The 9th Symposium of the 88th Academic Annual Congress of the Japan Society of the Hygiene: Various View Points of World Views

Introduction

In a time when diversity is emphasized, and so many administrative, semi-administrative and private services are prepared today, a methodology to narrow down the choice is needed practically. On the other hand, in individuals, families, communities, organizations, municipalities, and nations, it is impossible to lack multipolar direction to guide appropriate transformation. Here, we examined what something new become obvious when we slightly changed the methodology (mainly analytical method) in The 9th Symposium of the 88th Academic Annual Congress of the Japan Society of the Hygiene: Various View Points of World Views.

The 88th Academic Annual Congress of the Japanese Society for Hygiene was chaired by prof. K. Yokoyama at the Juntendo University School of Medicine Tokyo to highlight and secure hygiene’s identity as a scientific discipline on March 22–24, 2018 in Tokyo with 699 attendees, 3 special lectures including one oversea invited, 2 educational lectures, 21 symposiums, 231 general talks and a daily public lectures. The theme of this congress was “A recommendation of awareness comes only through practice is sophisticated hygiene. From Prof. Wang Yangming as the fundamental idea.”

The congress program asked “What is human health as a social being” including the interaction between community (social group) and individuals.

The title of each lecture and the name of lecturers and a commentator in the 9th Symposium were as the followings:

Lecture 1: What new insights have been gained by cutting edge technology manipulating specifies cells in the brain? By prof. dr. Tomohisa Mori

Lecture 2: What has benefited from nested analysis of data from benchtop experiments? By prof. dr. Satoshi Numazawa & dr. prof. Toshiko Sawaguchi

Lecture 3: Subjective QOL evaluation as PRO (Patient Reported Outcome). What was brought by utilizing the Evaluation of Individual Quality of Life (SEIQoL) such as subjective score? By prof. dr. Naoko Ideguchi

Lecture 4: What was brought from the nested approach & the sound approach-Listen to the voice of the state, cause of death & willful negligence by sound? By dr. prof. Toshiko Sawaguchi

Comment: What is lost and gained when the propensity score is used? By dr. professor Hideto Takahashi

What Changes Have Been Brought by Specific Cell Manipulation?

—Using Optogenetics—

Tomohisa Mori1, Toshiko Sawaguchi2,3

1) Department of Pharmacology, Hoshi University
2) Department of Legal Medicine, Showa University School of Medicine
3) National Institute of Public Health, Ministry of Health, Labour and Welfare

Behavioral changes induced by several abused drugs. Behavioral changes have been observed, which are depended on neurotransmitter release using the generalization test for evaluation of drug discrimination using mouse behavior. In addition, the development of neurotransmitter selective agonists and antagonists have been used as tools to lead the hypothesis. Recently, manipulation for neuronal activation by optogenetical technique such as Designer Receptors Exclusively Activated by Designer Drug (DREADD) system allows for better understanding for the underlying mechanisms of neuronal circuit. Using such advanced technologies by manipulating specific neural cells in the brain, it has been discussed which type of the new insight, especially for neuronal system could be gained. The present study was designed to study such as discriminative stimulus
effects and sensitization of locomotor activity, through D₁ and D₂ receptors, in mice. Furthermore, in order to produce the methamphetamine-induced behavioral changes, methamphetamine-activated “On cells” must have been identified. Interactional activation between dopamine D₁- and D₂-receptor containing medium spiny neuron plays an important role in the discriminative stimulus effects as well as locomotor activity induced by methamphetamine. In the present study, it was found that activation of D₁-receptors was taking part in the core role of discriminative stimulus effects and locomotor activity itself induced by methamphetamine. In contrast, other than D₁-receptors play a significant role in the expression of sensitization to locomotor activity induced by methamphetamine in mice.

**Key Words**: optogenetics, DREADD (Designer Receptors Exclusively Activated by Designer Drug) system, methamphetamine, dopamine D₁-receptor, drug discriminative procedure, optogenetics

Drug dependence can be defined as a syndrome in which the use of a drug is given a much higher priority than other behaviors that once had higher value. The intensity of dependence is gauged by the behaviors that are associated with the use of the drug. No sharp line separates drug dependence from nondependent but recurrent drug use. In its extreme form, drug dependence is associated compulsively with drug-using behavior, and it exhibits the characteristics of a chronic relapsing disorder.

It is notable that various drugs of abuse are more effective in raising extracellular dopamine in the nucleus accumbens, a terminal region of the mesolimbic dopaminergic system, compared with the striatum, the site of termination of nigrostriatal dopamine neurons. On the other hand, stereotype reactions are elicited by high doses of psychostimulants, which fully increase extracellular dopamine in the striatum. Thus, these terminals of the mesolimbic and nigrostriatal dopaminergic system are believed to play a significant role in several behavioral effects. However, exact neuronal mechanism to elicit the behavioral changes induced by abused drug has not been elucidated yet.

Most important determinant of abuse potential is the nature of the subjective effects that the drug produces. Psychostimulants such as cocaine, amphetamine and methamphetamine, and opioids such as morphine and heroin, produce a syndrome that includes feelings referred to euphoria. In view of the apparent relationship between drug-induced subjective effects and abuse potential, it is clearly desirable to develop animal models for studying components of action of abused drugs that bear on their effects in human. A methodology having considerable potential in this regard is drug discrimination procedures. In other words, drug discrimination procedures, in particular, have begun to provide relevant information about neuropharmacological mechanisms underlying the subjective effects of abused drug and are potentially useful techniques for identifying candidate therapeutics for the management of drug abuse.

Previous studies have demonstrated that mesolimbic dopaminergic system plays a significant role in the discriminative as well as reinforcing effects of psychostimulants in rats. Self-administration procedure as well as conditioned place preference procedure has provided a animal model for studying factors that influence the rewarding effects, which are thought to be linked to the psychic dependence, of drugs. Here, it is widely accepted that reinforcing effects of opioids are also mediated by activation of mesolimbic dopaminergic system, like those induced by psychostimulants. It should be noticed that discriminative stimulus effects of psychostimulants are different from those induced by morphine in rats. Thus, discriminative stimulus effects of abused drug do not always related to its reinforcing effects.

MDMA (3,4-methylenedioxymeth-amphetamine) and cannabinoids are both abused and classified as hallucinogens. Since MDMA exerts similar pharmacological effects those induced by methamphetamine, MDMA and psychostimulants may produce similar discriminative stimulus effects in animals. Cocaine and methamphetamine cross-substitutes each other in cross-substitution tests of rats. The research used Orexin KO mice & orexin/ataxin 3 mice on monoaminergic neuronal changes using MDMA was reported. However, MDMA and methylphenidate do not cross-substitute for each other. It is suggested that indicating that even though MDMA, exerts stimulant-like effects like psychostimulants, these findings clearly
indicate that the discriminative stimulus effects of MDMA are distinctly different from those of other psychostimulants in rats. As for the possible role relation to reinforcing effects and aversive effects, discriminative stimulus effects of hallucinogenic drugs including MDMA was also already reported. On the other side, MDMA and tetrahydrocannabinol do not cross-substitute each other. Furthermore, other hallucinogens, such as κ-opioid receptor agonist, phencyclidine and sigma-1 receptor ligands do not substitute for the discriminative stimulus effects of MDMA and tetrahydrocannabinol. These results suggest that each abused drug has characteristical subjective effects. So far mechanism of drugs dependence had been considered in a uniform way, each abuse drugs must have respective pathway to produce its abuse-related subjective effects. The abuse of designer drugs, which aim to mimic the subjective effects of psychostimulants (e.g., MDMA or amphetamines), has been still problematic.

Recently, manipulation of neuronal activity by optogenetical technique and/or Designer Receptors Exclusively Activated by Designer Drug (DREADD) system allows for better understanding for the underlying mechanisms of neuronal circuit. Such advanced technologies by manipulating specific cell in the brain give us strict information regarding which types of neuronal cell is taking a part in the behavioral effects. At least there are two dopamine receptors, such as D₁ and D₂ receptors, in the neuronal systems. It has been demonstrated that these dopamine receptors are localizing on the different types of medium spiny neurons (e.g., D₁-type medium spiny neuron and D₂-type medium spiny neuron). Although the behavioral pharmacology using methamphetamine could provide evidences for the pharmacological mechanism of its behavioral effect of methamphetamine, specific activated cells and/or cellular interactions following methamphetamine treatment is not fully elucidated yet. To pin-down the cellular mechanism of methamphetamine-induced discriminative stimulus effects, “On cell” analysis would be performed. It is possible that methamphetamine-induced discriminative stimulus would be suppressed by an optical suppression of the nucleus accumbens in cFos-eNpHR mice. These future studies will confirm that activation of D₁-receptors in the nucleus accumbens plays an important role in the behavioural effects induced by methamphetamine. Such step by step study may provide us further promising information to understand the mechanism of each drug for abuse.

Not only intracellular but also intercellular mechanism have been gained by advanced manipulation technology with high specificity with identified cells.

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Conflict of interest disclosure

None of the authors have a conflict of interest to declare.

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What Can Be Gained by Reanalysis with Nested Logistic Regression Analysis of Published Benchtop Experiments?
—Latent Time Navigation of a MetaRNA Study—

Satoshi NUMAZAWA1, Toshiko SAWAGUCHI2,3)
1) Division of Toxicology, Showa University School of Pharmacy
2) Department of Legal Medicine, Showa University School of Medicine
3) National Institute of Public Health, Ministry Health Labor & Welfare, JAPAN

The present study reanalyzes nested data in our published paper and proposes another interpretation following multilevel, multinomial, multivariate nested logistic regression analysis and self-regression error regression analysis. Our previous paper showed that an antiepileptic phenobarbital downregulated miR-122, a major miRNA expressed in the liver, leading to activation of AMP-activated protein kinase (AMPK), nuclear translocation of the transcription factor CAR, and eventually transactivation of the CYP2B gene encoding a drug-metabolizing enzyme. Because the AMPK activation and the miR-122 downregulation appeared within 4 h in the liver of C3H mice as well as HepG2 cells, we hypothesized in the previous paper that these early phase events would be involved in the subsequent CYP induction. In the present study, we further subjected the data to multilevel, multinomial, multivariate nested logistic regression analysis (SAS 9.4 : EG7.2) reconsidered for co-founding and bias. This analysis, which also included the actual time of reported measurements (0, 1, 4, 12, and 24 h) as a nested variable, indicated that data obtained 24 h after treatment was potentially meaningful. Thus, although the AMPK activation and miR-122 downregulation appeared simultaneously in the early phase of phenobarbital treatment, the present analysis implicated a data change that emerged after 24 h as significant. This assumption does not contradict the conclusion of our previous report, but rather suggests that additional time points be measured in future studies. Recently, activated CAR was shown to inhibit the transactivation of hepatocyte nuclear factor 4α, which suppresses transcription of the miR-122 gene. Positive application of multilevel, multinomial, multivariate analysis to wet lab data is therefore recommended for more accurate and meaningful
conclusions about similar datasets.

Key words: miR-122 downregulation, nuclear translocation of CAR, multihierarchical, multilevel, multinomial, multivariate nested logistic regression, latent time-series points, research navigation

Introduction

Multilevel analysis is a statistical method for samples with a hierarchical structure, although the level selected in such analysis is not always conceptual. In this study, we applied a nested logistic regression model\(^1\) to analyze samples with a nested hierarchical structure using a multilevel, multivariate, and multinomial approach. Such methods are often used in the social sciences to incorporate miscellaneous data such as human actions that have different reproducible characteristics and relatively small sample sizes compared to wet lab-type data. Nested data are also widely used in the experimental sciences, for example in whole animals and cell experiments, but a conclusion is often drawn based on results led from each separate level.

In a previously published study\(^4\), we concluded that an antiepileptic agent, phenobarbital, downregulates the expression of miR-122, a major miRNA expressed in the liver, leading to activation of AMP-activated protein kinase (AMPK), nuclear translocation of the transcription factor CAR, and the eventual transactivation of the CYP2B gene encoding a drug-metabolizing enzyme (Figure 1). These effects appeared within 4h in the liver of C3H mice as well as HepG2 cells, thus we hypothesized in the paper\(^4\) that these early-phase events would be involved in the subsequent CYP induction.

The present study focuses on nested data from our previous paper\(^4\) and considers an alternative possibility using nested logistic analysis as an analytical method. The particular data were selected for the following two reasons:

1. The molecular pharmacological results included plural nested biological levels, specifically different RNA levels such as mature and primary miRNA, and in vivo and in vitro levels of miRNA conceptualized as a part of metaRNA.
2. The time-dependent measurements were repeated for each nest level (Figure 2).

Generally, data analysis in molecular pharmacology considers each level separately, while herein we used a nested logistic regression model that includes analysis within levels and interactions between levels. We propose that using this additional statistical approach could extract a previously unidentified latent numerical association that might be scientifically significant.

Materials and methods

In the present study, we subjected data from our previous paper\(^4\) to multinomial, multilevel, multihierarchical, and multivariate nested logistic regression analysis (SAS 9.4: EG7.2) following reconsideration of bias and confounding variables. We used the categorized time measurement order as a response variable in the generalized linear model (GLM), assuming that those data would follow a multinomial distribution, used a cumulative logit model (logarithmic odds) as a link function, used the sample order in each group as an explanatory variable with the figure order (used as the nested variable),
and used the mean variable and the SE variable as qualitative variables. Distributions of the likelihood ratio were approximated by chi-square distribution and the significance level was set at 5%. The method for optimization used was the Newton-Raphson method.

Before the application of nested logistic regression analysis, we performed a standard logistic regression analysis with self-regression errors (SAS9.4EG7.2 AUTOREG procedure).

### Results

1) Multinomial, multilevel, multi-hierarchical, multivariate nested logistic regression analysis

The analysis included the actual time of measurement (0, 1, 4, 12, and 24 h) as a nested variable, and indicated that data obtained 24 h after treatment was potentially significant (Table 1, mean variable). The odds ratio was 1.00 and [95% CI] [0.99–1.00].

2) Regression analysis with self-regression errors

There was no positive time-dependent correlation based on the Durbin-Watson statistic value (2.271) shown by regression analysis with self-regression error between time-dependent inhibition of primary miR122 and administration of phenobarbital.

3) Conventional logistic regression analysis

We also calculated the positive contribution of microRNA quantitative variables (odds ratio = 4.956, 95% CI = [1.744–17.12]) to the time-dependent transition using the conventional logistic regression analysis (cumulative logit model, Newton-Raphson optimization method, SAS9.4EG7.2 logistic procedure).

| Parameter | Estimate value | t value | 95% CI |
|-----------|----------------|---------|--------|
| Mean (0 h) | 0.044 | 1.92 | −0.001 | 0.091 |
| Mean (1 h) | 0.043 | 1.92 | −0.001 | 0.087 |
| Mean (4 h) | 0.044 | 1.83 | −0.003 | 0.090 |
| Mean (12 h) | 0.075 | 1.00 | −0.072 | 0.22 |
| Mean (24 h) | 0.081 | 2.54 | 0.019 | 0.14 |
| SE (0 h) | −0.21 | −1.11 | −0.59 | 0.16 |
| SE (1 h) | −0.080 | −0.52 | −0.38 | 0.22 |
| SE (4 h) | −0.24 | −1.64 | −0.53 | 0.047 |
| SE (12 h) | −1.22 | −0.89 | −3.91 | 1.46 |
| SE (24 h) | −0.65 | −2.36 | −1.19 | −0.11 |

### Discussion

The AMPK activation and miR-122 downregulation appeared simultaneously in the early phase of the phenobarbital treatment, as detailed in our previous publication; however, the present analysis suggests that potentially significant changes are present at the 24-hour time point. This assumption does not contradict the conclusion of our previous report. It suggests that further time points should be measured. Indeed, the present multilevel analysis is consistent with a recent report that activated CAR inhibits transactivation of hepatocyte nuclear factor 4α, suppressing transcription of the miR-122 gene.

By using logistic regression analysis in this study, we calculated the positive contribution of miRNA quantitative variables to the time-dependent transitions and obtained results that were consistent with our previously published study. These types of virtual, nested logistic analyses on wet lab experimental data could therefore provide an additional, useful tool to establish the future directions of a given study. In general, nested analysis serves to restrain data, and initially we assumed that the benefit of additionally applying an optimized model would be much smaller. In contrast, we were fortunate to obtain an additional possible interpretation. We thus need to reconsider the viewpoint of latent structure, which reflects the background information of the data.

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### Conflict of interest disclosure

We have no conflicts of interest to disclose.
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Patient-based quality of life (QoL) measurement using the Schedule for the Evaluation of Individual QoL (SEIQoL) and response shift

- Naoko IDEGUCHI1), Yuki NAKAYAMA2), Takashi NAKAJIMA3)

1) Faculty of Pharmaceutical Sciences, Teikyo Heisei University
2) Tokyo Metropolitan Institute of Medical Science
3) Niigata National Hospital, National Hospital Organization

There has been increased recognition in recent years of the need for patient-reported outcomes (PRO) as a subjective evaluation of patients, not just evaluations of medical objectives, when evaluating the outcomes of therapeutic agents and therapies. Meanwhile, the issue remains as to what to do when the two measures are at odds. Moreover, even if quality of life (QoL) is evaluated based on PRO, evaluations using the EuroQol-5 Dimension (EQ-5D), a standardized instrument based on the concept of health, and the Schedule for the Evaluation of Individual QoL (SEIQoL), which is not affected by the concept of health, may yield completely different results. Therefore, the meaning of true outcome evaluation needs to be understood. In the present study, a seminar was conducted to help healthcare professionals understand the characteristics of the EQ-5D and SEIQoL and to use them properly in a clinical setting based on the PRO concept. During the seminar, participants used role play to evaluate the QoL of patients with amyotrophic lateral sclerosis (ALS). When the EQ-5D visual analogue scale (VAS) evaluation and derived utility index were compared before and after the seminar, mean QoL increased substantially from 38.61 to 56.17 in the same patient. When measured using EQSD, the mean (+ SD) of INDEX was a considerably low value (range 0-1) of 0.09 ± 0.18. However, when we performed measurement assuming the same patient using SEIQoL, the mean (+ SD) of INDEX was 52.99 ± 18.25, which was not low (range 0-100). PRO is an important endpoint of medical outcomes, but the present study demonstrated that there are substantial differences depending on the evaluation method used. Further, VAS results were affected by the evaluator learning about PRO and QoL, as evidenced by different values for this parameter before and after the seminar. In addition, we found that the seminar changed participants’ perceptions of QoL.

Key words : patient-reported outcome (PRO), SEIQoL-DW, ALS, SEIQoL

Introduction

The most important goals for medical treatment are considered to be: (1) the maintenance and prolongation of life, which is especially important when there is a prognosis of death at an early age; and (2) the maintenance of and increase in quality of life (QoL), especially avoiding suffering. QoL is considered to be the “true treatment outcome”, but can be evaluated by either physicians or patients; the results of the latter constitute patient-reported outcomes (PRO). There is a positive correlation between physicians’ evaluations and PRO, but the closeness of this correlation varies. For example, one study compared physicians’ evaluations
of the effects of anticancer agents administered to 467 cancer patients, based on Common Terminology Criteria for Adverse Events, with patient evaluations, with the former group rating adverse effects as more minor than the latter group. At the same time, there is the potential for low evaluations to be given for the efficacy of medical techniques that reduce adverse effects\(^9\). There are a number of methods to quantify QoL, but if methods involving unification from an objective perspective are applied to fields in which cure is not the aim, such as palliative care and the treatment of intractable disease, there is a risk of an evaluation lower than “death” being made, resulting in loss of the care perspective, and omission from the perspective of medical care allocation\(^9\).

The Schedule for the Evaluation of Individual QoL (SEIQoL) was developed in Ireland as a method to subjectively evaluate patients’ QoL\(^4\). SEIQoL is considered to be a representative PRO\(^5\).

Herein we report on a seminar to increase the understanding and practice of SEIQoL, with the aim of making its use more widespread. The seminar educated and trained medical personnel with regard to subjective QoL, and changes in participant perceptions of QoL after the seminar were evaluated.

**Methods**

On 10 February 2013, a seminar titled “A practical seminar for studying and using SEIQoL-DW: A patient subjective QoL evaluation method”, was held at the Tokyo International Forum. The data obtained are detailed below.

Quantification of the response shift in relation to subjective QoL

As part of the seminar, an amyotrophic lateral sclerosis (ALS) patient was introduced. The initial step was to achieve a full understanding of the patient’s perception of QoL using the EuroQol-5 Dimension (EQ-5D), which is widely used to measure QoL, to determine the utility value, based on summed scores for items on the EQ-5D, and scale datum on this basis. A lecture was then presented about the significance of PRO and comments were presented from representatives of patient advocacy organizations, after which the EQ-5D was again used to gain an understanding of the patient’s QoL, with the QoL determined before and after the lecture compared. The EQ-5D is a comprehensive evaluation tool used to quantify health-related QoL; it was developed and standardized by the EuroQoL group, established in 1987, to calculate health status scores. In the EQ-5D, complete health is given a score of 1, whereas death is given a score of 0.

The EQ-5D QoL measurement system includes questions on the following: (i) degree of movement; (ii) management of oneself and one’s immediate environment; (iii) daily activities, such as work, study, family life, and leisure activities; (iv) pain and discomfort; and (v) anxiety and unhappiness. Each of these items is scored as 0 (bedridden), 2 (problems to some degree), and 3 (if there are no problems), after which the data are combined, and an index, the utility value, is obtained using a conversion table. In addition, “health status today” is plotted, on a subjective basis, on a scale ranging from 0 (the worst state imaginable) to 100 (the best state imaginable).

In the seminar, information was presented about the ALS patient’s background factors, including an explanation of ALS and the patient’s disease progression, current living conditions, and the use of social resources (Table 1). The EQ-5D utility values and “health status today” scores of participants who had taken on the role of the ALS patient were then recorded, one at a time. The lecturer then explained about the risks of objective unification of QoL, points to bear in mind with regard to subjective QoL quantification, and the response shift, which is the change in perception, under similar conditions. The participants then repeated the quantification, using only the “health status today” scale, and the results were compared with those obtained before the lecturer’s explanation.

Quantification using SEIQoL.

The SEIQoL is a method to subjectively quantify patients’ QoL. In this study, seminar participants were paired up, with one taking the role of the “ALS patient” and the other taking the role of the interviewer. QoL was quantified using the SEIQoL, followed by calculation of the index\(^6\).

A provisional Japanese translation of the SEIQoL manual used in March 2007 in a seminar presented by O’Boyle et al. was used in the present study.

The SEIQoL involves a semistructured interview, with
the interviewer initially drawing information from the responder, including cues, as to the five most important lifestyle areas for the patient’s individual decision regarding QoL. The interviewer records the patient’s satisfaction in each of these areas on a scale from 0 to 100, and then weights each of these areas using five movable, colored disks, so that the relative importance of each area (cue) is determined. Values are recorded for each of three processes, shown as 0 to 1, and the index is finally calculated7.

Collation of participants’ questionnaires

Upon completion of the seminar, questionnaires were handed out to participants to obtain their opinions and impressions of patients’ QoL and the SEIQoL. The questionnaires were collected, and the data summarized and analyzed.

Ethical considerations

All data included in the analysis were obtained from participants who had provided informed consent after receiving both written and oral explanations that the questionnaires were not to be signed, about requests by study collaborators, that individuals could not be identified, and that the study results were to be made public.

Results

There were 63 participants in the seminar (1 physician, 18 nurses, 7 pharmacists, 7 occupational therapists, 8 care workers, 2 members of patient advocacy organizations, 8 students, 10 others, and 2 of unknown position or occupation). All 63 participants provided informed consent for the data obtained using the questionnaires and during the seminar to be used.

With regard to familiarity with SEIQoL, 73% of participants responded that “This is the first time I have heard of it” or “I knew a little about it, but this is the first time I have been to a seminar”. 6 participants had already studied SEIQoL, and 10 had actually used it (Fig. 1).

The motives for participating in the seminar are listed in Table 2.

Table 1. Motives for participation

| Motives for participation                                                                 |
|------------------------------------------------------------------------------------------|
| - I wanted to hear the opinion of an actual ALS patient.                                  |
| - I thought the seminar would be necessary for my future work.                           |
| - I am thinking about making use of SEIQoL-DW as a quantification index in my research. |
| - I thought SEIQoL would be useful for evaluation of the QOL of my current patients.     |
| - I am thinking about making use of SEIQoL in clinical practice.                         |
| - I intend to carry out research using SEIQoL.                                           |
| - I am interested in SEIQoL.                                                             |
| - In my research, I am thinking about making a connection with QOL, and I am therefore interested in SEIQoL as a method for objective QOL quantification. |
| - I want to carry out SEIQoL-DW as part of my research.                                  |
| - I am thinking about using SEIQoL for my graduation thesis, so no statement is needed. |
| - I was encouraged by an acquaintance to participate.                                    |
| - I am interested in QOL evaluation methods.                                             |
| - In providing occupational therapy on the basis of patients’ intrinsic motivations, I was very much aware of the difficulty involved in objective presentation of efficacy. |
| - I previously took a SEIQoL study course, and carried out an actual interview, but deciding upon the cues was very difficult, so I have little confidence in my ability, and I have not used the methods since. I would now like to learn about what would be appropriate for being able to decide upon the cues. |
| - I want to improve my support of patients with intractable diseases.                    |
| - I am participating on behalf of my laboratory at university.                           |
| - I hope to make use of SEIQoL in my research on nursing.                                |
| - If I learn how to use the SEIQoL-DW evaluation method, it should be useful for treating patients at this hospital. |
| - I wanted to learn about the details and methods of use, as a QOL evaluation method in the palliative care field. |
| - I hoped to achieve a deeper understanding of SEIQoL-DW.                                 |
| - I wanted to study.                                                                     |

Quantification of the response shift with regard to subjective QoL

The participants read the explanatory documents distributed to them, after which each participant took on the role of the appropriate patient, and the EQ-5D quantification was conducted. The mean ± SD health status score was found to be 0.01 ± 0.18.

Next, we compared the “health status today” scale data obtained before and after the lecture. Before the lecture, the mean ± SD score was 38.61 ± 24.63, whereas after the lecture it was 56.17 ± 23.04. These
Quantification by SEIQoL

Participants were allocated to pairs, with one taking the part of an ALS patient and the other taking the part of the interviewer. The SEIQoL was administered as a semistructured interview. The mean index value for the interviewer in the pair was 52.99, which is very close to the score of 56.05 obtained previously with the "ALS patients" in these pairs (Fig. 5).

Post-participation questionnaire

In the post-participation questionnaire, 80% of participants reported wanting to use SEIQoL in the future (Fig. 6). However, four participants noted that they would not be able to use the SEIQoL because of their working environment (Fig. 6).

Change in awareness before and after the seminar

To evaluate changes in awareness before and after the seminar, participants were asked the same questions. Figures 7-9 show the proportion of participants giving the following responses:

- good medical treatment is that which has a high efficacy to cost ratio
- QoL decreases as the disease state progresses
- QoL is objectively quantifiable.

There were particularly large changes from before to after the seminar with regard to awareness about figures show that the score on the "health status today" scale increased significantly after the lecture (P < 0.001, t-test; the one-sample Kolmogorov-Smirnov test indicated normal data distribution; Figs 2-4).

Table 2. Impressions about participation in the seminar

| Perception                                                                 | Number of Participants |
|---------------------------------------------------------------------------|------------------------|
| I would definitely like physicians also to take part in training courses on this evaluation method. | 5                      |
| I can now think about the general principles of QoL, and I understand the use of SEIQoL-DW (two participants gave this response). | 3                      |
| I now have a thorough understanding of SEIQoL. This was a significant and important training course, involving listening to the actual opinion of a patient with an intractable disease. | 4                      |
| My way of thinking has changed, and I think that my perspective has also changed. I have realized that measurement systems differ between individuals, and it is essential to think about what is actually good according to the person directly affected by a situation (four participants gave this response). | 6                      |
| The seminar confirmed the excellence of SEIQoL (two participants gave this response). | 1                      |
| The seminar was very good, enabling me to understand both the theoretical background to, and practical use of, SEIQoL (three participants gave this response). | 3                      |
| I thought that I was very interested in this method, so I would like to spend time learning about it in detail (four participants gave this response). | 4                      |
| I appreciated the ways that life is unpleasant for patients with intractable diseases. I hope to think about this more constructively. | 5                      |
| QoL is subjective, and in the past I have been unable to evaluate it even while providing care. There are disagreements even between health-care professionals, and no consistent approach has been presented. I think that, if the tools presented in this seminar are used, these problems can be resolved. | 6                      |
| It was good to study about methods for understanding patients’ subjective issues. I hope to make use of these professionally (four participants gave this response). | 4                      |
| I participated in the seminar thinking that I would like to use SEIQoL in my nursing research, but have now changed my mind, thinking that it would be best for SEIQoL to be the entire theme of my research. In general, when caring for patients the highest priority is given to life. However, I realized that, from patients’ points of view, life may not actually be the most important matter, and other issues may warrant higher priority. I think that approaches to medical treatment may change if this understanding becomes widespread. | 5                      |
| I found the seminar very easy to understand, and achieved a thorough understanding of SEIQoL. I would like more medical personnel to attend this type of lecture (three participants gave this response). | 3                      |
| The seminar was held with the style of the actual method, and an impression of the method was therefore readily obtained. | 4                      |
| My doubts were resolved to some extent by carrying out the QOL evaluation (five participants gave this response). | 5                      |
| I am involved with intractable neurological disease patients on the hospital ward. However, with respect to patients' QOL, I felt that I now want to take completely the opposite approach. I feel that there are major differences in QOL between hospitalized patients and patients cared for at home, and more thought must be given to hospitalized patients. | 6                      |
| I now understand the use of SEIQoL, and the importance of carrying out the "then-test". | 2                      |
| I was impressed that SEIQoL measures QOL on the basis of patients’ subjective perceptions. | 4                      |
| I previously had little motivation to evaluate QOL, but today’s seminar had a major impact on me, and I now want to use this method. | 5                      |
| It was valuable to have practical experience with SEIQoL, and to listen to the opinion of an actual patient. | 4                      |
| The slides included rather too much information, and time management was difficult. The seminar was at about my limit for comprehension and progress. | 3                      |
| It was good that the seminar focused on the practical aspects. I don’t think I would have understood half of this just by talking about the method. | 5                      |
the efficacy to cost ratio, and QoL decreasing with progression of the disease state.

Finally, 93% of participants reported a final level of satisfaction with the seminar as expected or higher than expected. Thus, it can be concluded that the seminar was important and significant for almost all participants. Participants’ own statements about changes in their impressions and perceptions are given in Tables 3a and shown in Fig. 10.

Discussion

Using PROs has recently become increasingly important in the evaluation of medical care. In this context, PROs have been verified and made more detailed by means of more quantitative assessments and statistical analyses. Among PROs, QoL measurement in particular offers advantages, such as enabling the patient him- or herself to decide upon the value of medical techniques, and the measurement of QoL is

![Fig. 2. Distribution of EQ-5D utility value](image)

![Fig. 3. EQ-5D scale before lecture](image)

![Fig. 4. EQ-5D scale after lecture](image)

![Fig. 5. Distribution of SEIQoL-DW index among participants](image)

![Fig. 6. Intend to use SEIQoL in future?](image)
important as an index of the efficacy of a wider range of medical techniques. In this study, people from a wide variety of backgrounds, including members of patient advocacy organizations, care workers, and medical personnel, met together and learned about PRO by practical demonstration. On the basis of changes in questionnaire results and scale data before and after the seminar, it is considered that the response shift in both cases involved increased awareness on the part of participants. The findings suggest that this PRO

![Fig. 7. Good medical treatment is that with high efficacy / cost ratio](image)

![Fig. 8. QOL decreases with disease state progression](image)

![Fig. 9. QOL is objectively quantifiable](image)

![Table 3. Changes in my awareness due to this seminar](image)

- The idea of achieving an objective and accurate judgment on the basis of the subjective perception of the actual person involved was completely new to me.
- I reached the understanding that, when a patient’s QOL is traced back into the past, it can be calibrated on that basis.
- The way I understand the term “QOL” has changed.
- I would like more time for communication with patients.
- I found it impressive that an ALS patient was living alone in his own home. He also had considerable satisfaction with his life. In future, I will aim to listen to the thoughts and feelings of patients.
- I appreciated that the efficacy of treatment is not solely objective, but varies with changes in the patient’s subjective experience and in the scale used. I wondered whether I myself could contribute to better changes in the scale (two participants gave this response).
- I had thought that therapeutic intervention results in decreased QOL, but I appreciated from listening to the patients’ own conversation that that is not in fact the case.
- I realized that one must try to be aware that one’s own opinion is inevitably subjective.
- It is widely held that, if a disease is intractable, its progression automatically results in decreased QOL, and a positive outcome of the seminar was that I realized that this is not necessarily the case.
- I was interested in the response shift. As a pharmacist, I hope to carry out my tasks without thinking solely about drug efficacy, but asking about the extent to which changes in QOL are connected to drug efficacy and intervention by the pharmacist.
- I thought about various issues, such as the question of what constitutes good medical treatment, and how to respond to patients.
- I realized that it is essential to think from the point of view of the patient rather than that of the health-care professionals (four participants gave this response).
- I realized that progress should be made, not for the sake of the hospital ward, but for the sake of establishing a positive living environment for the patient, in accordance with the patient’s psychological state.
- The usual intention was to converse with the patient, and to connect with the patient, thinking about what he/she considers to be important. However, I felt that my own subjective perception also played a major role.
- I thought that this method could be used with any type of disease.
- It is important to not be dragged along by the value judgment of the representative evaluator.
- I felt that it is essential to think about the fact that the feelings and level of satisfaction of a patient cannot readily be quantified by a stranger.
- I came to understand that subjective perceptions can be presented numerically.
- The method has the potential for use as an educational tool giving a sense of diversity.
- I had the feeling that the actual situation and the structural concept are very important, and it is always necessary to think about this meaning.
may help achieve a deeper understanding of areas such as treatment of intractable rare diseases, in which judgments cannot be made solely on the basis of a cost to efficacy ratio.

With regard to current and future evaluation of medical treatment, research on QoL measurement systems and other PROs is being undertaken to clarify relationships with evaluations conducted by physicians. It is considered that PROs and physicians’ evaluation are not entirely disparate, there being a close relationship between them. In addition, it is considered that PROs can be used for sensitive detection of changes to patients.

No one other than the patient him- or herself can know anything about his or her subjective experience or valuation of treatment. However, a physician’s objective evaluation is also important, and the most helpful information is therefore obtained by combining subjective and objective evaluations.

SEIQoL cannot yet be considered to be sufficiently widely used; therefore, in future, it will be necessary to take various opportunities to introduce SEIQoL to more medical and care personnel, as well as to the patients and their family members. Progress with effective research is also needed.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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What Have Been Brought Forth by the Nested Analysis and Propensity Score-matching?

Toshiko Sawaguchi1,2,3

1) Department of Legal Medicine, Showa University School of Medicine
2) National Institute of Public Health, Ministry of Health, Labour & Welfare
3) Department of Public Health, Juntendo University School of Medicine

In this report, nested approach and propensity score approach were selected as two methodologies in view of their impacts on confounding factors and biases. Selection of these two methodologies was based on a viewpoint that they both contain points of issue that are important for our providing an explanation to the general public regarding the recent trends in data science methodologies. In the pursuit of causal reference in the present-day society where bulk data are provided, any attempt towards large-capacity multivariate data handling with disregard for data selection bias and deflection bias may result in a reversed outcome. Both the above methodologies are capable of suggesting a way to cope with confounders to attain a positive effect. It is hoped that these two approaches concerning those confounders will give impetus to how to cope with and reconsideration of statistical causal relationships.

Key Words: nested approach, propensity score, multivisual prospects, survey observation, causal inference

Introduction

The nested approach and the propensity score approach have both been selected as important methodologies from the viewpoint of how to cope with confounders. It is of vital importance to maintain a viewpoint on how to cope when difficulties are encountered in conducting a survey study or an observational study in an ideal situation. Survey studies and observational studies often entail defects which impede the ability to deal with such measures as random allocation, random sampling, missing data processing, and selection bias under an ideal situation, so that a variety of background factors involving confounders need to be subjected to surveys. Both parametric and nonparametric methodologies have been and are adopted in making a statistical causal reference.

Many observational studies entail biases, missing data and statistical interventions, and such bias-affected data are sporadically seen even in scientific papers. This report deals with the two well-known methodologies, i.e., the nested approach1-10 and an approach using the propensity score11-17 included in a semiparametric methodology, to reconsider them from the viewpoint of their positive potentiality and negative potentiality.

Methods and subjects

The following items were settled through review of a retrieved plurality of published papers and inter-researcher discussions/debates pertaining to positive and negative potentialities of the approach that uses propensity scores11-17 contained in the two well-known methodologies: the nested approach1-10 and semiparametric methodologies.

1) Definition
2) Merits elucidated when the potentiality of this approach was considered as positive
3) Demerits elucidated when the potentiality of this approach was considered as negative

The thirty reference papers which were the subjects of the study were selected via Google, Google Scholar, and PubMed employed as the survey engines, using “propensity score” and “nested analysis” as the key words. Survey content analyses were carried out from the above-described three points of issue at the discretion of one of the authors of the current study.

Results

(1) Nested approach
*Definition

The term ‘nest’ refers to a structure or situation that embraces something of the same shape and of the same sort but of smaller sizes10. In structured programming, the term ‘nesting’ denotes a method for constructing programs whereby a different routine or data block is repeatedly fitted into a routine or data block10. In analytical epidemiology, a nested case control study is comprised of patients in an experimental group and a control group selected from the same cohort.

In a nested logistic regression analysis, hierarchical data are translated into a nest (nested structure) and then an upper categorical variable in each datum is entered into a lower categorical variable and subjected
to analysis together with a quantitative variable.

*Merits elucidated when the potentiality estimated with this technique is interpreted as positive.

In analytical epidemiology, a nested case control study is conducted on patients in an experimental group and a control group, both being selected from the same cohort, though the selection is done after initiation of the case. Using this approach, it is feasible to eliminate many confounding factors such as equilibrium between survival time for the control group and that for the case. Many confounders are eliminated in nested case control studies.

In nested approaches, it is practicable to reduce the number of variances by nesting qualitative variates in a multivariate situation, so that the approach may be applicable even to variates for a small number of samples.

By using nested logits, it is possible to evaluate the combination of a model parameter with a relative scale parameter.

A demerit elucidated when the potentiality of this approach is taken as negative

Nested treatment is involved in data reprocessing during the process of integrating a plurality of variables, and difficulty in attaining an optimization model for solvability (insolvability) may arise. Once a part of an optimization model is attained, nevertheless, message via the model may support the interpretation of results of hierarchical analysis. This would indicate the direction of research feasible in the future. However, the idea supporting the nested approach does not warrant induction of any significant improvement of the model.

(2) Propensity score

*Definition

Propensity scoring is a semiparametric methodology. In this methodology, it is necessary that the intercovariate regression function of a regression analysis and latent outcome variables are settled. Biases are likely to arise in consequence of a wrong model designation in the presence of many covariates. Propensity scoring is a system that follows a semiparametric law under the circumstances where it is neither practicable nor necessary to designate a regression model of covariates and outcome variables. Rosenbaum and Rubin developed a new concept called the propensity score, thereby exerting influence upon relevance studies in which random allocation is impracticable. If a single variate is capable of ruling a plurality of covariates, then this allows construction of a stratified structure over the single variate. It is possible, therefore, to interpret it as implying a concept revealed by the point at issue based on matching under the circumstance where such stratification does not occur.

In observational studies, as is well known, stratified analysis with matching exists as a device to generate a pair of comparable groups (groups A and B). The method is such that, for the comparison of variable y, 2 groups of subjects with equal distributions of z between them are arranged by regarding comparable information as subject background information z, whereby these 2 groups are compared using, for instance, difference in the outcome variable (mean absolute risk difference) as an index. A readily understandable method would be exemplified by gender-age matching (allowing a probability of 50% allocation to group A as well as to group B in terms of gender and age). Group A is taken here as a standard.

For propensity score (PS) matching, a method frequently employed in recent years is such that the probability of allocation to group A, \( p(z) \), is estimated from subject background information z, then 1 or a certain number \( n \) of subjects of group B, whose \( p(z) \) is apparently equal to that in each subject of group A, is selected to form group B and thereby to make comparison between groups A and B (the 2 groups are equal in distribution of z owing to the way B’ is generated). Consequently, the intergroup comparison is feasible because background information on each subject is equal between groups A and B in the light of background information z.

A elucidated forth when the potentiality of this approach is taken as positive

When using propensity score-matching, reaching a thorough understanding regarding the subject or item that has been revealed by the comparability study is of prime importance.

Concerning a disease, T, for example, group A is comprised of patients (experimental group) and group B consists of non-patients (control group), and an exposure factor is set as variable y. Variable z (vector value) is then considered as a factor (confounder) distorting the comparison. 1) In usual case control
studies, as to relevance of factor y in group A to group B, the odds ratio (OR) is evaluated after adjusting impact of variable z by such means as a logistic regression analysis. The comparison therein pertains to all subjects in groups A and B recruited as samples.  
2) As regards gender-age matching, the intergroup comparison is made with subjects extracted from group B who match in gender and age with subjects in group A. In these 2 groups, the OR pertaining to matched pairs is adjusted according to impact of variable z by such means as a logistic regression analysis, and evaluated.  
3) As for 2 groups formed via PS matching, subjects corresponding to a region allowing $0 < p(z) < 1$ among those in group B are allocated so that an equal distribution of p(z) between the 2 groups is attained for comparison.

Thus, the propensity scoring proved to be effective. It may be said that the procedure has proven so because it involves adjustment of confounders and verifies comparability in observational studies.

*A demerit elucidated when the potentiality of this approach is taken as negative

It should be noted that propensity scoring provides a limited comparison under stringent restriction to raise comparability. What can be seen as the outcome of the comparison varies with how the comparison has been performed; caution should therefore be exercised when interpreting the outcome.

In a Controlled Propensity matched retrospective cohort study published in the British Medical Journal (BMJ) in 2013, it was specified that only samples bearing a Propensity Score $> 0$ enabled comparison with a view to raising comparability of 2 groups, eventually leading to a decrease in representativeness of the samples in the general area.

Discussion

In a logistic regression analysis, data are analyzed to determine how a covariate pertaining to an explanatory variable participates in a regression equation using a nominal variable as an explanatory variable. In non-randomized retrospective backward studies, there is the possibility that being regarded as a confounding factor may affect the outcome. The propensity score analysis has been proposed as a method for adjusting confounders, where it is used as predictive probability being employed as propensity scoring in a logistic regression analysis. In the propensity score analysis, matching and/or stratification with the single variable are carried out by way of reducing a plurality of confounders into a one-dimensional term. As the consolidation into a single variable makes it unnecessary to set up hypotheses for various models suited to individual variables, hence enabling efficient elimination of the influence of confounders, it is possible to raise comparability for selective assessment of the impact of the causal relationship subject to attention. However, involvement of another influence by which the impact of a specific confounder is excessively underestimated may possibly occur. It is a common understanding in society as a whole that if one thing is gained, another should be abandoned; no one can always gain everything, all the time. It is virtually impracticable at present to gain a generalized outcome for a certain purpose in the presence of enforced incomplete matching due to propensity score matching. Trials with supercomputing would be needed for the generalization.

Integration by means of a multilevel nested logistic regression analysis may be regarded as a sort of meta-analysis in the practice of the nested approach in logistic regression analyses.

In the nested approach, upper hierarchical scale data are often nested into lower hierarchical data and, thereby, the upper and lower hierarchical data are processed simultaneously. Since inter-hierarchical nest processing allows the presumption that the nested hierarchies concur simultaneously (synchronously) and since it has been generally thought that a causal relationship holds between a temporal predecessor and a follower, there is the possibility that the temporal relationship of creation of cause-and-effect in the data structure may be disregarded in the nested approach. Whilst what we see through our subjectivity is a non-nest-processed relationship, we may succeed in some instances in seeing a previously undetected or overlooked inter-data relationship via the objective method termed logistic regression analysis. This seems likely to represent a methodology for finding latency by means of data integration.
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Conflict of interest disclosure

The authors state that they have no conflict of interest to declare.

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What Can Be Gained by Aurally Approach?
—Basis of Making the Aurally Information from Each Numerical Value of National Voice, the Causes of Deaths and Willful Negligence—
—Social Aurally Approach—
Toshiko SAWAGUCHI1,2,3,4,5

1) Department of Legal Meidicine, Showa University School of Medicine
2) Department of Public Health, Juntendo University School of Medicine
3) Post doctoral Course of Tsukuba University, Faculty of Business Science Research, Section of Enterprize Law, Course of Intellectual Property
4) Law School of Komazawa University
5) Ministry of Health, Labor and welfare, National Institute of Public Health

The world can be perceived in a significant number of ways. This paper discusses a ‘urally approach’, a technological framework for representing and communicating various types of data aurally, to provide a different perspective.

Public health policy has long been criticized: people sometimes feel that their government is unapproachable and unresponsive, while authorities have trouble communicating the benefits of their policies to citizens. Previously, health promotion campaigns in Japan have assessed such effects in terms of various statistics and performance indicators, and visually depicted the changes to communicate improvements in such values, to verify and demonstrate improvements following a policy’s introduction. On this quantitative basis alone, Sukoyaka 21 was successful, resulting in improvements to about 80% of the 74 metrics tracked1. However, the benefits achieved by the program were not readily apparent to the policy administrators themselves.

In fact, the outcomes in the indicator framework for Sukoyaka 21 were poor predictors of perceived effectiveness, with low odd ratios for each of the variables in the indicator framework. It takes effort to read text or interpret a graph; sound is instant and universally accessible. The proposed approach should assist in spreading health awareness among citizens: listeners can experience an ‘inner awakening’, going from ‘knowing by seeing’ to ‘knowing by hearing’, while still maintaining scientific rigour. This paper reports the technical basis of our model for communicating key performance indicators in musical form, as well as an applied example.

Key Words: Sound Approach, Multilevel nested logistic regression analysis, national voice, causes of death, willful negligence

Introduction

The world can be perceived in a significant number of ways. This paper discusses a ‘urally approach’, a technological framework for representing and communicating various types of data aurally, to provide a different perspective.

Individual citizens often fail to appreciate the magnitude of the effort put into developing national policies, prefectural initiatives, or municipal plans; likewise, the authorities are having trouble conveying to the citizens information about government services. These critiques are long-standing.

National campaigns for health promotion such as Sukoyaka Oyako 21 (‘Healthy parents and children 21’) and Kenkoh Nihon 21 (‘Healthy Japan 21’) are data-driven, incorporating a variety of statistics and performance indicators for health care policy. Typically, graphs or mappings are used to attempt to visualise empirical changes in such values, to verify and demonstrate improvements following a policy’s introduction. On this quantitative basis alone, Sukoyaka 21 was successful, resulting in improvements to about 80% of the 74 metrics tracked1. However, the benefits achieved by the program were not readily apparent to the policy administrators themselves.

In fact, the outcomes in the indicator framework for Sukoyaka 21 were poor predictors of perceived effectiveness, each showing low odd ratios2. However, pure numbers—which is to say, indicators—are not so appealing to the average reader, and it seems illogical.
to blame the lack of perceived effectiveness on the
tedium of numbers. On the other hand, numbers are
inherent to data-driven public health care policy. Maybe
the data’s visual media were to blame for viewers not
appreciating the numerical improvements in the Sukoyaka
21 outcomes. In this case, we propose the conversion
of visual, ‘indicator’ data into sound, or auralisation, to
communicate health-care and other data in an intuitive
way. The guiding principle behind the ‘sound approach’
was to present information in a different sensory
modality than usual. Listeners can experience an ‘inner
awakening’, going from ‘knowing by seeing’ to ‘knowing
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way. The guiding principle behind the ‘sound approach’
was to present information in a different sensory
modality than usual. Listeners can experience an ‘inner
awakening’, going from ‘knowing by seeing’ to ‘knowing
by hearing’ when the medium of the information
changes, while still maintaining scientific rigour.

The author has previously discussed the development
of the underlying methodology and applied topics in a
designated oral presentation at the 14th Annual Meeting of
the Japan Society of Fetal Therapy3, and in three general
presentations5 and symposia6, each at the 76th Annual
Meeting of the Japanese Society of Public Health2 and
88th Annual Meeting of the Japanese Society for Hygiene.

These studies were the launching point to develop
a sound approach to data auralisation, as a technology
to communicate various information. This report adds
six kinds of materials suitable for adaptation using the
sound approach, and records their trial attempts.

Materials and methods

Proposed Basic Approach

Five topics were considered as sources of data
suitable for auralisation.

1) Listen to: the voices of nations
2) Listen to: causes of death
3) Listen to: children’s expression of thoughts after
an unexpected death
4) Listen to: the outcomes of health promotion
campaigns
5) Listen to: wilful negligence

(1) Materials

The sound approach converts numerical data into acoustic
patterns. This data could be an indicator, or multiple
indicators, or analysis findings, which vary with respect
to statistical values, parameters, and time; they can also
include categorical values designating qualitative information.
Primary sources that cannot be captured by numbers alone,
such as text and mass spectra, are also included.

Specific primary sources are listed as follows, along
with their associated goals:
1) The International Wealth Index (IWI) : to hear the
   voices of nations
2) Causes-of-death and mass spectra from judicial
   autopsy reports (Satoko Sawaguchi, commissioned
   chief surgeon) : to hear mortality
3) Raw data from the 2011 / 13 Cabinet Office report
   Assisting children who lost their families in traffic
   accidents, and findings of nested (multinomial)
   logistic regression analysis: to hear children’s
   expression of thoughts after an unexpected death.
4) Multiple performance indicators from Sukoyaka
   Oyako 21 / Kenkoh Nihon 21: to hear the efficacy
   of health promotion campaigns.
5) Libet’s readiness potential: to hear wilful negligence.

(2) Methods

This paper will discuss the components of the
auralisation methodology that are commonly utilized by
applications of the five types of data above.

Auralisation consists of three steps:

1) Time composition
2) Multi-level composition
3) Polyphonic composition

This basic, three-step auralisation process can be
applied to all types of numerical data, as summarized
concisely below:

1) Time composition
   Observation data is plotted over time, with each point
   an equal distance apart; tone length configured by user.
2) Multi-level composition
   Triple musical scales are deployed to represent three
   levels of data.
   2-1) Major (Ionian) scale : 7 notes.
       (On a piano, white keys only, from C; 5 whole steps,
       2 half steps.)
   2-2) Chromatic scale: 12 notes
       (On a piano, all 7 white and 5 black keys in an octave.)
   2-3) Pentatonic (black key) scale: 5 notes.
       (On a piano, black keys only.)
   * Data will be segmented and zoned (‘zonated’) by
dividing the range (max-min) of each variable by the
number of notes in the respective musical scale (Table
1-1, Table 2-1, Table 3-1, Table 4-1).
* One zone corresponds to one note on the scale.
* Each data point belongs to one zone.
* Data points belonging to the same zone are assigned the same tone (Table 1-2, Table 2-2, Table 3-2, Table 4-2).
* Musical score is created (Figure 1, Figure 2, Figure 3).

Three scales are proposed in the methodology; each follows the protocol above. Users can choose whichever scale they prefer, and several if they would like.

The technology can be adapted to allow for fewer or more scales.

3) Polyphonic composition

Data encoded using multiple scales in level (2) could also give rise to polyphonic (harmonic) composition.

Alternatively, users could group several indicators or outcomes based on contextual similarity, and assign matching sounds to each to create harmonies.

4) General concerns

Several principles are necessary to maintain scientific rigour in each step of the auralisation process.

* Constant rules for assigning sound(s) to numerical data (as above)
* Minimal use of acoustic processing

Raw and refined data, alike, can be auralised: the approach also supports the conversion of verbal (linguistic) data.

Results

Our initial attempts at applying basic technology to create melody lines included five types of sources for auralisation. The conversion process worked equally well for test values (e.g. mass spectra)\(^5\)\(^,\)\(^6\) and non-numeric (linguistic) data\(^7\).

In addition, we successfully applied a process to auralise the performance metrics of two national health promotion campaigns, Sukoyaka Oyako 21 and Kenkoh Nihon 21.

We analysed a questionnaire about children’s mental health, following a traffic accident, using nested (multinomial) logistic regression, and looked at everyday challenges that affected the health of a surviving family as compared to traditional, percentage-based analysis. In addition, we recently discovered three other harmful factors: insomnia, loss of vitality / interest / enthusiasm, and physical deterioration.

The sound approach works best when there are significant numbers of sonic elements: not necessarily a small number of test values output by analysis, but a matrix or chart, including numerous data points. In addition, a listener would surely benefit from first looking at the musical notes on the page (itself an alternate way of graphing data), since finer distinctions in a ‘musical’ performance might escape the attention of uninitiated listeners.

The aurally approach has potential to supplement subtle differences (e.g. due to gender) present in a dataset yet invisible to the eye, highlighting certain patterns with distinct harmonies / rhythms even when the raw data resists clear interpretation. The proposed audio presentation technology could be employed as a means to bring Japan’s health consciousness to its citizens ears, especially those with disabilities, or who are bedridden, or living alone. This report will have served its purpose if this ‘musical data’ found a place in the hearts of the Japanese people: a unique way of listening to not only our minds and bodies, but also to society, originally rooted in indicator properties.

Discussion

Our sound approach’s benefits can be summarized as, below-mentioned.

When nested analysis detects commonalities between different elements, measures, or variables in health care policy, it strongly suggests that they are common components to some ‘global approach’. When multiple variables are linked in the nested or similar approach, and certain indicators or themes are extracted together, they are good candidates for efficacy assessments performed to advance national and international public health.

Listeners don’t need to set up an access point to hear audio; music transcends boundaries of nation, community, sect, and citizens. Our sound approach could serve as a universal approach to impart information intuitively and naturally into people’s minds. Official autopsies to determine causes of death are a sign not only of a medically competent government, but also good governance in general; this procedure’s benefits were severely limited in the former DDR, Eastern Europe, and a significant number of Asian countries. Auralisation could be used to convert cause-of-death and autopsy data into musical form (e.g. CD) for use in grief counselling, or as part of ‘virtual’ inquest proceedings\(^8\). Hygiene is meant to support personal health, by cultivating optimal conditions for people to flourish. Our sound approach allows
people to expand their arsenals for understanding and perceiving health care data, and could help achieve ‘breakthrough’ moments in the field of public health.

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COI

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Fig. 1. Music of causes of death from author’s own judicial forensic autopsy authentication

Fig. 2. Music of willful negligence via movement preparation potential using data from J Okayama Medical Association
Fig. 3. National Voice using the sound from GINI and associated INDICES with triple scale method
| Table 1-1. officially opened indicator |
|---------------------------------------|
| indicator                              | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
| Age-adjusted mortality ratio from     | 84.3 | 83.1 | 81.3 | 80.1 | 79   | 78   |
| Diabetic kidney complication          | 16247| 16003| 16171| 16035| 15899| 16072|
| rate of suicide                       | 23.4 | 22.9 | 21   | 20.7 | 19.5 | 18.5 |
| proportion of low birth weight in     | 9.6  | 9.6  | 9.6  | 9.6  | 9.5  | 9.5  |
| total birth number                    |      |      |      |      |      |      |
| trend of low nutrition < BMI20        | 17.4 | 18.2 | 16.5 | 16.8 | 17.8 | 16.7 |
| proportion of skinny citizens         | 29   | 21.9 | 21.8 | 21.5 | 17.4 | 22.3 |
| decrease of natri intake              | 10.6 | 10.4 | 10.4 | 10.2 | 10   | 10   |
| average of intake of vegetables       | 28.2 | 27.7 | 28.7 | 28.3 | 29.2 | 29.4 |

| Table 1-2. Ionial Major Scale |
|--------------------------------|
| Age-adjusted mortality ratio from   | 6    | A    | 6    | A    | 6    | A    | 6    | A    | 6    | A    |
| Diabetic kidney complication        | 7    | B    | 7    | B    | 7    | B    | 7    | B    | 7    | B    |
| rate of suicide                     | 2    | D    | 2    | D    | 2    | D    | 2    | D    | 2    | D    |
| proportion of low birth weight in   | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| total birth number                  |      |      |      |      |      |      |      |      |      |      |
| trend of low nutrition < BMI20      | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| proportion of skinny citizens       | 2    | D    | 2    | D    | 2    | D    | 2    | D    | 2    | D    |
| decrease of natri intake            | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| average of intake of vegetables     | 7    | B    | 7    | B    | 7    | B    | 7    | B    | 7    | B    |

| Table 1-3. Chromatic Scale |
|-----------------------------|
| Age-adjusted mortality ratio | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| Diabetic kidney complication  | 12   | B#   | 12   | B#   | 12   | B#   | 12   | B#   | 12   | B#   |
| rate of suicide              | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| proportion of low birth weight | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| total birth number           |      |      |      |      |      |      |      |      |      |      |
| trend of low nutrition < BMI20| 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| proportion of skinny citizens | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| decrease of natri intake      | 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |
| average of intake of vegetables| 1    | C    | 1    | C    | 1    | C    | 1    | C    | 1    | C    |

| Table 1-4. Pentatonic Black Key Scale |
|---------------------------------------|
| Age-adjusted mortality ratio from     | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| Diabetic kidney complication          | 5    | H#  | 5    | H#  | 5    | H#  | 5    | H#  | 5    | H#  |
| rate of suicide                       | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| proportion of low birth weight in     | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| total birth number                    |      |      |      |      |      |      |      |      |      |      |
| trend of low nutrition < BMI20        | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| proportion of skinny citizens         | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| decrease of natri intake              | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
| average of intake of vegetables       | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  | 1    | C#  |
Table 2. Changes from numericals to sounds in Maternal & Child Health using triple scale

| Table 2-1. officially opened indicator | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|----------------------------------------|------|------|------|------|------|------|
| suicide rate of teenagers              | 7.5  | 8.3  | 9.3  | 9.8  | 9.8  | 9.8  |
| abortion rate of teenagers             | 12.1 | 10.5 | 7.6  | 7.1  | 7.1  | 7.1  |
| smokers rate of teenagers              | 15.95| 9.25 | 5.175| 14.9 | 14.9 | 14.9 |
| drinkers rate of teenagers             | 33   | 25.5 | 16.9 | 14.15| 14.15| 14.15|
| number of junior high school with school counselors | 22.5 | 47.3 | 84.3 | 83.2 | 83.2 | 83.2 |
| number of outpatient clinics of adolescent health | 52.3 | 137.4| 1746 | 135.9| 135.9| 135.9|
| maternal mortality rate                | 6.3  | 4.3  | 3.5  | 4    | 4    | 4    |
| number of suspicious cases of postpartum depression | 13.4 | 12.8 | 10.3 | 9    | 9    | 9    |

| Table 2-2. Ionial Major Scale | correspondence of numerical value and phonetic sound |
|--------------------------------|-----------------------------------------------------|
| suicide rate of teenagers      | 0 B C 1 C 1 C 0 B 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |
| abortion rate of teenagers     | 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |
| smokers rate of teenagers      | 1 C 1 C 0 B 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |
| drinkers rate of teenagers     | 2 D 2 D 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |
| number of junior high school with school counselors | 2 D 3 E 6 A 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G 5 G |
| number of outpatient clinics of adolescent health | 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B |
| maternal mortality rate        | 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B |
| number of suspicious cases of postpartum depression | 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |

| Table 2-3. Chromatic Scale | correspondence of numerical value and phonetic sound |
|-----------------------------|-----------------------------------------------------|
| suicide rate of teenagers   | 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B |
| abortion rate of teenagers  | 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B |
| smokers rate of teenagers   | 1 C 0 B 0 B 0 B 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C |
| drinkers rate of teenagers  | 2 C# 1 C 1 C 1 C 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B 0 B |
| number of junior high school with school counselors | 1 C 12 B 6 F 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# 7 F# |
| number of outpatient clinics of adolescent health | 12 B 0 C 0 C 0 C 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# 9 G# |
| maternal mortality rate      | 0 B 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C |
| number of suspicious cases of postpartum depression | 0 B 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C 0 C |

| Table 2-4. Pentatonic Black Key Scale | correspondence of numerical value and phonetic sound |
|---------------------------------------|-----------------------------------------------------|
| suicide rate of teenagers             | 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| abortion rate of teenagers            | 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| smokers rate of teenagers             | 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| drinkers rate of teenagers            | 1 C# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| number of junior high school with school counselors | 0 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# 5 H# |
| number of outpatient clinics of adolescent health | 1 C# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| maternal mortality rate               | 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
| number of suspicious cases of postpartum depression | 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# 0 H# |
Table 3. Creation of sounds from GINI index & associated index as the reflection of the voice of each nation

| ISO-CODE | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence |
|----------|--------------|----------------------|--------------|----------------------|--------------|----------------------|--------------|----------------------|
| ARM      | 0.784        | 31.540112            | C            | 77.2                 | 8.8031356   | B                    | 0.71         | 1.06424436          | B            | 5009                 | 7.54038416       | B               |
| AZE      | 0.863        | 34.7189503           | E            | 67.1                 | 7.6498252   | A                    | –           | 0                    | rest         | 3940                 | 5.9311453        | G               |
| BDI      | 0.939        | 37.7760792           | A            | 15.8                 | 1.801308799 | C                    | 0.31         | 0.46476084          | C            | 359                  | 0.54024622       | C               |
| BEN      | 0.914        | 36.7730263           | G            | 28.7                 | 3.271997629 | E                    | 0.41         | 0.61546366          | D            | 1311                 | 1.97353565       | D               |
| BFA      | 0.951        | 38.2588406           | B            | 19.4                 | 2.211733589 | D                    | 0.3          | 0.449608727         | C            | 996                  | 1.49934516       | C               |

| unitvalue | 0.024857     | 8.7714               |              |                      |              |                      |              |                      |              |                      | 664.29            |                |

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| ISO-CODE | Life exp. | GINI | PHR$1.25 |
|----------|-----------|------|----------|
| ARM      | 74.1      | 21.525537 | B       |
| AZE      | 69        | 20.0412434 | A       |
| BDI      | 50        | 14.5226408 | C       |
| BEN      | 54.3      | 15.7715879 | D       |
| BFA      | 51.6      | 14.9673653 | C       |

| unitvalue | 3.4429     | 1.2429              | 13.1     |

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| ISO-CODE | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence |
|----------|--------------|----------------------|--------------|----------------------|--------------|----------------------|--------------|----------------------|
| ARM      | 0.784        | 36.33398             | C            | 77.2                 | 24.8612168  | B                    | 0.71         | 20.7845333          | B            | 5009                 | 10.1677394       | A               |
| AZE      | 0.863        | 67.4714378           | A            | 67.1                 | 13.1417738  | A                    | –           | 0                    | rest         | 3940                 | 9.079441452      | C#              |
| BDI      | 0.939        | 67.4714378           | A            | 15.8                 | 3.0899817   | C                    | 0.31         | 9.079441452         | C#           | 359                  | 3.92045163       | C               |
| BEN      | 0.914        | 65.7715879           | G            | 28.7                 | 5.696936905 | D                    | 0.41         | 12.00234192         | D#           | 1311                 | 3.38022806       | D               |
| BFA      | 0.951        | 68.3336926           | B            | 19.4                 | 3.791580366 | C                    | 0.3          | 8.782201405         | C            | 996                  | 2.570322581      | C#              |

| unitvalue | 0.013917   | 5.1166               | 0.03416  | 387.5               |

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| ISO-CODE | Life exp. | GINI | PHR$1.25 |
|----------|-----------|------|----------|
| ARM      | 74.1      | 36.9068787 | B       |
| AZE      | 69        | 34.8574167 | A       |
| BDI      | 50        | 24.9867986 | C       |
| BEN      | 54.3      | 27.0377932 | D       |
| BFA      | 51.6      | 25.6933725 | C#      |

| unitvalue | 2.0883     | 0.725               | 7.64     |

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| ISO-CODE | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence | Multi-valued | Voice Correspondence |
|----------|--------------|----------------------|--------------|----------------------|--------------|----------------------|--------------|----------------------|
| ARM      | 0.784        | 23.4705593           | C            | 77.2                 | 6.28644951  | A                    | 0.71         | 8.658536058         | A            | 5009                 | 53.6021505       | A               |
| AZE      | 0.863        | 25.8383234           | D            | 67.1                 | 5.46469381  | G                    | –           | 0                    | rest         | 3940                 | 42.3655914       | G               |
| BDI      | 0.939        | 28.1177252           | A            | 15.8                 | 1.28644951  | C                    | 0.31         | 3.786457085         | C            | 359                  | 3.86021504       | C               |
| BEN      | 0.914        | 27.3652695           | G            | 28.7                 | 2.33713355  | D                    | 0.41         | 5                    | E            | 1311                 | 14.9677419       | D               |
| BFA      | 0.951        | 28.4705593           | A            | 19.4                 | 0.35576768  | C                    | 0.3          | 3.658536058         | C            | 996                  | 10.79067742      | D               |

| unitvalue | 0.0334     | 12.28               | 0.082     | 93                  |

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| ISO-CODE | Life exp. | GINI | PHR$1.25 |
|----------|-----------|------|----------|
| ARM      | 74.1      | 15.373444 | A       |
| AZE      | 69        | 14.3153527 | G       |
| BDI      | 50        | 10.733444 | C       |
| BEN      | 54.3      | 11.2655602 | D       |
| BFA      | 51.6      | 10.7059422 | C       |

| unitvalue | 4.82       | 33.42              | 18.34    |

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**Table was made by Dr. Prof. Toshiko Sawaguchi**
Table 4. Creation of sounds from willful negligence using movement preparation potential (data extracted from Table 2 p.55 J Okayama Medical Association 93 (1-2) 1982 & arranged by Dr. Prof. Toshiko Sawaguchi, M.D.Ph.D.L.A.)

Table 4-1. Creation of sounds using movement preparation potential by right hand movement by seven notes

| value   | right central (µV) | Multi-valued voice correspondence | time (sec) | Multi-valued voice correspondence | Time (sec) | Multi-valued voice correspondence |
|---------|--------------------|-----------------------------------|-----------|-----------------------------------|-----------|-----------------------------------|
| 7       | 7.686433           | E                                 | 7.9       | 7.098989                      | F         | 89                               | 20.7652031 | G                               | 1.4 | 10.85271318 B                    |
| 4.3     | 4.7049529         | C                                 | 46        | 4.129023                      | C         | 93                               | 21.6955343 | A                              | 0.5 | 3.675969992 C                    |
| 8.6     | 9.4098937          | G                                 | 12.4      | 11.33509                       | B         | 69                               | 16.0982874 | C                              | 0.5 | 3.675969992 C                    |
| 10.7    | 11.306934          | B                                 | 10.8      | 9.699493                      | G         | 99                               | 23.0984601 | B                              | 0.7 | 5.42635689 D                    |
| 6       | 6.56455342         | D                                 | 8.5       | 7.630163                       | F         | 71                               | 16.956623  | C                              | 0.8 | 6.201550388 E                    |
| 5.5     | 6.03750847         | D                                 | 7.1       | 6.373429                       | E         | 77                               | 17.9645897 | D                              | 1   | 7.75193764 F                    |
| mean    | 7.686433           | E                                 | 86        | 7.719922                       | F         | 83                               | 19.3653764 | F                              | 0.8 | 6.201550388 E                    |
| SEM     | 0.94               | C                                 | 1.11      | 0.965132                      | G         | 5                                | 1.66953984 | G                              | 0.1 | 0.775193798 F                    |
| unit value | 1.14               |                                    | 4.266     |                                  |           |                                  |                  |                                | 0.129|                                    |

Table 4-2. Creation of sounds using movement preparation potential by left hand movement by seven notes

| value   | right central (µV) | Multi-valued voice correspondence | time (sec) | Multi-valued voice correspondence | Time (sec) | Multi-valued voice correspondence |
|---------|--------------------|-----------------------------------|-----------|-----------------------------------|-----------|-----------------------------------|
| 7.9     | 5.7621736          | D                                 | 7.7       | 4.854981                         | D         | 103                              | 14.7148571 | G                               | 1.3 | 10.0751938 B                    |
| 4.6     | 3.3552137          | C                                 | 57        | 3.595347                         | C         | 81                               | 11.5714287 | D                               | 1.1 | 8.52731783 A                    |
| 9.2     | 6.72643034         | E                                 | 10.7      | 6.746532                        | G         | 86                               | 12.28571429| E                              | 0.4 | 3.000795194 C                    |
| 14.8    | 10.7590401         | B                                 | 16.8      | 10.592866                       | E         | 88                               | 12.5714287 | E                              | 0.9 | 6.97644186 F                    |
| 8       | 5.68513682         | D                                 | 64        | 4.635309                        | C         | 125                              | 17.8754286 | B                              | 1   | 7.75193764 G                    |
| 6       | 4.53636761         | C                                 | 7.9       | 4.980584                        | D         | 76                               | 10.8754286 | C                              | 1.1 | 8.52731783 A                    |
| mean    | 8.4                | 6.12991466                      | 92        | 5.8007666                       | F         | 98                               | 13.28571429| F                              | 1   | 7.75193764 G                    |
| SEM     | 1.4                | 1.02115244                      | 1.7       | 1.0718389                       | G         | 7                                | 1               | G                              | 0.1 | 0.775193798 G                    |
| unit value | 1.37                |                                    | 1.596     |                                  |           |                                  |                  |                                | 0.129|                                    |
Table 5. sound from causes of deaths (date from author’s judicial medical authentication using the standard manual of judicial autopsy by Japan Society Legal Medicine) by 12 sound notes in chromatic scale

| Code of judicial autopsy | Contents of the code | Multi-valued of each code | Voice correspondence of each code | With description | Multi-valued | Voice correspondence | Without description | Multi-valued | Voice correspondence |
|--------------------------|----------------------|---------------------------|----------------------------------|-----------------|-------------|---------------------|---------------------|-------------|---------------------|
| 1.1 prevention of infection | 1 | C | existing | 1 | C |
| 1.2 management of instruments | 2 | C# | existing | 2 | C# |
| 2.1.1 body height | 1 | C | existing | 1 | C |
| 2.1.2 body weight | 2 | C# | existing | 2 | C# |
| 2.1.3 nutrition | 3 | D | existing | 3 | D |
| 2.1.21 sex | 1 | C | existing | 1 | C |
| 2.1.22 body characteristics | 2 | C# | existing | 2 | C# |
| 2.1.23 scar | 3 | D | existing | 3 | D |
| 2.1.24 hair | 4 | D# | existing | 4 | D# |
| 2.1.25 eye, nose, ear, mouth | 5 | E | existing | 5 | E |
| 2.1.26 diameter of pupils | 6 | F | existing | 6 | F |
| 2.1.27 tooth | 7 | F# | existing | 7 | F# |
| 2.1.28 genitals & anus | 8 | G | existing | 8 | G |
| 2.1.29 medical treatment | 9 | G# | existing | 9 | G# |
| 2.1.31 body temperature (rectum) | 1 | C | existing | 1 | C |
| 2.1.32 postmortem lividity | 2 | C# | existing | 2 | C# |
| 2.1.33 postmortem rigidity | 3 | D | without existing | 3 | rest |
| 2.1.34 corneal opacity | 4 | D# | existing | 4 | D# |
| 2.1.35 putrefactive coloring | 5 | E | without existing | 5 | rest |
| 2.1.36 late postmortem phenomenon | 6 | F | without existing | 6 | rest |
| 2.1.41.1 injury by sharp instrument findings | 1 | C | without existing | 1 | rest |
| 2.1.41.2 injury by sharp instrument cide | 2 | C# | without existing | 2 | rest |
| 2.1.41.3 injury by sharp instrument size | 3 | D | without existing | 3 | rest |
| 2.1.41.4 injury by sharp instrument shape | 4 | D# | without existing | 4 | rest |
| 2.1.41.5 injury by sharp instrument intrawound | 5 | E | without existing | 5 | rest |
| 2.1.42.1 injury by blunt instrument findings | 1 | C | without existing | 1 | rest |
| 2.1.42.2 injury by sharp instrument findings cite | 2 | C# | existing | 2 | C# |
| 2.1.42.3 injury by sharp instrument findings size | 3 | D | existing | 3 | D |
| 2.1.42.4 injury by sharp instrument findings shape | 4 | D# | existing | 4 | D# |
| 2.1.42.5 injury by sharp instrument surrounding | 5 | E | existing | 5 | E |
| 2.1.42.6 injury by sharp instrument findings | 6 | F | without existing | 6 | rest |
| 2.2.11 brain skin and scalp findings | 1 | C | without existing | 1 | rest |
| 2.2.12 epidural, subdural, subarachnoidal findings | 2 | C# | without existing | 2 | rest |
| 2.2.13 brain findings | 3 | D | without existing | 3 | rest |
| 2.2.14 spinal cord findings | 4 | D# | without existing | 4 | rest |
| 2.2.21 organ findings | 1 | C | existing | 1 | C |
| 2.2.22 fluid and cohesion | 2 | C# | existing | 2 | C# |
| 2.2.23 surgical operation | 3 | D | without existing | 3 | rest |
| 2.5.1 histological exermination | 1 | C | existing | 1 | C |
| 2.5.2 toxicological exermination | 2 | C# | without existing | 2 | rest |
| 2.5.3 microbiological exermination | 3 | D | existing | 3 | D |
| 2.5.4 biochemical exermination | 4 | D# | existing | 4 | D# |
| 2.5.5 serological and molecular biological exermination | 5 | E | existing | 5 | E |
| 2.5.6 other expertises opinions | 6 | F | without existing | 6 | rest |
| 2.6 suture and embemring | 1 | C | existing | 1 | C |