Morningness–eveningness questionnaire score correlates with glycated hemoglobin in middle-aged male workers with type 2 diabetes mellitus

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ABSTRACT

Aims/Introduction: ‘Morningness’ and ‘eveningness’ represent the sleep–wake patterns of the circadian rhythm; might also affect glycemic control in patients with type 2 diabetes. The aim of this study was to examine the relationship between the morningness–eveningness trait and metabolic parameters.

Materials and Methods: The study participants comprised 101 Japanese male workers with type 2 diabetes treated in an outpatient clinic. Blood samples were obtained, and a morningness–eveningness questionnaire (MEQ), where a high score represents morningness; and the Pittsburg Sleep Quality Index (PSQI), where the higher the score the worse the sleep quality, were carried out.

Results: MEQ correlated positively with age, and high-density lipoprotein cholesterol (HDL-C), and negatively with glycated hemoglobin (HbA1c) and PSQI. Multivariate regression analysis showed that MEQ was significantly associated with HbA1c and HDL-C. In addition, we classified the study patients into three groups: ‘morning type’, ‘neither type’ and ‘evening type’ according to the sum of the MEQ score, and analyzed the difference between morning type (n = 32) and evening type (n = 11). We found that HbA1c, low-density lipoprotein cholesterol and PSQI of the morning type group were significantly lower than those of the evening type group.

Conclusions: The present study suggests that ‘eveningness’ type male Japanese workers with type 2 diabetes suffer inadequate glycemic control. (J Diabetes Invest, doi: 10.1111/jdi.12047, 2013)

KEY WORDS: Japanese, Morningness–eveningness questionnaire, Type 2 diabetes mellitus

INTRODUCTION

The onset and development of type 2 diabetes is associated with numerous lifestyle problems. Although several reports have suggested the pathological role of sleep duration and/or quality in the onset of diabetes1–5, Knutson et al.6 reported that both sleep duration and quality affect blood glucose control in patients with type 2 diabetes, suggesting that the two aspects of sleep might be a possible target for improvement of glycemic control in type 2 diabetes.

Morningness–eveningness, which reflects the sleep–wake pattern of the circadian rhythm, might also affect metabolic state. Indeed, although it has been reported by several studies using experimental genetic models that the circadian clock in mammals is expressed in the brain and maintains proper phase alignment of peripheral tissue clocks present in nearly all cells7, clock disruption leads to disorders in glucose metabolism8. Based on these findings, we examined the circadian integration of glycemic control in a clinical setting to assess the relationship between morningness–eveningness and glycemic control in a cross-sectional study. Generally, older adults tend to show morningness; that is, being most active and alert during the morning9. In addition, a large sex difference is present in the percentage of workers in Japan. Thus, in the present study, we focused on male middle-aged workers with type 2 diabetes.

MATERIALS AND METHODS

Patients

This was a substudy of the study investigating the relationship among metabolic parameters, the health-related quality of life (HRQOL) and lifestyle in patients with type 2 diabetes. Briefly, the study participants were recruited from the Diabetes Outpa-
tient Clinic of Juntendo University in Tokyo, Japan. After being informed of the purpose and procedures of the study, 319 consecutive patients with type 2 diabetes volunteered to answer a questionnaire during an outpatient appointment, between June 2010 and August 2010. Among these patients, we selected study participants who fit the following inclusion criteria: (i) male; (ii) worker; and (iii) aged more than 40 years-of-age, but <65 years-of-age. Here, workers were defined as full-time employees, and shift workers were excluded from the present study. The work schedule of the participants was determined by a question in the questionnaire, ‘Which is your usual work schedule, day, evening, shift or permanent night work?’ Regular daytime workers were defined as participants without any evening and night work in their usual work schedule. We defined shift working as working patterns that differed from regular daytime working, including irregular or unspecified shifts, mixed schedules, evening shifts, night shifts and rotating shift. The present study plan excluded patients from the analysis who had chronic inflammatory or malignant diseases, and those had been diagnosed with type 2 diabetes within the past 1 year, because it is unlikely that they had achieved stable glycemic control. Blood samples were taken from the participants, and questionnaire surveys on their psychological status were carried out. The present study protocol was approved by the Institutional Review Board in Juntendo University Hospital and in accordance with the principles described in the Declaration of Helsinki. All patients provided written informed consent before participation.

Questionnaire Survey
The Morning Evening Questionnaire (MEQ)12 is a self-assessment questionnaire developed primarily for screening candidates for sleep-related experiments to evaluate circadian rhythm and sleep rhythm patterns in individuals, which consists of 19 items on sleep habits and fatigue. Scoring was based on an original questionnaire by Ostberg12. Briefly, 11 questions allowed for choice, and scored from 1 to 4. Two questions allowed for choice, and scored 0, 2, 4 and 6. One question allowed for choice and scored 0, 2, 3 and 5. The remaining five questions allowed for choice of time scales and scored from 1 to 5. The sum of all scores was converted into a five-point MEQ scale as follows: ‘definitely morning type’ (group 1), score 70–86; ‘moderately morning type’ (group 2), score 59–69; ‘intermediate (neither) type’ (group 3), score 42–58; ‘moderately evening type’ (group 4), score 31–41; and ‘definitely evening type’ (group 5), score 16–30. In the present study, we reduced the categories from five to three: morning type (groups 1 and 2), score 59–86; neither type (group 3), score 42–58; and evening type (groups 4 and 5), score 16–41, as reported previously13,14.

The Pittsburg Sleep Quality Index (PSQI)15 is a self-administered questionnaire designed to evaluate sleep quality consisting of 18 items that in turn are comprised of seven components, which include subjective sleep quality, sleep duration, sleep onset, habitual sleep efficiency, sleep disturbances, use of sleeping medications and daytime dysfunction, with each weighted equally on a 0–3 scale to be summed to yield a global PSQI score, which ranges between 0 and 21, where the higher the scores, the worse the sleep quality. Among the questions in PSQI, the question ‘how often have you had trouble sleeping because you had pain?’ identified patients with sleep disturbed by pain, representing those who responded ‘three or more times per week’. Knutson et al.8 investigated the roles of sleep duration and quality in the risk and severity of type 2 diabetes mellitus, and excluded individuals with chronic pain because the latter could influence sleep and glycemic control. To avoid the possible effect of this confounder, we followed the same rule and excluded two patients with chronic pain.

The Beck Depression Inventory (BDI)-II measures depressive symptoms in adults and adolescents16. BDI-II is a 21-item questionnaire to assess hopelessness, irritability, cognition, guilt, fatigue, weight loss and sexual interest17. Each of the 21 items measures the presence and severity of a somatic or cognitive symptom of depression, rated on a four-point scale ranging from 0 to 3. The ratings are summed, yielding a total score ranging from 0 to 63. A high score represents a depressive state: The BDI-II has been validated as a sensitive, specific and predictive tool for quantitative assessment of the severity of depression17. The Japanese version of the BDI-II has been cross-culturally validated18.

Individual physical activity levels were assessed with the International Physical Activity Questionnaire (IPAQ) that comprises four simple questions on physical activity19. The IPAQ results are expressed as metabolic equivalent scores (MET-min/week)19. We further converted these to daily energy expenditure (kcal/day).

Dietary habits during the preceding month were assessed with a validated, brief, self-administered diet history questionnaire (BDHQ)20. The BDHQ is a four-page structured questionnaire that asks about consumption frequency of selected foods to estimate the dietary intake of 56 food and beverage items with specified serving sizes described in terms of consumption in general Japanese populations. The dietary intakes of energy and selected nutrients were estimated using an ad hoc computer algorithm for the 56 foods and beverages of the BDHQ and the Standard Tables of Food Composition in Japan21.

Biochemical Tests
Blood samples were obtained at visit. High-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides and glycated hemoglobin (HbA1c) were measured with standard techniques. The value of HbA1c (%) was estimated as an National Glycohemoglobin Standardization Program equivalent value (%)22,23.

Statistical Analysis
Results are presented as mean ± standard deviation or number (proportion) of patients. To investigate the importance of metabolic and clinical parameters on MEQ, the correlation coefficients of MEQ scores were assessed by Pearson’s paramet-
The study participants comprised 101 Japanese male workers with type 2 diabetes mellitus who were being treated on an outpatient basis. Table 1 shows the characteristics of the study participants. The mean age was 53.9 ± 7.1 years and HbA1c was 7.3 ± 1.2%. The MEQ score was 53.7 ± 8.4 and PSQI was 5.2 ± 2.9.

MEQ correlated positively and significantly with age and HDL in 101 Japanese male workers with type 2 diabetes mellitus (Table 2). In addition, MEQ correlated negatively and significantly with HbA1c. Next, the aforementioned factors were entered into multivariate regression analysis. The results showed that MEQ correlated significantly with HbA1c and HDL in 101 Japanese male workers (Table 3).

Next, we also classified the participants into three groups, such as 'morning type', 'neither type' and 'evening type', based on MEQ score. Then, data obtained for the morning and evening groups were compared by the Mann–Whitney test or by chi-square test for non-continuous variables. Statistical tests were two-sided with a 5% significance level. Data were analyzed using the Statistical Package for Social Science computer software program, version 12 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

The study participants comprised 101 Japanese male workers with type 2 diabetes mellitus who were being treated on an outpatient basis. The mean age was 53.9 ± 7.1 years and HbA1c was 7.3 ± 1.2%. The MEQ score was 53.7 ± 8.4 and PSQI was 5.2 ± 2.9.

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Next, we also classified the participants into three groups, such as 'morning type', 'neither type' and 'evening type', according to MEQ score. The MEQ results showed that 32 individuals were 'morning type', 58 'neither type' and 11 'evening type'. To further clarify the feature of each chronotype, we further compared metabolic parameters and questionnaire survey scores between the 'morning type' group and the 'evening type' group. HbA1c, LDL-C and PSQI in the morning type group were significantly lower than those in the evening type group (Table 1). In addition, BDI-II tended to be higher in the morning group than the evening group. In contrast, there were no significant differences in sleep duration, energy intake and physical activity between the 'morning type' group and the 'evening type' group.

### Table 1 | Patient characteristics

| Total (n = 101) | Morning type (n = 32) | Evening type (n = 11) | Neither type (n = 58) |
|----------------|----------------------|-----------------------|----------------------|
| **Age (years)** | 53.9 ± 7.1 | 54.7 ± 7.2 | 50.6 ± 6.8 | 54.0 ± 7.0 |
| **Estimated duration of diabetes (years)** | 9.4 ± 7.4 | 9.7 ± 6.1 | 8.9 ± 5.8 | 9.4 ± 8.4 |
| **Body mass index (kg/m²)** | 25.5 ± 4.1 | 25.7 ± 3.9 | 26.4 ± 3.6 | 25.2 ± 4.3 |
| **HbA1c (NGSP;%)** | 7.3 ± 1.2 | 7.2 ± 0.8 | 8.3 ± 1.8* | 7.2 ± 1.1 |
| **Systolic blood pressure (mmHg)** | 131.7 ± 14.8 | 133.9 ± 14.9 | 126.9 ± 15.6 | 131.4 ± 14.6 |
| **Diastolic blood pressure (mmHg)** | 79.4 ± 10.0 | 80.5 ± 9.5 | 79.9 ± 7.8 | 80.7 ± 10.7 |
| **HDL-C (mg/dL)** | 51.2 ± 12.5 | 55.1 ± 12.7 | 47.4 ± 9.1 | 49.9 ± 12.7 |
| **LDL-C (mg/dL)** | 105.6 ± 28.5 | 100.0 ± 22.4 | 129.0 ± 24.1** | 104.1 ± 30.2 |
| **Triglyceride (mg/dL)** | 160.0 ± 92.9 | 137.6 ± 62.3 | 162.3 ± 75.7 | 171.2 ± 107.0 |
| **MEQ** | 53.7 ± 8.4 | 63.2 ± 3.3 | 385.1 ± 9.9** | 51.3 ± 4.1 |
| **PSQI** | 5.2 ± 2.9 | 4.2 ± 2.1 | 6.4 ± 2.1** | 5.5 ± 3.2 |
| **BDH** | 82.8 ± 7.8 | 65.4 ± 49 | 103.7 ± 78 | 88.8 ± 9.9 |
| **Sleep duration (min)** | 378.1 ± 54.4 | 389.6 ± 47.4 | 379.1 ± 47.0 | 371.6 ± 56.9 |
| **Energy intake (kcal/day)** | 1811.0 ± 586.1 | 1788.8 ± 654.6 | 1758.9 ± 436.1 | 1845.5 ± 577.3 |
| **Fat intake (g/day)** | 494 ± 18.9 | 496 ± 23.0 | 455 ± 11.5 | 500 ± 17.6 |
| **Carbohydrate intake (g/day)** | 235.5 ± 85.3 | 225.4 ± 82.1 | 235.2 ± 77.8 | 241.1 ± 88.9 |
| **Protein intake (g/day)** | 684 ± 23.3 | 702 ± 27.9 | 574 ± 22.5 | 693 ± 20.6 |
| **Physical activity (kcal/day)** | 324.1 ± 349.8 | 345.3 ± 277.5 | 219.6 ± 190.7 | 333.2 ± 403.8 |

BDI, Beck Depression Inventory; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MEQ, morningness–eveningness questionnaire; NGSP, National Glycohemoglobin Standardization Program; OHA, other hypoglycemic agents; PSQI, Pittsburg Sleep Quality Index. Data are mean ± standard deviation or number (proportion) of patients (n = 101). Data obtained for the morning and evening groups were compared by the Mann–Whitney test or by chi-square test for non-continuous variables. *P < 0.05, **P < 0.01, by the Mann–Whitney test.
in genetic studies of the circadian rhythm have led to the recognition that the circadian system tightly controls both sleep and metabolism26–28, thus disrupting the circadian system causes imbalance of energy intake and consumption28. One common clinical example suggestive of interactions between disrupted circadian rhythms and metabolic problems in humans is that of shift work29,30. Numerous studies have reported high incidences of diabetes, obesity, metabolic syndrome, cardiovascular and gastric disorders, and increased mortality as a result of cancer in shift workers9,31. Scheer et al. carried out a clinical experiment of simulation of shift work. In their study, participants subjected to circadian misalignment developed hypoleptinemia, insulin resistance, inverted cortisol rhythms and increased blood pressure32. Extrapolation of these findings suggests that sleep disturbances as a result of disrupted circadian rhythm can worsen the course or trigger the development of insulin resistance and diabetes33. Although the present cross-sectional study does not allow conclusions about the cause and effect relationship, MEQ correlated positively with HbA1c and negatively with HDL-C. On the basis of no significant differences in energy intake and physical activity among the group, abnormal circadian rhythm might have an unfavorable influence on metabolic disorder through mechanisms other than altering energy intake and physical activity. These relationships were still found after adjustment for age, which was strongly associated with morningness11.

In the present study, a high rate of the evening type (10.9%) was identified in middle-aged male workers with type 2 diabetes, compared with just 2.2% evening type in middle-aged French workers34. Whereas the exact reason for this difference is not clear at present, it is not difficult to imagine that social and cultural differences could affect the sleep–wake pattern of the circadian rhythm.

Disturbance of the sleep–wake pattern can be divided into at least two forms. Many adolescents do not obtain adequate sleep; they tend to stay up late during school nights and sleep in on weekends35,36. This could be called voluntary disturbance of circadian rhythm. Another situation is indirect disturbance of circadian rhythm caused by work and social status or mental problems, such as depression. Under any of these situations, such sleep disturbances could manifest as insomnia, daytime sleepiness, tiredness or other symptoms, together with a decline in HRQOL. It has been reported that eveningness is associated with a greater need for sleep, less time in bed during the week compared with ideal sleep needs, more time in bed at the weekend, later bedtime and waking-up time, especially at the weekend, more irregular sleep/wake habits, and greater caffeine consumption11. Consistent with these findings, depressive status evaluated by BDI-II tended to be higher in the morning group than the evening group, although not significantly. Further large sample sized studies are required to address this issue.

The present study had certain limitations. If we could know the feature of the patients according to the classification of morning group, neither group and evening group, it could be

**MEQ and type 2 diabetes**

**Table 2** Correlation between the morningness—eveningness questionnaire and various parameters

| Independent variable | MEQ               | Non-standardized regression coefficient (B) | 95% Confidence interval | P-value |
|----------------------|-------------------|---------------------------------------------|-------------------------|---------|
| Age                  | 0.197*            | -0.111 to -0.044                             | 0.062                   |
| Body mass index      | 0.051             |                                             |                         |
| Duration of disease  | 0.042             |                                             |                         |
| Systolic BP          | 0.179             |                                             |                         |
| HbA1c (%)            | -0.238*           | -0.390 to -0.111                             | 0.030                   |
| HDL-C (mg/dL)        | 0.264**           | 0.187 to 0.330                               | 0.003                   |
| LDL-C                | -0.190            |                                             |                         |
| Triglyceride         | -0.093            |                                             |                         |

MEQ, morningness–eveningness questionnaire. n = 101. *P < 0.05, **P < 0.01, by Pearson for age, body mass index, systolic blood pressure (BP), glycated hemoglobin (HbA1c), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), or Spearman for duration of disease and triglyceride product-moment correlations.

**Table 3** Multivariate regression analysis for the morningness–eveningness questionnaire

| Independent variable | MEQ               | Non-standardized regression coefficient (B) | 95% Confidence interval | P-value |
|----------------------|-------------------|---------------------------------------------|-------------------------|---------|
| Age (years)          | 0.217             | -0.011 to -0.044                             | 0.062                   |
| HbA1c (%)            | -1.540            | -2.390 to -0.151                             | 0.030                   |
| HDL-C (mg/dL)        | 0.147             | 0.018 to 0.276                               | 0.026                   |

HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol. n = 101. Multiple linear regression analysis was carried out to determine the independent and significant variables associated with the morningness–eveningness questionnaire (MEQ). Only variables with P < 0.05 in univariate analyses were included in the model.

**DISCUSSION**

In the present study, we reported that the sleep–wake pattern of the circadian rhythm correlates with inadequate glycemic control along with low HRQOL in patients with type 2 diabetes.

The relationship between sleep duration and quality, and the associated health outcomes such as onset of cardiovascular disease, obesity, metabolic syndrome, diabetes and all-cause mortality have been widely reported and discussed1–7,24,25. These studies conclude that sleep disturbance is strongly associated with the onset of diabetes, as well as severity of glycemic control. In addition to sleep duration and quality, the circadian rhythm (sleep–wake pattern of daily life) is regarded an important component of sleep. The ‘circadian clock’ was originally established in studies on plants; which confirmed that the 24-h periodic phenomenon arises from biological oscillators that internally track the rotation of the Earth. These clocks are entrained by light, and synchronize energy-harvesting and utilization processes with the rising and setting of the sun7. Advances
useful information for the treatment. However, the study comprised only a small number of participants. Thus, we could not analyze differences among each group. Our sample was collected from a single hospital in Tokyo, and thus several potential factors affected by regional differences within Japan should be taken into account. Further studies including a larger number of participants from more than one institution are required to confirm the relationship among sleep–wake patterns, glycemic control and lifestyle factors, such as dietary habit, physical activity and smoking habit.

Despite the presence of the limitations, our data suggests that the normal alignment of feeding and activity with the environment light cycle itself is important for the maintenance of glycemic control.

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