Association of eating behaviours with diurnal preference and rotating shift work in Japanese female nurses: a cross-sectional study

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ABSTRACT
Objectives: Our study examines differences in eating behaviour between day workers and rotating shift workers, and considers whether diurnal preference could explain the differences.

Methods: Japanese female nurses were studied (39 day workers and 123 rotating shift workers, aged 21–63 years) using self-administered questionnaires. The questionnaires assessed eating behaviours, diurnal preference and demographic characteristics. The questionnaire in the Guidelines for the management of obesity disease issued by the Japan Society for the Study of Obesity was used to obtain scores for the levels of obesity-related eating behaviours, including cognition of constitution, motivation for eating, eating as a diversion, feeling of satiety, eating style, meal contents and temporal eating patterns. The Japanese version of the Morningness–Eveningness (ME) questionnaire was used to measure self-rated preference for the degree to which people prefer to be active in the morning or the evening (ME).

Results: The scores for meal contents and temporal eating patterns in rotating shift workers were significantly higher than those in day workers. The ME score of rotating shift workers was significantly lower, indicating greater eveningness/less morningness among rotating shift workers. Multivariate linear regression revealed that the ME score was significantly negatively associated with temporal eating patterns and showed a negative association with the score for meal contents at a trend level, while current work shift was not significantly correlated with the scores.

Conclusions: These results suggest that eating behaviours for rotating shift workers are associated with more unbalanced diets and abnormal temporal eating patterns and that the associations may be explained by diurnal preference rather than by rotating shift work.

INTRODUCTION
The growth in the proportion of the population aged 65 years and older leads to an increase in the social demand for nurses in medical facilities. Among them, health problems can be caused by severe working conditions such as shifting of work schedules between the day and night (ie, rotating shift work). Previous studies have suggested that rotating shift work is related to higher risks of health problems, including obesity, increase in body mass index (BMI) and adiposity with abnormal metabolism, compared with fixed day work.1–3 One of the possible factors for increasing the risks of these health problems in rotating shift workers is their altered eating behaviour.4,5 Our previous studies demonstrated that female workers who engaged in rotating shift work consumed more sugar-sweetened beverages.

Strengths and limitations of this study
- There are few studies that have clarified whether the difference of diurnal preference explains changes in eating behaviours in rotating shift workers.
- The aim of the present study was to elucidate the differences in obesity-related eating behaviour between day workers and rotating shift workers, considering the diurnal preference, among Japanese female nurses.
- Eating behaviours for rotating shift workers were associated with more unbalanced diets and more abnormal temporal eating patterns, which may be explained by the diurnal preference rather than by rotating shift work.
- These findings have important implications for the development of novel strategies for preventing excessive weight gain in rotating shift workers.
- Variables, such as eating behaviours and diurnal preference, were self-reported. Continuous monitoring of dietary intake and the sleep–wake cycle may be needed in future research.
and snacks than day workers, and that the rate of persons who reported skipping breakfast almost every day (80–100%) on days on the day shift was significantly higher in rotating shift workers compared with day workers. Recent studies by other groups have also shown that rotating shift workers had irregular meal times (eg, skipping meals or midnight snacks), and unbalanced dietary intake (eg, greater intake of fats and oils and lower intake of vegetables) when compared with day workers. However, it is unclear which aspects of obesity-related eating behaviour change in rotating shift workers and which factors contribute to the altered eating behaviours in rotating shift workers.

One plausible mechanism contributing to the altered eating behaviours in rotating shift workers is a disturbed circadian rhythm. Our previous study revealed that rotating shift workers had a significant phase delay in the 24 hours rhythm of cardiac autonomic nervous system activity compared with fixed day workers, suggesting a phase delay of the circadian rhythm among rotating shift workers. The endogenous circadian clocks, controlled by the master circadian clock in the suprachiasmatic nuclei of the hypothalamus, play a significant role in regulating a number of circadian and daily physiological rhythms, including feeding behaviour. For example, a human laboratory study showed that the circadian clock regulated hunger and appetite independently of the fasting–feeding rhythm and the sleep–wake cycle, indicating that the phase delay of the circadian clock might modify the timing of eating. Moreover, a recent study revealed that a late midpoint of nocturnal sleep was associated with increases in energy intake from undesirable dietary contents such as alcoholic beverages, confectioneries, fats and oils and meats in individuals who did not engage in night shift work. Despite these available data, which suggest a possibility of a close association between eating behaviour and the circadian clock, there are few studies that have clarified whether the association explains changes in eating behaviours in rotating shift workers.

To investigate epidemiologically the phase of the circadian clock during daily life, individual preference in the sleep–wake cycle phase (ie, diurnal preference, morningness–eveningness (ME) or chronotype), which may be different from the actual sleep–wake cycle during daily life, was assessed using the Japanese version of the Morningness–Eveningness questionnaire by Torsvall and Akerstedt. Diurnal preference (eg, evening type or morning type) are attributed to differences in the phase of the circadian clock. Therefore, the aim of the present study was to elucidate the association between rotating shift work and obesity-related eating behaviours, considering the diurnal preference, among Japanese female nurses. Eating behaviours were investigated using the questionnaire in the Guidelines for the management of obesity disease issued by the Japan Society for the Study of Obesity. Characteristics of eating behaviour which were different between overweight and normal weight individuals were extracted from a survey and compiled to produce the questionnaire. Our hypothesis was that rotating shift workers would have obesity-related eating behaviours associated with meal contents (eg, greater intake of specific nutrients) and temporal eating patterns (eg, skipping breakfast and/or late dinner), and that diurnal preference would partially explain the differences in obesity-related eating behaviours between day workers and rotating shift workers.

METHODS
Participants
The study population consisted of nurses working at a general hospital in the centre of Ome city. Ome city is located in the western side of Tokyo metropolitan area and is the fifth largest city in the metropolis. Urbanisation and industrialisation is present in the plains, while the districts in the hilly area in the western region of the city have rural populations. A total of 506 nurses were given the questionnaires by the chief nursing officer of each ward. The purpose of this study and data handling procedures were described in a covering letter with the questionnaire. Agreement to participate in this study was assumed on the basis of receipt of an anonymous questionnaire. A total of 218 nurses (43.1%; age 19–63 years) responded. Among them, 56 were excluded from the analysis because of missing data (age (n=2), current work schedules (n=6), residential status (n=1), marital status (n=2), years of experience as a rotating shift worker (n=23), smoking status (n=2), alcohol status (n=4), number of night shifts during the previous month (n=6) and the questionnaire about diurnal preference (n=15)). Since the scoring method for the questionnaire about obesity-related eating behaviour was different for men and women, we decided to exclude the small data from male nurses (n=20). As a result, 162 female nurses (39-day workers and 123 shift workers) were analysed (figure 1). Their mean total duration of experience in their current job was 12.2±10.5 (SD) years. In this study, individuals who worked fixed day shifts only (ie, 08:30–17:15 hours) were defined as ‘day workers’, while those who worked in either a two-shift system (days and nights, at 08:30–17:15 and 16:30–09:15 hours) or a forward-rotating three-shift system (days, evenings and nights, at 08:30–17:15, 16:30–01:00 and 00:45–09:15, respectively) were classified as ‘rotating shift workers’. The mean number of night shifts was 7.6±3.1 during the previous month.

Assessments
A cross-sectional study using self-administered questionnaires on demographic characteristics, diurnal preference and eating behaviour was conducted in the general hospital at the beginning of September 2012. Completed questionnaires were returned within 2 weeks. Demographic characteristics of the participants included in the questionnaire were the following: age, height,
weight, current work schedule, years of experience in the current job and as a rotating shift worker, marital status, residential status, smoking status, alcohol status and the number of night shifts during the previous month. Body mass index (BMI) was calculated on the basis of self-reported height and weight (weight/height² (kg/m²)). The Japanese version of the ME questionnaire by Torsvall and Akerstedt was used to measure self-rated preference for activity in the morning or the evening (ME). Based on seven items about daily sleep habits or preference consisting of 0–5 Likert scales, the ME score was calculated (range: 7–28 points). A lower ME score indicates a tendency for a greater preference for activity in the evening (evening type), while a higher ME score indicates a greater preference for activity in the morning (morning type). We calculated the internal consistency for the ME questionnaire using the present data, which revealed a Cronbach’s α of 0.73.

Data about habitual eating behaviours during the previous month were obtained from the response to the eating behaviour questionnaire issued by the Japan Society for the Study of Obesity, which was developed to detect obesity-related eating behaviour. The details of the contents of the questionnaire have been shown in previous studies. In brief, each of the 55 items on eating habits is rated on a four-point scale ranging from ‘strongly disagree’ to ‘strongly agree’. These items form seven separate scales: cognition of constitution (range: 6–24), motivation for eating (range: 9–36), eating as a diversion (range: 4–16), feeling of satiety (range: 6–24), eating style (range: 5–20), meal contents (range: 7–28) and temporal eating patterns (range: 8–32). Higher scores indicate more improper eating behaviour in terms of a higher probability of obesity.

Statistical analysis

After the normal distribution of variables had been tested by Kolmogorov-Smirnov test, the t-test or Mann-Whitney U test and the χ² test or Fisher’s exact test were used for continuous and categorical variables, respectively, to compare the difference in demographic characteristics, the ME score and the scores for eating behaviour between day workers and rotating shift workers. For categorical variables, residuals between the observed and expected frequencies were standardised to determine cells which were statistically different from expected values. Effect sizes for the difference in the scores of eating behaviour between the groups were assessed using Cohen’s d. Simple and multivariate linear regressions (model 1) were performed with each score for eating behaviour (meal contents or temporal eating patterns) as dependent variables, and current work schedule (0=day work, 1=rotating shift work) and the ME score (continuous, in points) as independent variables. The model was extended (model 2) using an interaction term (shift work×ME score) with the following demographic characteristics for covariate adjustment: age (continuous, in years), years of experience as a rotating shift worker (continuous, in years), marital status (0=married, 1=unmarried or divorced), residential status (0=living alone, 1=not living alone), smoking status (‘Do you smoke?’, 0=no, 1=yes), alcohol status (‘Do you drink alcohol?’, 0=no, 1=yes) and the number of night shifts during the previous month (continuous, in days). All statistical analyses were performed with an SPSS statistical software package (IBM SPSS V.22.0 for Windows, SPSS Japan). p Values <0.05 were considered statistically significant using two-tailed tests.

RESULTS

The demographic characteristics of day workers and rotating shift workers are shown in table 1. Age was significantly higher in day workers compared with rotating shift workers (p<0.05). The years of experience in the current work schedule were significantly more in day workers compared with rotating shift workers (p<0.05). Marital status and residential status were significantly associated with the current work schedule (p<0.05). The ME score for rotating shift workers was significantly lower compared with day workers (p<0.05), indicating greater eveningness/less morningness among rotating shift workers compared with day workers. This significant difference was not attenuated after controlling for age as a confounding variable (data not shown).

Scores for the obesity-related eating behaviours of day workers and rotating shift workers are shown in table 2. The scores for meal contents and temporal eating patterns significantly differed between the groups (p<0.05), indicating an unbalanced diet and more irregular timing of meals among rotating shift workers compared with day workers. Scores for other eating behaviours did not differ between the groups (p>0.05).
We examined the relationship between rotating shift work, the ME score and scores for meal contents and temporal eating patterns using simple and multivariate linear regression. Simple linear regression (table 3, figure 2) showed that rotating shift work and a lower ME score were significantly (p<0.05) associated with higher

### Table 1 Demographic characteristics of day workers and rotating shift workers

|                         | Day workers | Shift workers | p Values |
|-------------------------|-------------|---------------|----------|
| Age† (years)            | 44.2±10.9   | 34.7±8.7      | <0.001   |
| Height† ‡ (cm)          | 156.7±5.6   | 157.5±5.5     | 0.175    |
| Weight† § (kg)          | 53.4±8.3    | 53.8±8.9      | 0.784    |
| BMI† ‡ (kg/m²)          | 21.7±2.7    | 21.7±3.5      | 0.676    |
| ME score** (points)     | 20.8±3.3    | 17.1±4.0      | <0.001   |
| Years of experience     |             |               |          |
| Current work† (years)   | 17.4±12.0   | 10.6±9.2      | 0.002    |
| Rotating shift work† (years) | 11.8±10.7 | 9.7±8.7       | 0.652    |
| Number of night shifts (day/month) | 0.0±0.0 | 7.6±3.1       |          |
| Marital status††        |             |               |          |
| Married                 | 32 (82)*    | 50 (41)*      | 0.001    |
| Unmarried or divorced   | 7 (18)      | 73 (59)       |          |
| Residential status††    |             |               |          |
| Living alone            | 3 (8)       | 33 (27)*      | 0.014    |
| Not living alone        | 36 (92)*    | 90 (73)       |          |
| Smoking status          |             |               |          |
| Yes                     | 4 (10)      | 17 (14)       | 0.785    |
| No                      | 35 (90)     | 106 (86)      |          |
| Alcohol status††        |             |               |          |
| Yes                     | 21 (54)     | 51 (41)       | 0.198    |
| No                      | 18 (46)     | 72 (59)       |          |

Values are means±SD or number (%).

* p<0.05.
† Mann-Whitney U test.
‡ Shift workers, n=120.
§ Shift workers, n=118.
** A lower ME score is indicative of the evening type.
†† χ² test or Fisher’s exact test (When p<0.05, standardised residuals were determined for each cell.).
BMI, body mass index; ME score, Morningness–Eveningness score.

### Table 2 Scores for habitual eating behaviour in day workers and rotating shift workers

|                         | Normal (Ref. 23) | Day workers | Shift workers | Cohen’s d | p Values |
|-------------------------|------------------|-------------|---------------|-----------|----------|
|                         | n=39             | n=123       |               |           |          |
| Cognition of constitution† ‡ (points) | 14             | 14.3±3.4    | 13.6±3.7      | −0.19     | 0.328    |
| Motivation for eating† ‡ (points) | 18             | 19.5±4.9    | 18.8±5.6      | −0.13     | 0.384    |
| Eating as a diversion† ‡ (points) | 7              | 7.4±2.4     | 7.1±2.9       | −0.11     | 0.310    |
| Feeling of satiety† ‡ (points) | 10             | 10.9±3.1    | 11.3±3.2      | 0.13      | 0.427    |
| Eating style† ‡ (points) | 9               | 9.8±3.5     | 9.7±3.6       | −0.03     | 0.629    |
| Meal contents† ‡ (points) | 12             | 13.9±3.9    | 15.6±4.5      | 0.39      | 0.045    |
| Temporal eating patterns† ‡ (points) | 16             | 16.5±4.5    | 19.5±4.8      | 0.63      | 0.001    |

Values are means±SD.

Higher scores indicate more improper eating behaviour in terms of a higher probability of obesity: Cognition of weight and constitution, having false recognition of and assumptions about reasons for weight gain; Motivation for eating, having behavioural factors which can induce over-eating; Eating as a diversion, being subject to psychological factors which increase appetite (ie, perceived mental stress); Feeling of satiety, being prone to have an appetite and to eat as much as possible; Eating style, being prone to eat fast; Meal contents, having a preference for a high fat diet and sweets (eg, confectioneries and sweet buns); Temporal eating patterns, irregularity of timing and number of meals taken during the day and delay in timing of meals.

†t-test.
‡Mann-Whitney U test.
§Shift workers, n=122.
‖Day workers, n=38.
**Shift workers, n=119.
scores for meal contents and temporal eating patterns. Multivariate linear regression (model 1) showed that the ME score was significantly (p<0.05) associated with the score for meal contents, while the effect of rotating shift work was not (p=0.245). Regarding temporal eating patterns, the ME score was significantly associated with the score (p<0.05), while rotating shift work was attenuated to a trend level only (p=0.060). In model 2, in which the variables of demographic characteristics (p<0.05) differed significantly between the groups (ie, age, years of experience as a rotating shift worker, marital status, residential status, smoking status, alcohol status and number of night shifts during the previous month) and smoking and alcohol status were controlled, the correlations with the ME score decreased slightly but remained significantly negative (β=−0.338, p<0.001) for temporal eating patterns or at a trend level (β=−0.196, p=0.051) for meal contents, while there were no significant interactions between shift work and the ME score with the scores for meal contents and temporal eating patterns.

### Table 3  Association of current shift schedule (rotating shift work) and diurnal preference with scores for meal contents and temporal eating patterns in multivariate linear regression models

| Independent variables | Crude | Model 1 | Model 2* |
|-----------------------|-------|---------|----------|
|                       | Unstandardised coefficients | Standardised coefficients | p Values |
| Meal contents         | B     | SE      | β        | p Values |
| Rotating shift work   | 1.689 | 0.804   | 0.164    | 0.037 |
|                      | −0.223 | 0.082   | −0.210   | 0.007 |
| ME score              | 1.007 | 0.862   | 0.098    | 0.245 |
|                      | −0.183 | 0.089   | −0.172   | 0.041 |
| Rotating shift work   | 1.486 | 1.441   | 0.144    | 0.304 |
|                      | −0.208 | 0.106   | −0.196   | 0.051 |
| ME score              | 0.222 | 0.247   | 0.100    | 0.371 |
| Shift work×ME score  | 0.222 | 0.247   | 0.100    | 0.371 |
| Temporal eating patterns |         |         |         |
| Rotating shift work   | 3.211 | 0.867   | 0.284    | <0.001 |
|                      | −0.465 | 0.086   | −0.397   | <0.001 |
| ME score              | 1.698 | 0.897   | 0.150    | 0.060 |
|                      | −0.395 | 0.093   | −0.338   | <0.001 |
| Rotating shift work   | 1.426 | 1.500   | 0.126    | 0.342 |
|                      | −0.395 | 0.110   | −0.338   | <0.001 |
| ME score              | −0.061 | 0.255   | −0.025   | 0.811 |
| Shift work×ME score  | 0.222 | 0.247   | 0.100    | 0.371 |

*Adjusted by age, years of experience as a rotating shift worker, marital status, residential status, smoking status, alcohol status and number of night shifts during the previous month. Years of experience in the current work schedule were not included in model 2 because of a high level of multicollinearity (Variance inflation factor=8.101).

**Figure 2**  The relationship between the Morningness–Eveningness (ME) score and the meal contents and temporal eating patterns scores.

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DISCUSSION

Our cross-sectional study explored the differences in obesity-related eating behaviour between day workers and rotating shift workers, considering diurnal preference, among Japanese female nurses. Scores for meal contents and temporal eating patterns were significantly higher in rotating shift workers than in day workers (p<0.05). The ME score of rotating shift workers was significantly (p<0.05) lower compared with day workers, indicating greater eveningness/less morningness among rotating shift workers. Multivariate linear regression revealed that the correlation with the ME score was significantly negative (β=-0.338, p<0.05) for the score for temporal eating patterns and showed a negative association with the score for meal contents at a trend level (β=-0.196, p=0.051), while current work shift (ie, rotating shift work) was not significantly correlated with the scores. These results suggest that eating behaviours for rotating shift workers are associated with a more unbalanced diet and abnormal temporal eating patterns and that the associations could be explained by diurnal preference (eg, greater eveningness/less morningness) rather than by rotating shift work. To the best of our knowledge, this is the first study to show the associations between rotating shift work, diurnal preference and eating behaviour.

Given the fact that the evening type closely correlates with delays in the phase angle of the circadian rhythm and that the phase delay can be caused by light exposure and sleep/dark schedules during nights on the days of the night shift, our study indicates that being of greater eveningness/less morningness, or the phase delay of the circadian rhythm, may correlate with altered eating behaviour in rotating shift workers. This indication is supported by previous studies. For example, one previous study revealed that rotating shift workers showed a phase delay in the circadian rhythm compared with day workers. In addition, rotating shift workers have a tendency for more evening types compared with day workers, which is consistent with our results. We also demonstrated that a greater phase delay of the circadian rhythm was associated with a later timing of breakfast among rotating shift workers. However, causality between diurnal preference or phase angle of the circadian rhythm and altered eating behaviour could not be examined, although these may have interactive effects. It should be explored in future studies whether changes from the evening type to the morning type in diurnal preference or the phase advance of the circadian rhythm would improve eating behaviour in rotating shift workers.

Our results show that rotating shift work is associated with higher scores for meal contents and temporal eating patterns. A higher score for meal contents represents a greater preference for a high-fat diet and sweets (eg, confectioneries and sweet buns). A higher score for temporal eating patterns represents a greater irregularity in the timing and number of meals consumed and a later timing of meals. Consistent with these changes in obesity-related eating behaviour in rotating shift workers, our previous studies have shown that rotating shift workers consumed more confectioneries and sugar-sweetened beverages compared with day workers, and that the rate of skipping breakfast on days on the day shift in rotating shift workers was significantly higher compared with day workers among female nurses, in large population studies. Furthermore, the preference for a high-fat diet was confirmed following a simulated night shift.

Chronic positive energy balance is one of the well-known causes of lifestyle-related diseases which are mediated by obesity. The positive energy balance is caused by the excess dietary intake relative to energy expenditure, and can be relatively easily induced by consuming large portions of food and/or high energy-dense food such as snacks and confectioneries. In our samples, the score for meal contents was significantly and positively associated with BMI (Pearson’s correlation=0.186, p=0.031). Recently, studies have shown that the timing of meal intake (ie, skipping breakfast, greater caloric intake at dinner or later timing of dinner) also contributed to increases in BMI and the higher risk of obesity after statistically controlling for total energy intake, in individuals who do not engage in night shift work. In our samples, the score for temporal dietary patterns was significantly and positively associated with BMI (Pearson’s correlation=0.281, p=0.005). Regarding rotating shift workers, it has been found that nocturnal energy intake (00:00-04:00) on days on the night shift was associated with increases in body weight. Another recent study found that the significant effects of rotating shift work on BMI remained after controlling for daily total energy intake and daily physical activity. With regard to the physiological background of these relations, the timing of meals might change the lipid metabolism. Considered together with higher scores for meal contents and temporal eating patterns in rotating shift workers (table 2) compared with those scores of day workers and normal-weight women, the timing of meal intake, as well as meal contents, may be an important factor in prevention and improvement of obesity and lifestyle-related diseases in rotating shift workers and this should be examined in the future. In particular, studies on the effects of the timing of meal intake on days on the night shift on BMI may be needed.

The means of BMI for day workers and rotating shift workers in our samples were not significantly different and fell in the normal range of BMI. However, it should be noted that age was significantly higher in day workers, and that years of experience of rotating shift work were significantly longer in day workers compared with rotating shift workers (table 1). Previous studies have indicated that the duration of rotating shift work may have a positive relationship with overweight/obesity and increasing BMI, indicating that there may be cumulative effects of rotating shift work on BMI in
day workers (table 1). In addition, in Japan, more than 20% of women in their 20s are overweight (BMI<18.5 kg/m²). This percentage is much higher than in most developed countries. Also, in epidemiological studies using a larger sample size, mean BMI scores for rotating shift workers in Japanese female nurses (eg, Tada et al; 21.6±3.2 kg/m², n=1579; Lee et al 22.3±3.0 kg/m², n=18 108) were in the normal range, while this value in other countries was higher than the normal range (eg, Australian and New Zealand nurses; 26.4±5.3 kg/m², n=320; Canadian nurses; 25.7 ±5.1 kg/m², n=411)26. Considered together with the higher percentage of body fat levels, especially at lower BMI, in Japanese compared with Caucasians and African-Americans, Japanese female nurses engaging in rotating shift work should be careful of gains in BMI and/or the percentage of body fat as well as BMI.

There were several limitations to this study. First, variables, such as eating behaviours and diurnal preference, were self-reported. Continuous monitoring of dietary intake and the sleep–wake cycle may be needed in future research. Second, the effect of other rotating shift systems on eating behaviours remains unclear. Morikawa et al24 reported that people working on a rotating two-shift system had a higher risk of increased BMI compared with people working on a rotating three-shift system, indicating that the type of rotating shift system might affect eating behaviour. Third, the current participants were all Japanese female nurses at a particular city hospital. Studies in other populations may be required to clarify to what extent the present results can be generalised. Fourth, the unbalanced sample size between day and shift workers may have contributed to a decrease in the statistical power to detect significant differences in dietary behaviours between the groups, even though we could not detect differences of a negligible effect size (absolute Cohen’s d<0.15) or a lower range of a small effect size (0.15≤absolute Cohen’s d<0.02) using statistical tests. Finally, potential confounding variables, such as habitual sleep duration, daily variation in sleep timing, psychological stress and sensations of fatigue, may not have been fully considered.

Conclusions

In conclusion, eating behaviours for rotating shift workers were associated with more unbalanced diets and more abnormal temporal eating patterns, which may be explained by the diurnal preference rather than by rotating shift work. These findings have important implications for the development of novel strategies for preventing excessive weight gain in rotating shift workers.

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Contributors

TY, VK, ON, JQ, RT and FT designed the research. TY, AS, YY, AH and YT conducted the research. TY, YT and FT analysed the data. TY, VK and FT wrote the manuscript. TY had primary responsibility for the final content. All the authors read and approved the final manuscript.

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Competing interests

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