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An Application of Rough Set Analysis to a Psycho-physiological Study - Assessing the Relation between Psychological Scale and Immunological Biomarker

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Abstract—This study aims at an application of rough set theory to illustrate the relationship between human psychological and physiological states. Recent behavioral medicine studies have revealed that various human secretory substances change according to mental states. These substances, the hormones and immune substances, show temporal increase against mental stress. Thus, it is frequently introduced as biomarkers of mental stress. The relationship between these biomarkers and human chronic stress or daily mental states was also suggested in the previous studies. However, the results of these studies were inconsistent. Some technical reasons were indicated for this discrepancy. Among that, we focused on the analysis technique investigating the relationship between human psychological state, i.e., scores of a psychological scale, and physiological state, i.e., level of the secretory biomarkers. In this paper, we introduced Rough Set analysis method instead of using a conventional linear correlation analysis method. In the experiment, the salivary secretory immunoglobulin A (IgA), which is a major stress biomarker, of 20 male students was assessed before and after a short-term stressful mental workload. Also, 65 items of psychological mood scale was assessed as a psychological index. The result showed that some items strongly related with the change in the IgA, while no significant linear correlation among that was obtained.

I. INTRODUCTION

In this study, we introduced Rough Set theory [1], [2] as a new methodological approach to extract the embedded relationships between human psychological and physiological states.

For over a century, behavioral medicine studies have been made to investigate the relationship between human psychological and physiological states. Consequently, it has revealed that human secretory substances sensitively change accompanying with the change in his/her mental states. For example, human secretory immunoglobulin (IgA) shows transient increase against a short-term experimental stressor like arithmetic task [3], [4], [5]. Recently, this bio-behavioral medicine studies are drastically developing according to the improvement of biochemical analysis techniques such as radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA). Nowadays, at least a dozen of human secretory substances, which are hormones, immune substances, and digesting enzymes, are considered as candidates of the biomarker of human psychological state [6]. Most of these studies have Because most of these biomarkers showed increase against short-term stressor, it is also called as an objective stress-marker. While these stress-markers can be found in any human secretory fluids, such as blood, urine, and saliva, salivary biomarkers is expected to be a practical stress-marker because of its easy-to-get nature unlike blood and urine. On the other hand, as against studies on the short-term laboratory stressors, studies investigating the effects of long-term stressors or rather daily stressful experience on biomarkers have frequently shown inconsistent results. Some reasons were indicated for this discrepancy, such as small number of studies, variation of biomarker determination techniques, subjects’ control, specimen sampling, and so on. Above all, one could say that, in all these studies, the only method introduced for evaluating the degree of relationship between somatic and mental state is the correlation analysis by which a sort of strength in the relationship between the score of psychological questionnaire and the amount of secretory substance can be quantified. The correlation analysis is though a one-to-one factorial evaluation method based on linearity between the target factor and another. In other words, one can easily imagine that the correlation analysis suggests no result if a target factor such as the change in secretory substance would be mediated by several psychological factors, or if the relationship would be in the form of non-linearity. Therefore, it can be worth introducing independent analytical methodology. In this study, we introduced rough set theory as an attempt to extract the relationship between the score of psychological questionnaire and the amount of a salivary biomarker. The factors and elements of data for analyzing by
rough set theory have no statistical restriction such as the number of elements, linearity and independency of factors. Also, relationship among multiple factors can be analyzed simultaneously.

In this study, we introduced the "the profile of mood state" (POMS) as for the psychological questionnaire and the concentration of salivary immunoglobulin A (IgA) as for the biomarker, and analyzed the relation among them by rough set theory. In the next, we briefly review the past IgA studies.

II. SALIVARY IMMUNOglobulin A (IGA) AS AN IMMUNOLOGICAL BIOMARKER

Immunoglobulin A (IgA) is one of the most important substances in human immune system. It exists in various secretion fluids, such as serum, saliva and breast milk. The IgA in these secretory fluids normally exist in dimeric form combined with a glycoprotein named J-chain. Also, IgA is combined with secretory component (SC) which stabilizes IgA molecular and protects it from degradation in those fluids [7]. The salivary IgA antibodies work non-specifically and, therefore, play a very important role for our health, e.g., for preventing bacteria from forming colonies, neutralizing toxins and enzymes produced by bacteria, and inhibiting pathogenic viruses to penetrate into the epithelial cell. That is the reason why salivary IgA called as the "first line of defense" against the influenza or other respiratory tract infection (URTI) illnesses. In fact, clinical studies have suggested the negative correlation between the level of salivary IgA and the incidence of an acute URTI [8]. It was also suggested that the relevance between the level of salivary IgA and caries or periodontitis [9].

On the other hand, by the 70's behavioral medicine studies, it has been found that salivary IgA changes its level accompanying with various types of psychological factors [5], such as desirable or undesirable daily events [10], daily hassles [11], negative or positive moods [12], academic stresses such as examination [13] and presentation [14], a short-term stress [8] and relaxation [15], [16]. A review article has concluded that there are distinguishable two types of stress effects on IgA: 1) increasing IgA secretion immediately after a shot-term stress, termed "immediate stress effect", and 2) decreasing IgA secretion several days after stress, termed "delayed stress effect" [7]. However, even though the immediate stress effect has been successfully observed almost all studies targeting on variety of short-term stressors, the delayed stress effect has not been directly observed yet as far as we know. Some studies showed the negative relationship between the IgA level and a long-term or chronic stress. However, as the other reviews on IgA study pointed out, these studies had methodological defects such as less control of subjects' physical conditions like as sleep and diet, using inappropriate saliva sampling methods, and introducing non-standardized psychological questionnaire [5]. So far as we know, no clear relationship between IgA and any psychological state has ever shown before.

However, as mentioned above, these studies frequently investigated the relationship all that by the correlation analysis, which was based on the linearity of one factor to another. Because scores of questionnaire are subjective, it is not improbable that some sort of uncertainty would affect the results. We then introduced the rough set theory which is a non-parametric analysis method and is thought to be suitable for classifying the data sets including such uncertainty.

III. ROUGH SETS

In this section, we review the rough set theory, in particular, on decision tables, relative reducts, and degrees of contribution of condition attributes to relative reducts as an evaluation criterion for condition attributes proposed by the authors [17]. Note that contents of this section are based on [18], [19].

A. Decision tables and lower and upper approximations

Generally, subjects of data analysis by rough sets are illustrated by decision tables. Formally, a decision table is the following quadruple:

$$DT = (U, C \cup D, V, \rho), \quad (1)$$

where $U$ is a finite and non-empty set of elements, $C$ and $D$ are finite and non-empty sets of condition attributes and decision attributes such that $C \cap D = \emptyset$, respectively, $V$ is a set of all values of attributes $a \in C \cup D$, and $\rho : U \times (C \cup D) \rightarrow V$ is a function which assigns a value $\rho(x, a) \in V$ at the attribute $a \in C \cup D$ to the element $x \in U$.

Classification of elements in decision tables are done based on indiscernibility relations. For any set of attributes $A \subseteq C \cup D$, the indiscernibility relations $R_A$ is the following binary relation on $U$:

$$R_A = \{(x, y) \mid \rho(x, a) = \rho(y, a), \forall a \in A\}. \quad (2)$$

If a pair $(x, y)$ is in $R_A$, then two elements $x$ and $y$ are indiscernible with respect to all attributes in $A$. It is well-known that any indiscernibility relation is an equivalence relation, and equivalence classes by an equivalence relation consists of a partition on the domain of the equivalence relation. In particular, the indiscernibility relation $R_D$ based on the set of decision attributes $D$ provides a partition $D = \{D_1, \cdots, D_k\}$, and each element $D_i \in D$ is called a decision class.

Classifying elements with respect to condition attributes provides approximation of decision classes. Formally, for any set $A \subseteq C$ of condition attributes and any decision class $D_i \in D$, we let

$$\Delta(D_i) = \{x \in U \mid [x]_A \subseteq D_i\}, \quad (3)$$

$$\overline{\Delta}(D_i) = \{x \in U \mid [x]_A \cap D_i \neq \emptyset\}. \quad (4)$$

where the set $[x]_A$ is the equivalence class of $x$ by the indiscernibility relation $R_A$. The set $\Delta(D_i)$ and the set $\overline{\Delta}(D_i)$ are called the lower approximation and the upper approximation of the decision class $D_i$ with respect to $A$, respectively. Note that the lower approximation $\Delta(D_i)$ illustrates the set of elements which are correctly classified to the decision class $D_i$ by checking all attributes in $A$. 

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B. Relative reducts

By checking values of all condition attributes, we can classify all discernible elements in a given decision table to those correct decision classes. However, not all condition attributes may need to be checked in the sense that some condition attributes are essential to classify, and the other attributes are redundant. A minimal set of condition attributes to classify all discernible elements to correct decision classes is called a relative reduct of the decision table.

To introduce the concept of relative reducts, for any subset \( X \subseteq C \) of condition attributes in a decision table \( DT \), we let

\[
POS_X(D) = \bigcup_{D_i \in D} X(D_i).
\]

The set \( POS_X(D) \) is called the positive region of \( D \) by \( X \). All elements \( x \in POS_X(D) \) are classified to correct decision classes by checking all attributes in \( X \). In particular, the set \( POS_C(D) \) is the set of all discernible elements in DT.

Here, we define relative reducts formally. A set \( A \subseteq C \) is called a relative reduct of the decision table \( DT \) if the set \( A \) satisfies the following conditions:

1) \( POS_A(D) = POS_C(D) \).
2) \( POS_B(D) \neq POS_C(D) \) for any proper subset \( B \subset A \).

Note that, in general, there are plural relative reducts in a discernibility matrix \( n \times n \) matrix whose element at \( i \)-th row and \( j \)-th column is the following set of condition attributes to discern between two elements \( x_i \) and \( x_j \):

\[
\delta_{ij} = \begin{cases} 
\{a \in C \mid \rho(x_i, a) \neq \rho(x_j, a)\}, \\
\emptyset,
\end{cases}
\]

if \( \exists d \in D \) such that \( \rho(x_i, d) \neq \rho(x_j, d) \), otherwise.

Each element \( a \in \delta_{ij} \) represents \( x_i \) and \( x_j \) are discernible by checking the value of \( a \). Using the discernibility matrix, we get all relative reducts of the decision table as follows:

1) Construct the following logical formula \( L(\delta_{ij}) \) from each non-empty set \( \delta_{ij} = \{a_{k1}, \cdots, a_{kl}\} \) \( (i > j \) and \( l \geq 1 \) in the discernibility matrix:

\[
L(\delta_{ij}) : a_{k1} \lor \cdots \lor a_{kl}.
\]

2) Construct a conjunctive normal form \( \bigwedge_{i > j} L(\delta_{ij}) \).

3) Transform the conjunctive normal form to the minimal disjunctive normal form:

\[
\bigwedge_{i > j} L(\delta_{ij}) \equiv \bigvee_{p=1}^{s} \bigwedge_{q=1}^{t_p} a_{pq} \quad (8)
\]

4) For each conjunction \( a_{p1} \land \cdots \land a_{pt_p} \) \( (1 \leq p \leq s) \) in the minimal disjunctive normal form, construct a relative reduct \( \{a_{p1}, \cdots, a_{pt_p}\} \).

C. Degree of contribution of attributes to relative reducts

We use the following criterion for condition attributes based on all relative reducts called the degree of contribution of attributes to relative reducts [17].

Definition 1: Let \( DT = (U, C \cup D, V, \rho) \) be a decision table, and \( R \) be the set of all relative reducts of the decision table \( DT \). For each condition attribute \( a \in C \), we define the degree of contribution of the attribute \( a \) to relative reducts \( DoC_R(a) \) as follows:

\[
DoC_R(a) = \frac{|\{R \in R \mid a \in R\}|}{|R|},
\]

where \( |X| \) is the cardinality of the set \( X \).

The degree of contribution of \( a \in C \) is the ratio of relative reducts which contain \( a \), therefore the range of values of \( DoC_R(a) \) is \( 0 \leq DoC_R(a) \leq 1 \) for any \( a \in C \). Moreover, it is clear that \( DoC_R(a) = 1 \) if and only if \( a \) belongs to the core of relative reducts.

We intend to use the degree of contribution as a criterion to evaluate an “importance” of condition attributes. Because the set \( R \) of all relative reducts in the decision table provides all minimal combinations of condition attributes to classify all discernible elements to correct decision classes, attributes with high degree of contribution, that is, attributes which belong to many relative reducts are frequently used for classification of elements based on relative reducts. Thus, we consider that attributes with high degree of contribution as essential attributes for classification of elements to decision classes, which corresponds to the “importance” of condition attributes [17].

Example 1: Table I illustrates an decision table we use in this paper, and consists of the following elements: \( U = \{s1, \cdots, s19\}, C = \{Q.5, Q.10, Q.25, Q.32, Q.40, Q.45, Q.60\}, D = \{\text{IgA}\}, V = \{0, 1, 2, 3, 4\} \), and the function \( \rho : U \times (C \cup D) \rightarrow V \) illustrates values of elements at attributes such that \( \rho(s1, Q.5) = 1 \). The decision attribute IgA provides the following four decision classes:

\[
\begin{align*}
D1 & : \{s1, s7, s12, s14\} \quad \text{(IgA=1)}, \\
D2 & : \{s2, s3, s5, s11, s13, s17, s18\} \quad \text{(IgA=2)}, \\
D3 & : \{s4, s6, s8, s15, s19\} \quad \text{(IgA=3)}, \\
D4 & : \{s9, s10, s16\} \quad \text{(IgA=4)}. 
\end{align*}
\]

By constructing the discernibility matrix of Table I, we have the set of all relative reducts \( R \) with the following 10 relative reducts:

\[
\begin{align*}
r1 & : \{Q.5, Q.10, Q.25, Q.45\}, \quad r2 : \{Q.5, Q.10, Q.32, Q.45\}, \\
r3 & : \{Q.5, Q.10, Q.40, Q.45\}, \quad r4 : \{Q.5, Q.10, Q.45, Q.60\}, \\
r5 & : \{Q.5, Q.25, Q.32, Q.45\}, \quad r6 : \{Q.5, Q.25, Q.40, Q.45\}, \\
r7 & : \{Q.5, Q.35, Q.45, Q.60\}, \quad r8 : \{Q.5, Q.32, Q.40, Q.45\}, \\
r9 & : \{Q.5, Q.32, Q.45, Q.60\}, \quad r10 : \{Q.5, Q.40, Q.45, Q.60\}. 
\end{align*}
\]

The degrees of contribution of condition attributes are
calculated as follows:

\[ DoC_R(Q.5) = \frac{|R|}{|R|} = 1, \]

\[ DoC_R(Q.60) = \frac{|\{r1, r3, r7, r9\}|}{|R|} = \frac{4}{10}. \]

IV. METHOD

Twenty healthy male students aged from 20 to 26 participated in this study. They were well informed about the aim and contents of this study before the experiment, and confirmed their participation by subscribing to the agreement.

In the experiment, subjects were required to conduct 18 min of mental arithmetic task as a short-term stressor. Saliva was taken before and after the task. Collected saliva was kept in a freezer at -20 Celsius immediately after saliva sampling before biochemical assay. The concentration of IgA was determined by the enzyme-linked immunosorbent assay (ELISA). With some data of IgA might vary because of the failure of biochemical determination procedure. The rest data obtained from 19 subjects were introduced to the correlation and rough set analysis. Table II shows the correlation coefficients between IgA concentration and the six identified mood factors of POMS. As the table shows, there is no relevant correlation between the IgA concentration and the mood factors of POMS. Therefore as the same as the past studies, it was suggested that there was no linear relation between factors of POMS and secretion of IgA.

In the next, we categorized IgA data into four nonparametric scales for applying rough set theory, because rough set analysis was basically done by non-parametric data. So far as we know, there is no epidemiological study assessing huge number of subject and showing the distribution (or normal range) of human salivary IgA. We thus simply categorized IgA at regular intervals as Table III shows. Table IV shows the degrees of contribution (DoC) calculated by rough set theory and the Spearman’s rank-correlation coefficients between each items of POMS and non-parametrically allocated IgA. It also shows the average DoC of the six mood factors and dummy items. The correlation coefficients are shown only if they are statistically significant (\( p < .05 \)). There were only two items showing statistically significant correlation in factor T-A and D respectively, while the correlation coefficients were still small. Note that such a correlation was a result of simple one-to-one correlation between each item and IgA. Therefore, it is not necessary to think that the items with higher correlation had closer relationship with IgA than the other items. By this result of Table II again, it could be suggested that almost all the items and factors of POMS might not have relevant linear relation with IgA.

On the other hand, there were several items with higher DoC (DoC > 0.7) such as the item No. 8 in A-H, No. 19 in V, No. 22 in F, and No. 5 and No. 45 in C. In addition, the dummy items No. 1 and No. 31 also had higher DoC.

V. RESULT

As a result of biochemical analysis, the average IgA concentrations during a short arithmetic task was significantly increased from 123.5 [µg/dL] (SD = 63.5) to 173.2 [µg/dL] (SD = 92.9) \(( p < .01 \) by t-test). It was consistent result with numerous past studies. Note that the IgA of a subject was lost because of the failure of biochemical determination procedure. The rest data obtained from 19 subjects were introduced to the correlation and rough set analysis. Table II shows the correlation coefficients between IgA concentration and the six identified mood factors of POMS. As the table shows, there is no relevant correlation between the IgA concentration and the mood factors of POMS. Therefore as the same as the past studies, it was suggested that there was no linear relation between factors of POMS and secretion of IgA.

VI. DISCUSSION

Our result of correlation in Table II supports the suggestion of the past studies indicating no clear evidence showing the
Actually, the higher the average of DoC scores, the smaller the contribution (DoC) based on rough set theory, and found that there were some items with higher DoC scores. In contrast to the simple one-to-one correlation analysis shown in Table II, the DoC represents items relatively more important than the other items in the corresponding mood factor of POMS. In other words, these items marked higher DoC scores could consist of the seven questions, which are not categorized into the six mood factors. Nevertheless, these items are not just unclassifiable. Six items out of the seven dummy items are the questions about personal relationship with others, such as "Are you getting along with others?" or "Do you trust in others?" Some studies showed that the psycho-social support affected the salivary IgA secretion against long-term [21] and short-term [22] stressors. The high DoC scores in the dummy items might suggest the importance of such a psycho-social support to IgA secretion. Actually, the item No.1 asking "Are you getting along with others?" is the most relevant and typical question about the psycho-social support, and it marked the maximum DoC (1.0).

This study is the first step introducing rough set theory into the biomarker study. There must be hundreds of stuffs to develop this study, such as analyzing the other piece of psychological questionnaires with large number of subjects, assaying the other biomarkers which are thought to be changed to develop this study, such as analyzing the other piece of psychological states, introducing physiological indices such as heart rate and blood pressure, and taking account of all the possible mediators such as gender, age, race, and/or life styles and habits. The advantage of using rough set analysis is that one could compare among any non-parametric factors. In addition, any factor could be assigned as the condition or decision attributes. Moreover, there is no restriction of the number of decision attributes. One can choose several factors as the decision attributes. This property

<table>
<thead>
<tr>
<th>The factor A-H</th>
<th>The factor D</th>
<th>The factor A-H</th>
<th>The factor V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q.14  0.43</td>
<td>Q.2  0.30</td>
<td>Q.3  0.31</td>
<td>Q.4  0.56</td>
</tr>
<tr>
<td>Q.18  0.70</td>
<td>Q.7  0.27</td>
<td>Q.8  0.78</td>
<td>Q.15  0.69</td>
</tr>
<tr>
<td>Q.23  0.48</td>
<td>Q.12  0.29</td>
<td>Q.11  0.31</td>
<td>Q.19  0.88</td>
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<tr>
<td>Q.33  0.65</td>
<td>Q.16  0.56</td>
<td>Q.17  0.28</td>
<td>Q.26  0.38</td>
</tr>
<tr>
<td>Q.36  0.17</td>
<td>Q.20  0.39</td>
<td>Q.21  0.56</td>
<td>Q.39  0.38</td>
</tr>
<tr>
<td>Q.49  0.43</td>
<td>Q.24  0.25</td>
<td>Q.28  0.38</td>
<td>Q.50  0.44</td>
</tr>
<tr>
<td>Q.53  0.52</td>
<td>Q.29  0.28</td>
<td>Q.38  0.31</td>
<td>Q.54  0.63</td>
</tr>
<tr>
<td>Q.58  0.57</td>
<td>Q.37  0.32</td>
<td>Q.41  0.34</td>
<td>Q.61  0.06</td>
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<tr>
<td>Q.65  0.57</td>
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<td>Q.46  0.48</td>
<td>average 0.50</td>
</tr>
<tr>
<td>Q.47  0.05</td>
<td>Q.48  0.22</td>
<td>Q.52  0.65</td>
<td>Number of Reducts: 16</td>
</tr>
<tr>
<td>Q.51  0.59</td>
<td>Q.56  0.35</td>
<td>Q.63  0.36</td>
<td>Number of Reducts: 80</td>
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<tr>
<td>Q.55  0.39</td>
<td>Q.59  0.23</td>
<td>average 0.42</td>
<td></td>
</tr>
<tr>
<td>Q.64  0.30</td>
<td></td>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>The factor F</th>
<th>The factor C</th>
<th>Dummy questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q.9  0.67</td>
<td>Q.5  1.00</td>
<td>Q.1  1.00</td>
</tr>
<tr>
<td>Q.22  1.00</td>
<td>Q.10  0.40</td>
<td>Q.6  0.43</td>
</tr>
<tr>
<td>Q.27  0.33</td>
<td>Q.25  0.40</td>
<td>Q.13  0.57</td>
</tr>
<tr>
<td>Q.34  0.33</td>
<td>Q.32  0.40</td>
<td>Q.30  0.57</td>
</tr>
<tr>
<td>Q.44  0.67</td>
<td>Q.40  0.40</td>
<td>Q.31  0.71</td>
</tr>
<tr>
<td>Q.57  0.50</td>
<td>Q.45  1.00</td>
<td>Q.35  0.43</td>
</tr>
<tr>
<td>Q.62  0.33</td>
<td>Q.60  0.40</td>
<td>Q.43  0.57</td>
</tr>
<tr>
<td>average 0.55</td>
<td>average 0.57</td>
<td>average 0.61</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE III</th>
<th>CATEGORIZED IgA CHANGE AT REGULAR INTERVALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>change of IgA concentration [μg/dL]</td>
<td>score</td>
</tr>
<tr>
<td>Small</td>
<td>&lt; 0</td>
</tr>
<tr>
<td>Relatively Small</td>
<td>0 – 50</td>
</tr>
<tr>
<td>Relatively Large</td>
<td>50 – 100</td>
</tr>
<tr>
<td>Large</td>
<td>&gt; 100</td>
</tr>
</tbody>
</table>
would be useful especially to eliminate or detect the possible mediators.

VII. CONCLUSION

In this study, we introduced rough set theory to extract the embedded non-linear relation between human psychological state and salivary immune secretion. We then found several items that might be deeply relevant to IgA secretion level, while no clear correlation was found between the six mood factors of POMS and IgA secretion. It could assume that the classification of the 65 items of POMS by mood factors would be not adequate to presume human immune or, probably, physiological state.

However, we do not claim that rough set analysis must be more effective or useful methodology to investigate human body-mind relationship than the conventional correlation analysis. Rough set analysis is considerably different idea from correlation analysis. It is not the method to estimate the linearity among factors but the method to eliminate dominant condition attributes (each item in POMS) from a set of them (a mood factor). Thus, the result of rough set analysis certainly gives the information about the relative “importance” among a set of items. In contrast, it does not give any information about “how” important the item is, e.g., if it has a positive or negative relation. In another aspect, rough set analysis method would be suitable method to extract dominant factors or underlying mediators from a set of factors. The correlation analysis would be an adequate method for investigating the relationship between a given factor and its target. To summarize, by introducing both methods to the other kinds of psychological questionnaires, it might be possible to make an all-new questionnaire which is closely relevant to human immune or physiological state. There are numbers of psychological questionnaires including dozens of items. Most of these questionnaires were standardized by the factor analysis among the items. Thus, it has been originally made focusing on the subjective literature information. However, the close relationship between human psychological state and immune-endocrine secretion has been recently found as described at Introduction. Therefore making an all-new questionnaires being closely relevant with human unconscious physiological state must be quite valuable in terms of complementation of diagnosis or self-regulating the mental and somatic health.

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