clarify these cold cases, we introduced the notion, a "weather index".

The definition of our weather index was based on the SOM applied to meteorological data [3,4]. In these works, the weather data were grouped into six patterns (or units in the terminology of SOM): (1) warm cases of high air pressure, (2) cold cases of high air pressure, (3) cold cases of low air pressure, (4) rainy cases, (5) warm cases of low air pressure, and (6) humid cases. The order or numbering (1), (2) ,..., (6) of these six groups were determined by SOM according to the position in the lattices in the target plane. These numbers acquired meaning through SOM, because SOM mapped the similar/dissimilar patterns of meteorological data into near/far units among six units. Therefore it was natural to assign these numbers from 1 to 6 the term "weather index". The daily meteorological data were transformed to daily data of the weather index. We further considered the sum of weather indices during three preceding days, and associated to each day this sum, giving a daily data again. We abbreviated "this sum of three preceding weather indices" simply as the "weather index" as long as there was no confusion.

According to the number of patients, we grouped them as "high-risk", "low risk" and "mid risk". The thresholds were determined by calculating distribution of the numbers of patients during winter seasons. The values of thresholds were defined so that the ratio of low risk occupied 20%, high-risk 20%, and mid risk 60%.

The mean temperature had been useful information but not enough to forecast the onset of diseases. If we combine the mean temperature and weather index, then the information may be more useful to identify the risk of diseases. Thus, we plotted both high-risk and low-risk cases in a plane of weather index and mean temperature.

The results are shown in Figures 1 and 2 where the cross mark represents high risk and the circle mark, low risk. We calculated the distribution of the weather index of high-risk cases for winter from 2009 to 2011, for both cerebral infarction and ischemic heart disease. Further in the same figures, we described the distribution function of the weather index of high risk, where only cold cases were calculated. Here "cold" implied that the mean temperature was less than the mean temperature during the winter season in each year (as expressed by a horizontal dashed line).

In most cases, distributions were divided into two groups: high weather index (> 10), low weather index (<10). The features of the first group included humid, rainy and of low air pressure. The features of the second group were relatively dry and of high air pressure. In order to examine details of these patterns, we extracted data of weather charts from the Japan Meteorological Agency. It was found that in most cases of the first group, a cold front or traveling cyclone passed over Nagoya City. In most cases

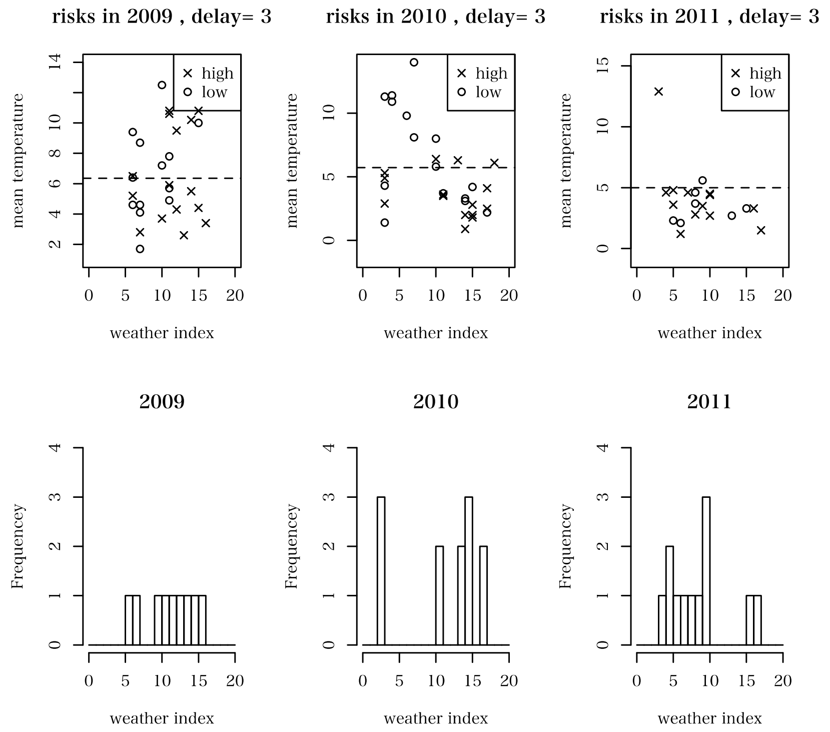

Figure 1: Distribution of weather index 2009-2012 winter seasons for cold cases (cerebral infarction). The marks of points cross or circle represent the risks of days. Cross means high risk, and circle low risk. The days are plotted at points of two coordinates (x, y)=(weather index, mean temperature). The lower graphs show the distribution functions of the weather index of high-risk cold days. The horizontal dashed lines imply the mean of mean temperature in winter.

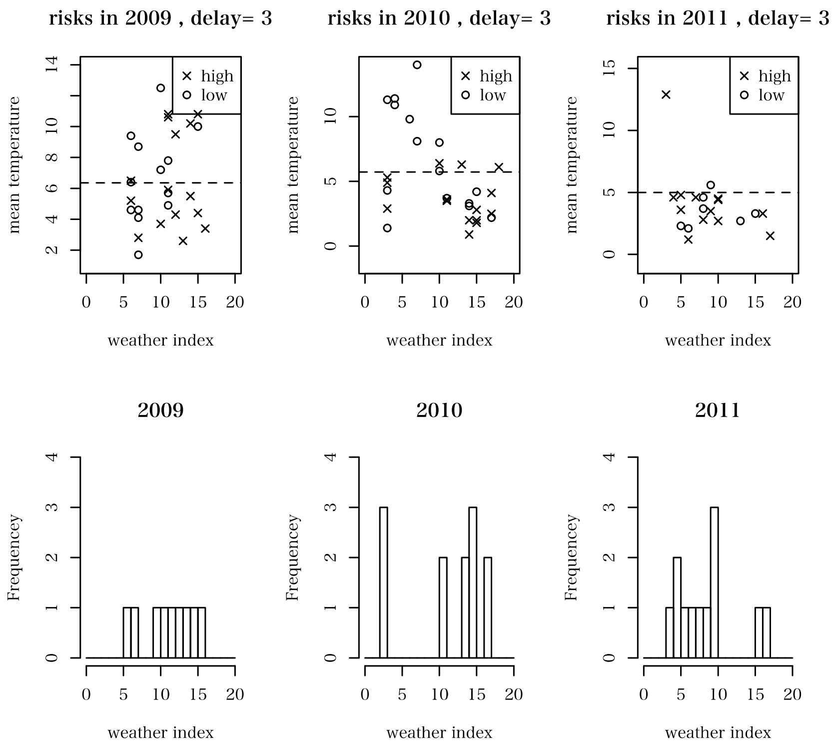

Figure 2: Distribution of weather index 2009-2012 winter seasons for cold cases (ischemic heart disease).

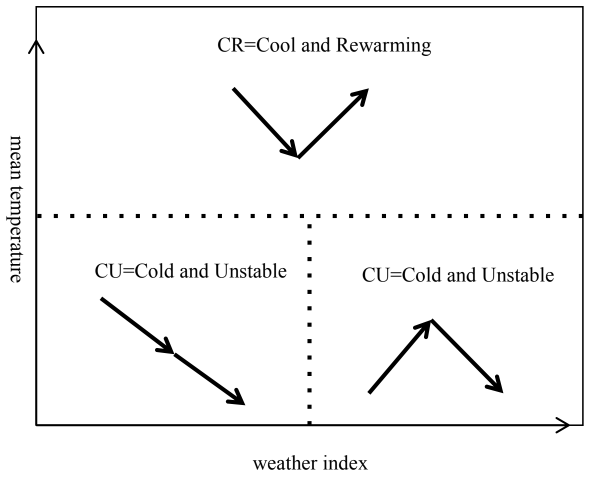

Figure 3: Classification of weather patterns of high risk. Three types of weather patterns were identified: CR, CU, and CS. The "up" and "down" of arrows implies the increase and decrease of mean temperature. For example, in the case of CR, the temperature increases after cold exposure.

of the second group, a steady winter pattern (west high and east low air temperature) was observed.

The results are summarized as follows. The patterns of weather which resulted in high-risk of diseases were classified into three groups (Figure 3):

Three types of high-risk weathers

(1) Cool and Rewarming (CR)

(2) Cold Unstable weather: Migratory Cyclone, Cold Front, Dry (CU)

(3) Cold Stable weather: Steady Winter Type (west high east low air pressure) (CS)

Temperature itself cannot forecast the risk of diseases, because there are cool and rewarming cases.

Our weather index might be expected to encounter this difficulty. To discriminate among high and low-risk cases, we used a "naive Bayes" classifier.

From a viewpoint of forecasting the onset of diseases from change of weather, it is important to distinguish days of high risk from those of low risk. This sort of problem is called "discrimination". We adopted a probabilistic method, a naive Bayes classifier, for this purpose. A naive Bayes classifier is a method based on Bayes' theorem.

Let C be the class of an instance = {high risk, low risk} (cf. method section).

C={high risk,low risk}

Let X be a vector of random variables denoting the observed attribute values. In our case, X is a vector (X_1, X_2), where X_1 = mean temperature, X_2=weather index.

$X=(X_1, X_2)$, X_1 = *mean temperature*, X_2 = *weather index*

Our main concern is the representation of the conditional probability $P(X|C)$, and the problem of estimating it from the training data. Here, the Bayes theorem plays an important role. Given $X=(X_1, X_2)$,, the problem is to calculate the probability of the class to which the given X belongs. In our case, given the data of mean temperature and weather index, the problem is to forecast whether the incidence of disease is of high risk or low risk from the data of mean temperature and weather index.

In other words, the discrimination problem is a problem to distinguish the area of high risk from the area of low risk in the plane of (X_1, X_2) = (mean temperature, weather index). Therefore, describing the boundary of these areas becomes important. The boundary corresponds to the set of the points with P(X|C) = 0.5. The results of these calculation are shown in Figure 4, where curves correspond to the boundaries of high or low risk, i.e., P(X|C) = 0.5. The hitting ratio of forecasting was also calculated. The delay was applied only for mean temperature (shifting three days) because our definition of weather index includes already three days as a sort of delay.

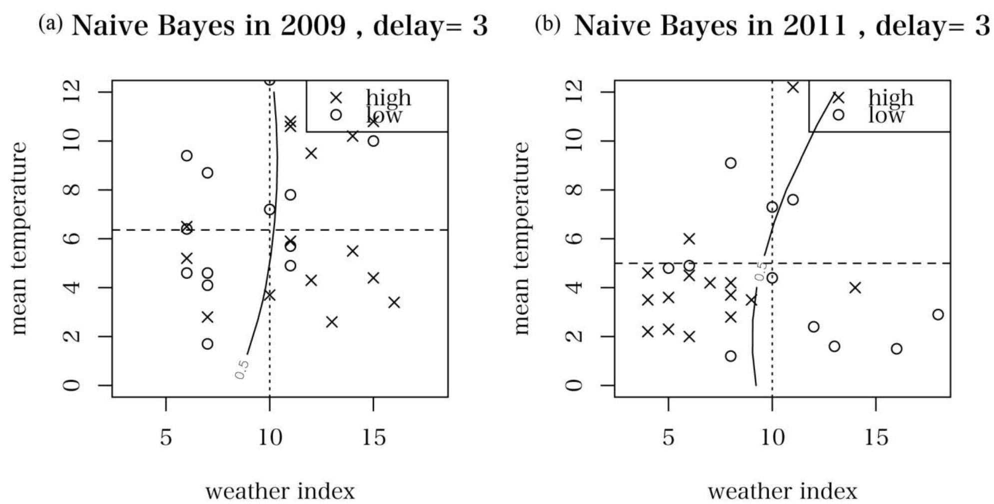

Figure 4: The discrimination of high and low risk using weather index and mean temperature. The values of mean temperature were shifted three days (delay = 3). The curves in the graphs imply the boundary points of areas of high risk (cross) and low risk (circle).

In Figure 4 (a), the cross marks represents high-risk days of cerebral infarction during 2009 winter seasons, and the circle marks, low-risk days. The values of mean temperature were shifted three days (delay = 3). The horizontal line meant weather index and the vertical line shows temperature. The horizontal dashed lines imply the mean of mean temperatures during winter. The curve in the figure traces the points, where the probabilities forecasted by naive Bayes are equal to 0.5, i.e., the points of boundaries of areas of high risk or low risk. The hitting ratio by the naive Bayes was 0.75, and hitting ratio restricted to only cold days (i.e., days, the temperature of which were less than the mean of mean temperature) was 0.73.

Figure 4 (b) was the same as Figure 4 (a), but the term was during 2011 winter season, dealing with myocardial infarction. The hitting ratio by naive Bayes was 0.79, and hitting ratio, restricted to only cold days, was 0.82.

Discussion

Exploring weather conditions that might trigger the incidence of disease, the works [7-9] found a pattern of cool and rewarming (CR) among high-risk cases of cerebral infarction and ischemic heart disease. If we excluded the "cool and rewarming" cases from high-risk cases, then the remaining high-risk cases become "cold days". In the current paper, these cold cases were mainly investigated by introducing a new notion, a "weather index". These cold cases were found to be more complex than one expected from the term "cold exposure".

The weather index was calculated from the results of the self-organized mapping (SOM) applied to meteorological data [3,4]. The sum of weather indices during three preceding days was also considered as a useful index, and this sum was associated with each day, which was also called as a "weather index" as long as there was no confusion. The weather index highlighted differences among high-risk cases of cold days. It divided these cold cases into two groups: (1) cold and unstable cases (CU) and (2) cold and stable cases (CS) . If we added the group of cool and rewarming (CR) together, the total groups consisted of three group: CR (cool and rewarming), CU (cold and unstable) and CS (cold and stable) (cf., Figure 3).

CU (Cold and Unstable cases)

The CU cases had a feature of high humidity, low temperature and low air pressure. We examined weather patterns of these high-risk cases in the database of weather charts of the Japan Meteorological Agency. It was found that this type was distinguished by events of a traveling low atmospheric pressure and moving cold front. These features resulted in a rapid change of weather, especially temperature. The events of the traveling low atmospheric pressure and moving cold front caused rapid weather changes. It was reported that rapid weather changes are associated with increased ischemic stroke risk [10].

CS (Cold and Stable cases)

The stable dry cases had a feature of low humidity, low temperature and mostly high air pressure. This type was characterized by a stable position of high and low air pressure, i.e., high air pressure in the west and low air pressure in the east. This layout of air remained stable for several days. Onset of atrial fibrillation- the primary cause of cardioembolic strokes – can be provoked by cold weather. In addition, a low relative humidity is known to increase human blood viscosity which is an established predictor for ischemic strokes.

CR (cool and rewarming cases)

The cool and rewarming pattern was discussed earlier [7-9], In these cases, the cold exposure occurred, but the temperature and humidity increased while air pressure decreased. It has been argued [9 Morimoto5] that cool and rewarming corresponded to a recovery process at DNA levels.

The U-shape graph of risk v.s. air pressure was observed for stroke [2]. Hgt850hPa decrease was found to be nonlinearly associated with ischemic stroke and other stroke increases. Hgt850hPa disclosed characteristic "U-shaped" relationships with PIH and other strokes.

The geopotential height considered in their study represents the height at which the isobaric measure corresponds to 850 hPa (average 1500 m asl). An increasing/decreasing Hgt850hPa indicates an increasing/decreasing sea level atmospheric pressure, corresponding to high/low atmospheric pressure, respectively. It has been found that the incidence of non-lacunar stroke was related to daily falls in atmospheric pressure whereas the incidence of ischemic heart disease was related to daily rises in atmospheric pressure [1]. They found that total stroke showed a U-shaped relation with air pressure.

These findings suggest that there are different mechanisms for the incidence of disease according to the groups CU, CS and CR. Therefore, it is reasonable to discuss the relationship between these three types of weather and the features of gene expression.

CR(cool and rewarming) and Gene expression

Gene expression related to CR(cool and rewarming) may be due to the effects of relatively high humidity and warming temperature. It has been reported [11] that the relative humidity association with ICAM-1 methylation was stronger on hot days than mild days. They found that the interaction between temperature and relative humidity, which gave rise to stronger decreases in ICAM-1 methylation during hot and humid days, ICAM-1 encodes a cell surface glycoprotein that is overexpressed during inflammatory responses. Temperature increases were associated with TLR-2 hypomethylation. TLR-2 hypomethylation may activate TLR-2 gene expression and induce biologic processes enhancing IL-6 and C-reactive protein after exposure to warm temperatures. These features correspond to cool and rewarming.

An increase in relative humidity (1 week) was associated with ICAM-1 hypomethylation. Humid weather conditions may lead to F3 and ICAM-1 hypomethylation that would increase tissue factor and ICAM-1 expression, respectively.

Research [12] showed that HSP70, a heat shock protein, was induced by cold shock, and was more highly induced with heat than with cold. Maximal induction of HSP70 occurred 4-6 h following recovery. They showed that HSP70 mRNA and protein are induced upon cooling neonatal cardiomyocytes to temperatures between 4°C and 25°C, and then rewarming to 37°C. The maximal HSP70 levels occurred after 90 min of recovery from cold shock, returning to normal levels by 3 h. Another study [13] reported that IL-8 is induced only after rewarming to 37°C for 6 h.

CU (Cold Unstable) and Gene expression

Research [11] found that humidity and low temperature caused decrease of DNA methylation, increase of protein. Temperature or relative humidity levels were associated with methylation on, intercellular adhesion molecule 1 (ICAM-1), toll-like receptor 2 (TRL-2), carnitine O-acetyltransferase (CRAT), LINE-1. A temperature decrease was associated with ICAM-1 hypomethylation. Similarly, a decrease in temperature was associated with CRAT hypermethylation. An increase in relative humidity (1 week) was associated with ICAM-1 hypomethylation. Humid weather conditions may lead to F3 and ICAM-1 hypomethylation that would increase tissue factor and ICAM-1 expression, respectively.

CS (Cold and Stable) and Gene expression

CS cases were characterized by stable cold states. A temperature decrease was associated with ICAM-1 hypomethylation. Similarly, a decrease in temperature was associated with CRAT hyper methylation.

Cold cases (both CU and CS) and Gene expression

Research [12] found that the induction of this response in cold-shocked neonatal cardiomyocytes may be due to cold-induced damage of cellular proteins. Therefore, it is possible that either cells cannot synthesize new proteins at cold temperatures, or that a cold-induced heat shock response could be due to cellular protein damage from rewarming.

One study [14] found that 32°C induces expression of CIRP (cold-inducible RNA-binding protein), and that with decreasing temperature from 37 to 28°C, cell proliferation gradually decreases. When human HeLa cells are placed at 4°C, there is a gradual decline in their ability to synthesize protein. They also reported APG-1 mRNAs were induced by a temperature shift from 32 to 39°C.

Thus, the groups, CR, CU, and CS correspond to different processes of gene expressions, including inflammatory processes. This finding suggests the different mechanisms for the onset of diseases according to weather patterns. The classification of weather by the "weather index" may provide a new forecasting scheme of the onset of diseases by weather, and a new aspect of gene networks affected by weather.

Conclusion

By introducing a new index, a "weather index", we have identified and classified highly risky weather patterns that trigger the incidence of cerebral infarction and ischemic heart disease. The three groups of weather patterns were obtained:

(1) Cool and Rewarming (CR),

(2) Cold Unstable weather: Migratory Cyclone, Cold Front, Dry (CU),

(3) Cold Stable weather:, steady winter type (west high east low air pressure)

This finding suggests the existence of different mechanisms for the onset of diseases. Each group, CR, CU, and CS corresponds with different patterns of gene expression. Thus the classification of weather by the "weather index" may contribute to the forecasting of the onset of diseases by weather. The relation of the classification of weather with gene expression may be expected to prompt further interest.

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