Effects of Work Stress and Period3 Gene Polymorphism and Their Interaction on Sleep Quality of Non-Manual Workers in Xinjiang, China: A Cross-Sectional Study

Juan Wang 1,2, Jiwen Liu 2, Huiling Xie 2 and Xiaoyan Gao 1,2,*

1 Xinjiang Key Laboratory of Special Environment and Health Research, Urumqi 830011, China; 13139638739@163.com
2 Department of Public Health, Xinjiang Medical University, Urumqi 830011, China; liujwendr@163.com (J.L.); sherilyn@tom.com (H.X.)
* Correspondence: 15199142607@163.com

Abstract: Work stress has been found to be associated with sleep quality in various occupational groups, and genetic factors such as variable number tandem repeat polymorphism in the Period3 (Per3) gene also influence the circadian sleep-wake process. Therefore, the present study aimed to evaluate the sleep quality status of non-manual workers in Xinjiang, China and to analyse the effects of work stress and Per3 gene polymorphism and their interaction on sleep quality. A cluster sampling method was used to randomly select 1700 non-manual workers in Urumqi, Xinjiang. The work stress and sleep quality of these workers were evaluated using the Effort–Reward Imbalance Inventory (ERI) and the Pittsburgh Sleep Quality Index (PSQI). Next, 20% of the questionnaire respondents were randomly selected for genetic polymorphism analysis. The polymerase chain reaction-restriction fragment length polymorphism technique was used to determine Per3 gene polymorphism. The detection rate of sleep quality problems differed between the different work stress groups (p < 0.05), suggesting that non-manual workers with high levels of work stress are more likely to have sleep quality problems. Regression analysis revealed that the Per3 gene (OR = 3.315, 95% CI: 1.672–6.574) was the influencing factor for poor sleep quality after adjusting for confounding factors, such as occupation, length of service, education, and monthly income. Interaction analysis showed that Per34/5,5/5 × high work stress (OR = 2.511, 95% CI: 1.635–3.855) had a higher risk of developing sleep quality problems as compared to Per34/4 × low work stress after adjusting for confounding factors. The structural equation modelling showed no mediating effect between work stress and Per3 gene polymorphism. The results of this study show that both work stress and Per3 gene polymorphism independently affect sleep quality of nonmanual workers from Xinjiang, and the interaction between these two factors may increase the risk of sleep quality problems. Therefore, to improve sleep quality, individuals with genetic susceptibility should avoid or reduce as much as possible self-stimulation by work-related exposures such as high levels of external work stress.

Keywords: work stress; sleep quality; Per3 gene polymorphism; non-manual workers

1. Introduction

Sleep is an integral part of maintaining the physiological functions of the body and is essential for our physical and mental health. Good sleep quality can reduce the risk of adverse diseases such as cardiovascular diseases, diabetes, mental and cognitive disorders, and accidental injuries [1]. Poor sleep quality is usually characterized by difficulties in falling asleep and maintaining sleep [2], which can easily lead to significant discomfort and thus affect daily life. The prevalence of sleep quality problems in occupational groups varies by region, with 58.2% of employees over the age of 18 years in the United States reporting sleep problems in the past month [3], and 30–45% and 40.2% of corporate employees and civil servants in Japan reporting sleep-related issues, respectively [4,5]. Sleep quality
problems are becoming a major concern in today’s society, and the chronic occurrence of sleep problems increases the risk of many diseases and places a heavy burden on health services worldwide [6].

Sleep quality problems in the occupational population can lead to increased absenteeism and reduced productivity, which can affect the ability to work [7] and can even lead to workplace accidents, thereby putting workers’ own lives at risk [8]. Non-manual workers are a specific type of occupational group whose physical and mental health, literacy, and quality of life can greatly affect economic and social development. With the rapid development of technology, the proportion of work based on mental ability is gradually increasing, which has minimised the need to perform manual work and thus has greatly improved work efficiency and industrial performance. However, fierce business competition in the industry has also overloaded the workforce with a heavy work schedule, thereby creating an imbalance between work capacity, coping resources, and demand, which can affect physical and mental health and consequently influence sleep quality.

Factors affecting sleep quality are multifaceted. In addition to demographic characteristics such as gender and age, work-related factors such as job stress and effort–reward imbalance may also affect sleep quality [9,10]. In early studies, most researchers in China and abroad focused on the effects of environmental exposure factors on sleep quality in occupational populations, and work stress, as one of the exposure factors, is a common cause of sleep difficulties. Work stress, also known as work stress and occupational strain, is the physical and psychological response of an individual due to a perceived incongruity between the demands and conditions of work and his or her own abilities and resources [11]. Many studies have found an association between work stress and insomnia, sleep disturbance, and poor sleep quality [12–14]. A non-randomised pilot study of adults concluded that prolonged exposure to stress with high work demands and low work rewards could affect sleep quality [15]. Stressors resulting from the imbalance between high work demands and low rewards were found to be associated with shorter sleep duration and insomnia [16,17]. Work stress can affect sleep quality by acting on the body through factors such as stress response and stress coping. When stress is excessive and lasts for too long, it can cause an imbalance in the body’s neuroendocrine regulation, with the occurrence of adverse reactions such as anxiety and depression [18], ultimately leading to sleep problems. All these results suggest a close link between work stress and sleep quality.

With the rapid development of molecular biology, studies have shown that both genetic and environmental factors affect sleep quality [19]. The system that regulates biological rhythms in the body is called the biological clock, which plays a leading role in regulating circadian rhythms. The Period3 (Per3) gene, one of the core genes of the biological clock, is located on chromosome 1p36, with a total length of 60,475 bp and 21 exons and having four or five tandem repeats (variable number tandem polymorphism [VNTP]) in exon 18. This region has a series of predicted phosphorylation sites and is polymorphically expressed in the population. Various studies have reported that Per3 gene polymorphism is strongly associated with sleep physiology and individual circadian preferences [20,21]. However, some studies have reported no evidence of an association between Per3 gene polymorphism and sleep quality and daytime preferences [22]. In a Japanese study, a variable number tandem repeat (VNTR) genotyping of the Per3 gene in subjects revealed no significant correlation between VNTR and ‘morning and evening’ preferences [23]. Therefore, the relationship between Per3 gene polymorphism and sleep quality needs to be further investigated.

Previous studies have reported the relationship between work stress, Per3 gene polymorphism, and sleep quality; however, fewer studies have examined the effects of work stress, Per3 gene polymorphism, and their interaction on sleep quality in non-manual workers. Therefore, the present study was conducted to analyse the effects of work stress and Per3 gene polymorphism on sleep quality of non-manual workers by combining epidemiological surveys and molecular biology experiments to further explore the effects of the interaction of these two factors on sleep quality and provide a theoretical basis for
better improving the sleep quality of non-manual workers and improving their physical and mental health and quality of life.

2. Materials and Methods

2.1. Subjects

This study was conducted in Urumqi, Xinjiang, China, and the survey period was from January 2021 to December 2021. The study protocol was approved by the Ethics Committee of Xinjiang Medical University, and all participants voluntarily completed a written informed consent form prior to the survey. Occupational groups in the first and second major categories (administrative state organizations, party and mass organizations, enterprises, institutions, professional, and technical personnel, etc.) were selected as the target population according to the Dictionary of Occupational Classification of the People’s Republic of China. A cluster sampling method was used to select non-manual workers in Urumqi, Xinjiang for the questionnaire survey.

Inclusion and exclusion criteria: Active workers aged 20–60 years with ≥1 year of service who were willing to cooperate with the completion of the questionnaire and the collection of blood samples were included in the study. Workers with a history of traumatic brain injury, hypertension, coronary heart disease, diabetes mellitus, thyroid disease, asthma, chronic bronchitis, and tumours that may cause sleep disorders; a history of other psychiatric disorders (schizophrenia, depression, mania, etc.) that may cause sleep disorders; and having other serious physical illnesses, sleep apnoea syndrome, episodic sleeping sickness, restless leg syndrome, etc. were excluded based on the past history survey. Workers who had been treated for their sleep quality problems with medication or hospitalisation within the last 3 months were also excluded.

Before administering the questionnaire, the investigator questioned the respondents according to the inclusion and exclusion criteria and administered the questionnaire to those who met the inclusion criteria and did not meet the exclusion criteria. Finally, a total of 1700 questionnaires were distributed; after excluding incomplete questionnaires and those with less than 80% of the content filled, the number of valid questionnaires was 1458, with an effective response rate of 85.76%. Twenty percent of the questionnaire respondents; i.e., 292 participants, were randomly selected for the polymorphism detection experiment. After eliminating samples with substandard concentration and purity of the extracted DNA, a total of 251 samples were tested for Per3 gene polymorphism, and the 251 participants were matched 1:1 using gender and age as the matching factors. A total of 113 pairs were successfully matched, resulting in a case-control study of 226 participants.

2.2. Methods

2.2.1. Assessment of Work Stress

A self-administered Effort–Reward Imbalance Inventory (ERI) based on the Effort–Reward Imbalance model was developed by Siegrist in Germany [24]. Currently, the ERI model is the dominant model for assessing work stress in many countries and is used to describe the relationship between workplace characteristics and individual psychological well-being [25,26]. The questionnaire consists of three dimensions: effort, reward, and overcommitment, with 23 items. Of these, the first six items rate ‘effort’, the middle 11 items rate ‘reward’ and the last six items rate ‘overcommitment’. In addition, the first 17 items are scored on a 5-point scale and the last 6 items are scored on a 4-point scale. The effort–reward imbalance index is calculated as: the score of effort/(the score of reward × C), where C is the number of effort items over the number of reward items, i.e., 6/11. If ERI > 1, the person is a high effort-low reward person (high work stress); if ERI ≤ 1, the person is a low effort-high reward person (low work stress).

2.2.2. Assessment of Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI), developed by Dr Buyee in 1989 [27], was used to assess sleep quality. This scale is currently more commonly used in psychiatric
clinical assessment abroad because of its ease of use in terms of survey methods and its high correlation with the results of polysomnographic electroencephalography (EEG) tests [28]. The scale is used to evaluate the quality of sleep in the previous month and consists of 19 self-rated and 5 other-rated entries (not involved in scoring), which include 7 sub-items of subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, hypnotic use, and daytime dysfunction. Each entry is scored on a scale of 0 to 3, and the cumulative score is the total PSQI score, which ranges from 0 to 21, with higher scores indicating poorer sleep quality. In accordance with international standards, the threshold for defining a sleep quality problem is 5. In this study, a total PSQI score of ≥5 was defined as poor sleep quality.

2.2.3. Genotyping

Genomic DNA (gDNA) was extracted using the Blood Genomic DNA Extraction System (non-centrifugal column type) kit (Tiangen Biotech, Beijing, China). Per3 gene polymorphism analysis was performed using the polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) technique. The total volume of each reaction mixture was 25 µL, and gDNA was amplified using PCR instruments (MyCycler, Bio-Rad, Hercules, CA, USA). The PCR reaction conditions were as follows: pre-denaturation at 94 °C for 5 min, followed by denaturation at 94 °C for 40 s, annealing at 58 °C for 30 s, extension at 72 °C for 40 s for a total of 30 cycles, followed by final extension at 72 °C for 12 min. The PCR amplification products were detected by 1.5% agarose gel electrophoresis and observed on a gel imager. The primers and genotypes for the Per3 gene are listed in Tables 1 and 2, respectively.

Table 1. Primer sequences.

| Gene | Sequence (5’-3’) | Amplified Fragment Length |
|------|------------------|--------------------------|
| Per3 | F TGT CTT TTC ATG TGC CCT TAC TT | 347/401 |
|      | R TGT CTG GCA TTG GAG TTT GA      |            |

Table 2. Genotype information of Per3.

| Gene | Enzyme Fragment Length | Genotype |
|------|------------------------|----------|
| Per3 | 347 bp                  | 4/4      |
|      | 347 bp, 401 bp         | 4/5      |
|      | 401 bp                 | 5/5      |

2.2.4. Quality Control

Before the survey was formally conducted, the investigators were professionally trained to learn the content of the questionnaire, the survey language, and the survey method. During the survey, the surveyor clarified the purpose, content, and significance of the survey to the respondents and explained in detail the requirements for completing the questionnaire; the surveyor also attempted to seek the cooperation of the respondents and respected their wishes as far as possible during the survey. The questionnaires were centrally distributed and collected on the spot. The questionnaires were reviewed, and those that were less than 80% completed were excluded and those that passed the survey were numbered. For the polymorphism detection experiment, the researchers wore a white laboratory apron, mask, and gloves before entering the laboratory. The researchers received safety training from the laboratory supervisor in advance of the experiment and familiarised themselves with the laboratory equipment and its operating procedures. During the experiments, the researchers were required to strictly observe the instructions of the laboratory supervisor and the safety regulations of the laboratory. The blood samples were carefully marked; the reagents were prepared in strict accordance with the instructions, and the names of the reagents were checked carefully. To avoid cross-contamination, reagents and samples were stored properly.
2.2.5. Statistical Analysis

Data entry was performed using Epidata 3.1 (The Epidata Association, Odense, Denmark), and data analysis was performed using the statistical software SPSS 26.0 (IBM, Armonk, NY, USA). Comparisons of sleep quality problem detection rates and Hardy–Weinberg genetic equilibrium tests for the Per3 gene and comparisons of genotypes between the sleep quality groups were performed using chi-square tests. The PSQI scores were statistically expressed as $\bar{x} \pm s$, and two independent samples $t$-test was used for comparison between the groups. Multiple regression analysis was used to determine the effect of the interaction between work stress and Per3 gene polymorphism on sleep. Pathway analysis between gene–environment–sleep quality was performed using SPSS Amos 24.0 (IBM). Subjects for gene polymorphism analysis were matched using propensity score matching (PSM) with a matching error of 0.02. The significance level was taken as $\alpha = 0.05$ (two-sided).

3. Results

3.1. Detection of Sleep Quality Problems among Non-Manual Workers with Different Demographic Characteristics

The results of the survey showed that 1038 of 1458 non-manual workers had sleep quality problems, with a detection rate of 71.19%. The detection rate of sleep quality problems among non-manual workers differed between the smoking groups, but the difference in the detection rate was not statistically significant for the remaining demographic characteristics ($p > 0.05$). The detection rate of sleep quality problems was higher in non-manual workers who smoked (77.5%) than in non-smokers (69.9%) (Table 3).

| Characteristics                               | Number | Poor Sleep Quality (n, %) | $\chi^2$ | p-Value |
|-----------------------------------------------|--------|---------------------------|---------|---------|
| Gender                                        |        |                           |         |         |
| Male                                          | 566    | 398 (70.32)               | 0.346   | 0.557   |
| Female                                        | 892    | 640 (71.75)               |         |         |
| Age/(years old)                               |        |                           |         |         |
| <30                                           | 456    | 320 (70.18)               | 0.772   | 0.680   |
| 30–40                                         | 683    | 485 (71.01)               |         |         |
| >40                                           | 319    | 233 (73.04)               |         |         |
| Education level                               |        |                           |         |         |
| College and below                             | 141    | 105 (74.47)               | 0.816   | 0.366   |
| Undergraduate and above                       | 1317   | 933 (70.84)               |         |         |
| Occupation                                    |        |                           |         |         |
| Teacher                                       | 120    | 84 (70.00)                | 0.831   | 0.975   |
| Civil Servants                                | 307    | 222 (72.31)               |         |         |
| Medical staff                                 | 102    | 70 (68.62)                |         |         |
| Finance, economic operations staff            | 116    | 83 (71.55)                |         |         |
| Administrative staff                          | 239    | 173 (72.38)               |         |         |
| Electrical, construction engineer             | 574    | 406 (70.73)               |         |         |
| Professional title                            |        |                           |         |         |
| Elementary                                    | 836    | 608 (72.73)               | 3.525   | 0.172   |
| Intermediate                                  | 458    | 311 (67.90)               |         |         |
| Advanced                                      | 164    | 119 (72.56)               |         |         |
| Length of service/(years)                     |        |                           |         |         |
| <5                                           | 331    | 235 (71.00)               | 3.361   | 0.339   |
| 5~                                           | 372    | 252 (67.74)               |         |         |
| 10~                                          | 314    | 230 (73.25)               |         |         |
| ≥15                                          | 441    | 321 (72.79)               |         |         |
Table 3. Cont.

| Characteristics            | Number | Poor Sleep Quality (n, %) | \(\chi^2\) | p-Value |
|----------------------------|--------|---------------------------|------------|---------|
| Marital status             |        |                           |            |         |
| Unmarried                  | 480    | 350 (72.92)               | 1.036      | 0.309   |
| Married                    | 978    | 688 (70.35)               |            |         |
| Monthly income/(yuan)      |        |                           |            |         |
| \(\leq 5000\)              | 593    | 430 (72.51)               | 0.848      | 0.357   |
| >5000                      | 865    | 608 (70.29)               |            |         |
| Smoking                    |        |                           |            |         |
| No                         | 1205   | 842 (69.88)               | 5.881      | 0.015   |
| Yes                        | 253    | 196 (77.47)               |            |         |
| Alcohol consumption        |        |                           |            |         |
| No                         | 938    | 661 (70.47)               | 0.673      | 0.412   |
| Yes                        | 520    | 377 (72.50)               |            |         |
| Total                      | 1458   | 1038 (71.19)              |            |         |

3.2. Association between Work Stress and Sleep Quality

The distribution of sleep quality among non-manual workers differed between the work stress groups, and the differences were statistically significant \((p < 0.05)\). The number of non-manual workers with sleep quality problems was significantly higher in the high work stress group than in the low work stress group. This finding suggests that non-manual workers with high levels of work stress are more likely to have sleep quality problems (Table 4).

Table 4. Condition of sleep quality between different work stress groups (n, %).

| Work Stress | Number | Non-Poor Sleep Quality | Poor Sleep Quality | \(\chi^2\) | p-Value |
|-------------|--------|------------------------|--------------------|------------|---------|
| Low         | 805    | 301 (37.39)            | 504 (62.61)        | 64.589     | <0.001  |
| High        | 653    | 119 (18.22)            | 534 (81.78)        |            |         |
| Total       | 1458   | 420 (28.81)            | 1038 (71.19)       |            |         |

3.3. Association between Work Stress and the Dimensions of Sleep Quality and PSQI Score

The Pittsburgh Sleep Quality Index (PSQI) contains subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, hypnotic use, and daytime dysfunction, and then the final sum of all dimensions is the total PSQI score. The PSQI scores on all dimensions differed between the different work stress groups, except for the sleep efficiency score, and the differences were statistically significant \((p < 0.05)\). All PSQI scores in the high work stress group were higher than those in the low work stress group, thus suggesting that high work stress is associated with poorer sleep quality (Table 5).

Table 5. Conditions of PSQI scores between different work stress groups (\(\bar{x} \pm s\)).

| Work Stress | PSQI Scores | Subjective Sleep Quality | Sleep Latency | Sleep Duration | Sleep Efficiency | Sleep Disturbances | Daytime Dysfunction |
|-------------|-------------|--------------------------|---------------|----------------|------------------|--------------------|---------------------|
| Low \((n = 805)\) | 5.68 ± 2.84 | 1.08 ± 0.69              | 1.00 ± 0.87   | 0.77 ± 0.64    | 0.40 ± 0.75      | 0.99 ± 0.56        | 1.45 ± 0.91         |
| High \((n = 653)\) | 7.24 ± 3.12 | 1.37 ± 0.75              | 1.24 ± 0.99   | 0.99 ± 0.69    | 0.43 ± 0.78      | 1.19 ± 0.63        | 2.01 ± 0.90         |
| \(t\)       | −9.871      | −7.719                   | −4.956        | −6.404         | −0.579           | −6.424             | −11.850             |
| \(p\)-value | <0.001      | <0.001                   | <0.001        | <0.001         | 0.563            | <0.001             | <0.001              |
3.4. Hardy–Weinberg Genetic Equilibrium Test

The Hardy–Weinberg genetic equilibrium test was used to analyse the distribution of genotypes at the 54 bp-VNTR locus of the Per3 gene. The results showed that the actual and expected values of each genotype in this study were in good agreement, with no statistically significant differences \((p > 0.05)\); this finding suggests that the gene frequencies of the 226 subjects were in genetic equilibrium in accordance with the law of genetic equilibrium (Table 6).

| Table 6. Hardy–Weinberg equilibrium test. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Gene  | Genotype | Actual Value | Expected Value | \(\chi^2\) | \(p\)-Value |
|-------|-----------|--------------|----------------|--------|----------|
| Per3  | 4/4       | 157          | 158.9          |        |          |
|       | 4/5       | 65           | 61.2           | 0.871  | 0.647    |
|       | 5/5       | 4            | 5.9            |        |          |

3.5. Distribution of Sleep Quality across Genotypes and Alleles of the Per3 Gene

The differences in the distribution of sleep quality among genotypes and alleles at the 54bp-VNTR locus of the Per3 gene were statistically significant. \((p < 0.05)\) (Table 7).

| Table 7. The distribution of sleep quality across genotypes and alleles of the Per3 gene. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Gene  | Genotype | N | Non-Poor Sleep Quality \((n, \%)\) | Poor Sleep Quality \((n, \%)\) | \(\chi^2\) | \(p\)-Value |
|-------|----------|---|-----------------|-----------------|--------|----------|
| Per3  | 4/4      | 157 | 87 (55.41) | 70 (44.59) | 6.287 | 0.043     |
|       | 4/5      | 65  | 24 (36.92)  | 41 (63.08)  |        |           |
|       | 5/5      | 4   | 2 (50.00)   | 2 (50.00)   |        |           |
|       | 4        | 379 | 198 (52.24) | 181 (47.76) | 4.721 | 0.030     |
|       | 5        | 73  | 28 (38.36)  | 45 (61.64)  |        |           |

3.6. Logistic Regression Analysis of Work Stress, Per3 Gene, and Poor Sleep Quality

Of the 226 experimental study subjects, the sleep quality status (Poor sleep quality and non-poor sleep quality) served as the dependent variable, while work stress and Per3 gene genotypes were considered to be independent variables. Genotype 4/5 and genotype 5/5 were grouped together due to the low number of genotypes 5/5. Multivariate logistic regression analysis was performed. The results showed that both work stress \((OR = 3.088, 95\% CI: 1.639–5.820)\) and Per3 gene \((OR = 3.315, 95\% CI: 1.672–6.574)\) were influencing factors for poor sleep quality after adjusting for confounding factors, such as occupation, length of service, education, and monthly income (Table 8).

| Table 8. Logistic regression analysis of work stress, Per3 gene, and poor sleep quality. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variables | \(\beta\) | SE  | Wald | \(p\)-Value | OR \((95\% CI)\) |
| Work stress | 1.128 | 0.323 | 12.165 | <0.001 | 3.088 \((1.639, 5.820)\) |
| Per3 gene | 1.199 | 0.349 | 11.777 | 0.001 | 3.315 \((1.672, 6.574)\) |

\(OR\), odds ratio; \(CI\), confidence interval.

3.7. Interaction of Work Stress and Per3 Gene Polymorphism on Sleep Quality in Non-Manual Workers

3.7.1. Logistic Regression Analysis of the Interaction between Work Stress and Per3 Gene Polymorphism on Sleep Quality

The interaction terms for work stress and Per3 gene genotype were further introduced into the multiple regression model. The results showed that, after adjusting for confounding factors, such as occupation, length of service, education, and monthly income, Per3\(^{4/5, 5/5}\) × high work stress \((OR = 2.511, 95\% CI: 1.635–3.855)\) had a higher risk of developing sleep quality problems as compared to Per3\(^{4/4}\) × low work stress. This finding
suggested that there is an interaction between work stress and Per3 gene polymorphism, and this interaction increases the risk of developing sleep quality problems (Table 9).

**Table 9. Interaction between work stress and Per3 gene polymorphism on poor sleep quality.**

| Comparison Group | β   | Wald | p-Value | OR (95% CI) |
|------------------|-----|------|---------|-------------|
| Per3 × work stress | -   | -    | -       | Ref         |
| Per3<sup>4/4</sup> × low work stress | -   | -    | -       | -           |
| Per3<sup>4/5,5/5</sup> × high Work stress | 0.921 | 17.705 | <0.001 | 2.511 (1.635–3.855) |

3.7.2. Structural Equation Modelling of the Relationship between Work Stress, Per3 Gene, and Sleep Quality

Pathway analysis between work stress, the Per3 gene, and sleep quality based on structural equation modelling was performed on 226 experimental study subjects. The reference evaluation criteria for the structural equation model were $\chi^2/df < 3.0$, RMSEA (root-mean-square error of approximation) <0.08, AGFI (adjusted goodness-of-fit index) >0.9, and GFI (goodness-of-fit index) >0.9. The following model was obtained through continuous revision of the model in accordance with the principles of accuracy and simplicity (Figure 1). The model fitted closest to the reference standard among all the models, thus indicating a good fit ($\chi^2/df = 1.716$ (41.184/24), RMSEA = 0.056, AGFI = 0.928, GFI = 0.962), and the model was statistically significant ($p < 0.05$).

As shown in Figure 1, in this survey, a direct effect was observed between work stress and sleep quality ($p < 0.05$) with a path coefficient of 0.47, thus suggesting a strong association between work stress and sleep quality among the non-manual workers in Xinjiang.
Urumqi, Xinjiang. A direct effect was also observed between Per3 gene polymorphism and sleep quality \((p < 0.05)\), with a pathway coefficient of 0.14, thus suggesting an association between Per3 gene polymorphism and sleep quality among the non-manual workers in Urumqi, Xinjiang; however, no direct effect was observed between Per3 gene polymorphism and work stress \((p > 0.05)\), with a pathway coefficient of \(-0.07\).

4. Discussion

The present study aimed to evaluate the sleep quality of non-manual workers in Urumqi, Xinjiang, China, and to analyse the effects of work stress and Per3 gene polymorphism on sleep quality to further explore the effects of their interaction on sleep. The results of the present study showed that 1038 of 1458 non-manual workers had sleep quality problems, with a detection rate of 71.19%, which shows that the sleep quality problems of non-manual workers in Xinjiang are more serious. Currently, sleep quality problems have become a more common health problem. Sleep quality problems can cause adverse effects such as drowsiness and fatigue, easily trigger psychological problems such as anxiety and depression, and increase the risk of cardiovascular diseases such as hypertension and coronary heart disease and death [29–33]. Therefore, it is particularly important to develop targeted preventive and intervention measures for non-manual workers in Xinjiang to improve their sleep quality.

Previous studies have shown that higher job demands, lower job satisfaction, and work-related psychological factors such as the effort–reward imbalance are associated with the development of sleep quality problems [34]. Several epidemiological studies have shown that work stress is a major risk factor for poor sleep quality [35–37]. Work stress is a work-related factor that negatively affects the physical and mental health of people who are exposed to high pressure environments for long periods of time. While moderate stress can motivate workers, excessive stress can have a significant impact on their physical and mental health and quality of life, leading to the suboptimal states of lethargy, drowsiness, and anxiety [38,39]; sleep disorders [40–42]; onset of various diseases [43,44]; increased health care and insurance costs; and increased costs for national health services. Currently, a number of domestic and international studies on different occupational groups have shown that work stress directly affects their sleep quality [42,45]. Gao et al. [46] obtained the same results in their study on the sleep quality of doctors. In daily work and life, individuals are prone to sleep problems if they are not relieved of their negative somatic reactions and psychological stress caused by work-related factors such as work stress and burnout. Although work stress does not cause specific occupational diseases, it can affect the physical and mental health of occupational groups, thus increasing the risk of mental disorders, sleep disorders, and cardiovascular disease [47]. Previous studies have also suggested that some alterations in the nervous system, such as dysregulation of the individual autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, could explain the effects of work stress on poor sleep quality [48]. Kalmbach et al. [49] reported that changes in cortical activity as a response to stress exposure increased the likelihood of future sleep quality problems. Another study [50] suggested that stress is associated with reduced parasympathetic activation, which may have a detrimental effect on voluntary arousal during sleep, which in turn leads to shorter sleep duration.

The circadian biological clock adjusts its circadian profile in response to changes in external environmental stimuli. As a key member of the feedback loop of the biological clock, several studies have reported an association between Per3 gene polymorphisms and human circadian phenotypes, including early and late night preferences and sleep homeostasis regulation [51,52]. Per3 VNTR variants are associated with circadian preferences, nonvisual responses to light, and brain and cognitive responses to sleep deprivation/circadian rhythm dysregulation. Per35/5 carriers are more likely to go to bed early and wake up earlier than Per34/4 carriers [53–55]. Cheng et al. [56] reported that the Per35/5 genotype was associated with an increased risk of daytime sleep disturbance in night shift workers. An association between Per3 gene polymorphism and sleep quality was also found in a
study on sleep quality in Chinese oil workers [57]. Animal studies on this topic have shown that Per3 protein loss of function in Per3 knockout mice is associated with altered sleep homeostasis [58,59]. In the current study, regression analysis revealed that the Per3 gene (OR = 3.315, 95% CI: 1.672–6.574) was the influencing factor for poor sleep quality. The reason for this finding may be related to differences in the Per3 VNTR genotype in relation to sleep duration and homeostatic response to sleep loss [20].

The occurrence of sleep quality problems is often influenced by a combination of genetic and environmental factors. In the current study, both work stress and Per3 gene polymorphisms were found to affect sleep quality in non-manual workers. To further investigate the potential interaction between work stress and Per3 gene polymorphism in predicting the risk of developing sleep quality problems, the effect of their interaction on sleep was further analysed. Logistic regression analysis showed that, compared to Per3^4/4 × low work stress, Per3^4/5,5/5 × high work stress (OR = 2.511, 95% CI: 1.635–3.855) had a higher risk of developing sleep quality problems as compared to Per3^4/4 × low work stress. This finding suggested that an interaction occurs between work stress and Per3 gene polymorphism and that this interaction increases the risk of developing sleep quality problems. This result is consistent with the findings of a recent study [48]. A study in Greece identified an interaction between Per3 gene and stressful events in the risk of sleep changes in women [60]. Further pathway analysis between gene–environment–sleep quality based on structural equation modelling revealed a direct association between work stress, Per3 gene, and sleep quality; however, no direct association was observed between work stress and Per3 gene, i.e., there was no mediating effect between them. This implies that work stress may not affect sleep quality by affecting the expression of the Per3 gene. Combining the results of the regression analysis and the pathway analysis, the present study showed an interaction between work stress and the Per3 gene, but no mediating effect between them.

This study used a cross-sectional approach to investigate the effects of work stress, Per3 gene polymorphism, and their interaction on sleep quality. Both work stress and Per3 gene polymorphism were found to affect sleep quality in non-manual workers, and there may be a potential interaction in the risk of sleep quality problems, i.e., there is a cumulative effect of work stress and Per3 gene on sleep quality, but this interaction may not be achieved through the effect of work stress on the expression of the Per3 gene. The results of this study have practical implications for improving the sleep quality of non-manual workers in Xinjiang. For individual non-manual workers, it is important to pay attention to the psychological changes caused by their stress in time to prevent sleep quality problems as early as possible; for employers, they should arrange the work tasks of workers reasonably to avoid exposing employees to high work stress environmental stress.

The present study also has some limitations. First, this study relied solely on the PSQI questionnaire to investigate the sleep quality of non-manual workers and was based on respondents’ self-reported sleep, which was too subjective and one-sided. In the future, objective indicators such as polysomnograms could be added to the sleep quality survey to better and more comprehensively analyse the sleep quality of non-manual workers. Second, when investigating the potential mechanisms of gene–environment interactions on sleep, only the effect of Per3 gene–environment interaction on sleep was studied. In the future, the Per3 gene and other biological clock genes can be combined to construct gene-gene and gene-environment interactions to investigate the potential mechanisms in the sleep–wake process.

5. Conclusions

The current study showed that both work stress and Per3 gene polymorphism affect sleep quality in non-manual workers in Xinjiang. Moreover, while the findings suggest that there is an interaction between work stress and Per3 gene polymorphism on sleep quality and that the interaction may increase the risk of poor sleep quality, this effect may not be achieved by a mediating effect. Therefore, avoiding or reducing the stimulation of
work-related exposure factors such as high external work stress can effectively reduce the occurrence of sleep quality problems. On the basis of the above results, relevant experts should further develop and improve management systems for non-manual workers and allocate work tasks rationally, and also actively conduct psychological seminars for non-manual workers to provide adequate humanistic care and social support to promote the development of their physical and mental health.

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References
1. Chaput, J.P.; Dutil, C.; Featherstone, R.; Ross, R.; Giangregorio, L.; Saunders, T.J.; Janussen, I.; Poitras, V.J.; Kho, M.E.; Ross-White, A.; et al. Sleep duration and health in adults: An overview of systematic reviews. Appl. Physiol. Nutr. Metab. 2020, 45, S218–S231. [CrossRef] [PubMed]
2. Barros, M.; Lima, M.G.; Ceolim, M.F.; Zancanella, E.; Cardoso, T. Quality of sleep, health and well-being in a population-based study. Rev. Saude Publica 2019, 53, 82. [CrossRef] [PubMed]
3. Knudsen, H.K.; Ducharme, L.J.; Roman, P.M. Job stress and poor sleep quality: Data from an american sample of full-time workers. Soc. Sci. Med. 2007, 64, 1997–2007. [CrossRef]
4. Doi, Y.; Minowa, M.; Tango, T. Impact and correlates of poor sleep quality in japanese white-collar employees. Sleep 2003, 26, 467–471. [CrossRef] [PubMed]
5. Saijo, Y.; Chiba, S.; Yoshioka, E.; Nakagi, Y.; Ito, T.; Kitaoka-Higashiguchi, K.; Yoshida, T. Synergistic interaction between job control and social support at work on depression, burnout, and insomnia among japanese civil servants. Int. Arch. Occup. Environ. Health 2015, 88, 143–152. [CrossRef] [PubMed]
6. Tan, X.; van Egmond, L.T.; Cedernaes, J.; Benedict, C. The role of exercise-induced peripheral factors in sleep regulation. Mol. Metab. 2020, 42, 101096. [CrossRef] [PubMed]
7. Van Laethem, M.; Beckers, D.G.; Kompier, M.A.; Dijksterhuis, A.; Geurts, S.A. Psychosocial work characteristics and sleep quality: A systematic review of longitudinal and intervention research. Scand. J. Work Environ. Health 2013, 39, 535–549. [CrossRef]
8. Parkes, K.R. Work environment, overtime and sleep among offshore personnel. Accid. Anal. Prev. 2017, 99, 383–388. [CrossRef]
9. Akerstedt, T. Psychosocial stress and impaired sleep. Scand. J. Work Environ. Health 2006, 32, 493–501. [CrossRef]
10. Soehner, A.M.; Harvey, A.G. Prevalence and functional consequences of severe insomnia symptoms in mood and anxiety disorders: Results from a nationally representative sample. Sleep 2012, 35, 1367–1375. [CrossRef]
11. Kourmousi, N.; Darviri, C.; Varvogli, L.; Alexopoulos, E.C. Teacher stress inventory: Validation of the greek version and perceived stress levels among 3,447 educators. Psychol. Res. Behav. Manag. 2015, 8, 81–88. [CrossRef] [PubMed]
12. Dong, H.; Zhang, Q.; Sun, Z.; Sang, F.; Xu, Y. Sleep disturbances among Chinese clinical nurses in general hospitals and its influencing factors. BMC Psychiatry 2017, 17, 241. [CrossRef] [PubMed]
13. Magnusson Hanson, L.L.; Chungkham, H.S.; Akerstedt, T.; Westerlund, H. The role of sleep disturbances in the longitudinal relationship between psychosocial working conditions, measured by work demands and support, and depression. Sleep 2014, 37, 1977–1985. [CrossRef] [PubMed]
14. Ota, A.; Masue, T.; Yasuda, N.; Tsutsumi, A.; Mino, Y.; Ohara, H.; Ono, Y. Psychosocial job characteristics and insomnia: A prospective cohort study using the demand-control-support (DCS) and EffortReward imbalance (ERI) job stress models. Sleep Med. 2009, 10, 1112–1117. [CrossRef] [PubMed]
15. Halonen, J.I.; Lallukka, T.; Pentti, J.; Stenholm, S.; Rod, N.H.; Virtanen, M.; Salo, P.; Kivimäki, M.; Vahtera, J. Change in job strain as a predictor of change in insomnia symptoms: Analyzing observational data as a Non-randomized Pseudo-Trial. Sleep 2017, 40, zsw007. [CrossRef]
16. Ota, A.; Masue, T.; Yasuda, N.; Tsutsumi, A.; Mino, Y.; Ohara, H. Association between psychosocial job characteristics and insomnia: An investigation using two relevant job stress models—the demand-control-support (DCS) model and the effort-reward imbalance (ERI) model. Sleep Med. 2005, 6, 353–358. [CrossRef]
17. Utsugi, M.; Saijo, Y.; Yoshioka, E.; Horiyaka, N.; Sato, T.; Gong, Y.; Kishi, R. Relationships of occupational stress to insomnia and short sleep in Japanese workers. Sleep 2005, 28, 728–735. [CrossRef]
18. Hu, Y.; Visser, M.; Kaiser, S. Perceived stress and sleep quality in midlife and later: Controlling for genetic and environmental influences. Behav. Sleep Med. 2020, 18, 537–549. [CrossRef]
19. Genderson, M.R.; Rana, B.K.; Panizzon, M.S.; Grant, M.D.; Toomey, R.; Jacobson, K.C.; Xian, H. Genetic and environmental influences on sleep quality in middle-aged men: A twin study. J. Sleep Res. 2013, 22, 519–526. [CrossRef]
20. Hida, A.; Kitamura, S.; Katayose, Y.; Kato, M.; Ono, H.; Kadotani, H.; Uchiyama, M.; Ebisawa, T.; Inoue, Y.; Kamei, Y.; et al. Screening of clock gene polymorphisms demonstrates association of a per3 polymorphism with morningsness-eveningness preference and circadian rhythm sleep disorder. Sci. Rep. 2014, 4, 6309. [CrossRef]
21. Maire, M.; Reichert, C.F.; Gabel, V.; Viola, A.U.; Strobel, W.; Krebs, J.; Landolt, H.P.; Bachmann, V.; Cajochen, C.; Schmidt, C. Sleep ability mediates individual differences in the vulnerability to sleep loss: Evidence from a per3 polymorphism. Cortex 2014, 52, 47–59. [CrossRef] [PubMed]
22. Barclay, N.L.; Eley, T.C.; Mill, J.; Wong, C.C.Y.; Zavos, H.M.S.; Archer, S.N.; Gregory, A.M. Sleep quality and diurnal preference in late adolescence and circadian rhythm sleep disorder. J. Sleep Res. 2019, 82, 1005–1013. [CrossRef]
23. Ge, J.; He, J.; Liu, Y.; Zhang, J.; Pan, J.; Zhang, X.; Liu, D. Effects of effort-reward imbalance, job satisfaction, and work engagement on self-rated health among healthcare workers. BMC Public Health 2021, 21, 195. [CrossRef]
24. Fortunatti, C.P.; Palmeiro-Silva, Y.K. Effort-reward imbalance and burnout among ICU nursing staff: A cross-sectional study. Occup. Med. 2018, 68, 686–689. [CrossRef] [PubMed]
25. Hida, A.; Kitamura, S.; Kadotani, H.; Uchiyama, M.; Ebisawa, T.; Inoue, Y.; Kamei, Y.; Mishima, K. PER3 lack of association between variable number tandem repeat and circadian rhythm sleep-wake disorders. Hum. Genom. Var. 2018, 5, 17. [CrossRef] [PubMed]
26. Buyssse, D.J.; Reynolds, C.F.; Monk, T.H.; Berman, S.R.; Kupfer, D.J. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Res. 1989, 29, 193–213. [CrossRef]
27. Min, A.; Hong, H.C.; Son, S.; Lee, T. Sleep, fatigue and alertness during working hours among rotating-shift nurses in Korea: An observational study. J. Nurs. Manag. 2021, 29, 2647–2657. [CrossRef]
28. Linton, S.J.; Kecklund, G.; Franklin, K.A.; Leissner, L.C.; Sivertsen, B.; Svensson, A.C.; Hansson, S.O.; Sundin, O.; Hetta, J.; et al. The effect of the work environment on future sleep disturbances: A systematic review. Sleep Med. Rev. 2018, 41, 3–38. [CrossRef]
29. Ran, L.; Chen, Q.; Zhang, J.; Tu, X.; Tan, X.; Zhang, Y. The multimorbidity of hypertension and osteoarthritis and relation with sleep quality and hyperlipemia/hyperglycemia in China’s rural population. Sci. Rep. 2021, 11, 17046. [CrossRef] [PubMed]
30. Buysse, D.J.; Reynolds, C.F.; Monk, T.H.; Berman, S.R.; Kupfer, D.J. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Res. 1989, 29, 193–213. [CrossRef]
31. Mehra, R.; Marcus, G.M. Novel insights into sleep disorder and atrial fibrillation risk: More than sleep apnea. Chest 2019, 156, 421–423. [CrossRef] [PubMed]
32. Linton, S.J.; Kecklund, G.; Franklin, K.A.; Leissner, L.C.; Sivertsen, B.; Svensson, A.C.; Hansson, S.O.; Sundin, O.; Hetta, J.; et al. The effect of the work environment on future sleep disturbances: A systematic review. Sleep Med. Rev. 2018, 23, 10–19. [CrossRef] [PubMed]
33. Garefelt, J.; Platt, L.G.; Hyde, M.; Hanson, L.L.M.; Westerlund, H.; Akerstedt, T. Reciprocal relations between work stress and insomnia symptoms: A prospective study. J. Sleep Res. 2020, 29, e12949. [CrossRef] [PubMed]
34. Yang, B.; Wang, Y.; Cui, F.; Huang, T.; Sheng, P.; Shi, T.; Huang, C.; Lan, Y.; Huang, Y. Association between insomnia and job stress: A meta-analysis. Sleep Breath. 2018, 22, 1221–1231. [CrossRef]
35. Han, Y.; Yuan, Y.; Zhang, L.; Fu, Y. Sleep disorder status of nurses in general hospitals and its influencing factors. Psychiatr. Danub. 2016, 28, 176–183. [PubMed]
36. Gärtner, F.R.; Nieuwenhuijsen, K.; van Dijk, F.J.; Sluiter, J.K. The impact of common mental disorders on the work functioning of nurses and allied health professionals: A systematic review. Int. J. Nurs. Stud. 2010, 47, 1047–1061. [CrossRef]
37. Boyle, D.A. Occupational stress in oncology nurse caregiving: Caring for ourselves. Clin. J. Oncol. Nurs. 2015, 19, 499. [CrossRef] [PubMed]
38. Li, Y.; Cao, Z.; Wu, S.; Wang, C.; He, S.; Dong, Y.; Zhang, X. Association of job stress, clockgene polymorphism and their interaction with poor sleep quality. J. Sleep Res. 2021, 30, e13133. [CrossRef] [PubMed]
39. Iwasaki, S.; Deguchi, Y.; Inoue, K. Association between work role stressors and sleep quality. Occup. Med. 2018, 68, 171–176. [CrossRef] [PubMed]
42. Zare, R.; Choobineh, A.; Keshavarzi, S. Association of amplitude and stability of circadian rhythm, sleep quality, and occupational stress with sickness absence among a gas company employees—a cross-sectional study from Iran. *Saf. Health Work* **2017**, *8*, 276–281. [CrossRef] [PubMed]

43. Wu, W.; Tsai, S.; Wang, C.; Lin, Y.; Wu, T.; Shih, T.; Liou, S. Professional driver’s job stress and 8-year risk of cardiovascular disease: The taiwan bus driver cohort study. *Epidemiology* **2019**, *30*, S39–S47. [CrossRef] [PubMed]

44. Zaitseva, N.S.; Siziakina, L.P. The influence of acute professional stress on the immune system. *Allergy* **2018**, *73*, 469.

45. Deng, X.; Liu, X.; Fang, R. Evaluation of the correlation between job stress and sleep quality in community nurses. *Medicine* **2020**, *99*, e18822. [CrossRef] [PubMed]

46. Gao, X.; Ge, H.; Jiang, Y.; Lian, Y.; Zhang, C.; Liu, J. Relationship between Job stress and 5-HT2A Receptor Polymorphisms on Self-Reported Sleep Quality in Physicians in Urumqi (Xinjiang, China): A Cross-Sectional Study. *Int. J. Environ. Res. Pub. Health* **2018**, *15*, 1034. [CrossRef] [PubMed]

47. Kim, C.J.; Schlenk, E.A.; Kang, S.W.; Park, J.B. Effects of an internet-based lifestyle intervention on cardio-metabolic risks and stress in korean workers with metabolic syndrome: A controlled trial. *Patient Educ. Couns.* **2015**, *98*, 111–119. [CrossRef] [PubMed]

48. Peng, X.; Li, J.; Han, B.; Zhu, Y.; Cheng, D.; Li, Q.; Du, J. Association of occupational stress, period circadian regulator 3 (PER3) gene polymorphism and their interaction with poor sleep quality. *J. Sleep Res.* **2022**, *31*, e13390. [CrossRef]

49. Kalmbach, D.A.; Anderson, J.R.; Drake, C.L. The impact of stress on sleep: Pathogenic sleep reactivity as a vulnerability to insomnia and circadian disorders. *J. Sleep Res.* **2018**, *27*, e12710. [CrossRef]

50. Mellman, T.A.; Bell, K.A.; Abu-Bader, S.H.; Kobayashi, I. Neighborhood stress and autonomic nervous system activity during sleep. *Sleep* **2018**, *41*, zsy059. [CrossRef] [PubMed]

51. Archer, S.N.; Robilliard, D.L.; Skene, D.J.; Smits, M.; Williams, A.; Arendt, J.; von Schantz, M. A length polymorphism in the circadian clock gene Per3 is linked to delayed sleep phase syndrome and extreme diurnal preference. *Sleep* **2003**, *26*, 413–415. [CrossRef]

52. Ebisawa, T.; Uchiyama, M.; Kajimura, N.; Mishima, K.; Kamei, Y.; Katoh, M.; Watanabe, T.; Sekimoto, M.; Shibui, K.; Kim, K.; et al. Association of structural polymorphisms in the human period3 gene with delayed sleep phase syndrome. *EMBO Rep.* **2001**, *2*, 342–346. [CrossRef] [PubMed]

53. Pereira, D.S.; Tufik, S.; Louzada, F.M.; Benedito-Silva, A.A.; Lopez, A.R.; Lemos, N.A.; Korczak, A.L.; D’Almeida, V.; Pedrazzoli, M. Association of the length polymorphism in the human Per3 gene with the delayed sleep-phase syndrome: Does latitude have an influence upon it? *Sleep* **2005**, *28*, 29–32. [PubMed]

54. Viola, A.U.; Chellappa, S.L.; Archer, S.N.; Pugin, F.; Gotz, T.; Dijk, D.J.; Cajochen, C. Interindividual differences in circadian rhythmicity and sleep homeostasis in older people: Effect of a per3 polymorphism. *Neurobiol. Aging* **2012**, *33*, 1010.e17. [CrossRef] [PubMed]

55. Weiss, C.; Woods, K.; Filipowicz, A.; Ingram, K.K. Sleep quality, sleep structure, and per3 genotype mediate chronotype effects on depressive symptoms in young adults. *Front. Psychol.* **2020**, *11*, 2028. [CrossRef] [PubMed]

56. Cheng, P.; Tallent, G.; Burgess, H.J.; Tran, K.M.; Roth, T.; Drake, C.L. Daytime sleep disturbance in night shift work and the role of period3. *J. Clin. Sleep Med.* **2018**, *14*, 393–400. [CrossRef] [PubMed]

57. Ning, L.; Shi, L.Y.; Tao, N.; Li, R.; Jiang, T.; Liu, J.W. Effects of occupational stress and circadian clock gene polymorphism on sleep quality of oil workers in xinjiang, china. *Med. Sci. Monit.* **2020**, *26*, e924202. [CrossRef]

58. Hasan, S.; van der Veen, D.R.; Winsky-Sommerer, R.; Dijk, D.J.; Archer, S.N. Altered sleep and behavioral activity phenotypes in per3-deficient mice. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **2011**, *301*, R1821–R1830. [CrossRef]

59. van der Veen, D.R.; Archer, S.N. Light-dependent behavioral phenotypes in PER3-deficient mice. *J. Biol. Rhythm.* **2010**, *25*, 3–8. [CrossRef]

60. Antypa, N.; Mandelli, L.; Nearchou, F.A.; Vaiopoulos, C.; Stefanis, C.N.; Serretti, A.; Stefanis, N.C. The 3111T/C polymorphism interacts with stressful life events to influence patterns of sleep in females. *Chronobiol. Int.* **2012**, *29*, 891–897. [CrossRef]