Abstract We have previously reported that there may be a relationship between bowel habits including functional constipation (FC) and irritable bowel syndrome and sleep health. However, our previous studies were based on only subjective parameters by self-reported questionnaire. The aim of this study is to investigate the relationship between bowel habits such as FC and sleep health using objective parameters. Sleep health was assessed by actigraphy measurement and bowel habits by fecal flora analysis. The FC and control subjects, whose bowel habits were defined at Rome II, were recruited from evaluated respondents in our previous study directed at middle-aged Japanese women, ten FC and ten control subjects participating in this study. Wake after sleep onset (WASO) and WASO (%) (WASO/total sleep time multiplied by 100) in FC subjects was significantly longer and greater than those in control subjects, respectively. Average activity during sleep in FC subjects was significantly higher than that in control subjects. FC had no effect on total sleep time. Bifidobacterium is broadly accepted to be useful intestinal bacteria for human health and one of the indices showing that the intestinal environment is in a desirable condition. Bifidobacterium counts per gram of wet feces and proportion in total bacterial cell counts in FC subjects were significantly lower than those in control subjects. In conclusion, these results suggest that corresponding to low Bifidobacterium counts and proportion, sleep in FC subjects may be worse than that in control subjects. There may be a relationship between bowel habits and sleep health. Bowel habits such as FC might be a risk factor for sleep disorders. J Physiol Anthropol 27(3): 145–151, 2008 http://www.jstage.jst.go.jp/browse/jpa2 [DOI: 10.2214/jpa2.27.145]

Keywords: sleep health, bowel habits, functional constipation, Bifidobacterium, actigraphy

Introduction

Sleep is influenced and modulated by a number of factors. It is well known that in particular, environmental factors such as the light-dark cycle, meal timing and exercise play an important role in sleep regulation as time cues. On the other hand, previous reports have demonstrated that gastrointestinal motility has circadian rhythms as well as sleep-wake cycles. The motor activities of the stomach (Goo et al., 1987), small intestine (Keller et al., 2001) and large intestine (Furukawa et al., 1994; Rao et al., 2001) are high during the day and low during the night. In addition, it has been reported that muramyl peptides, which are derived from the cell walls of intestinal bacteria, peptidoglycan enhance slow wave sleep (SWS) [stage 3 and 4 non-rapid eye movement sleep (NREM sleep)] via IL-1β (Krueger et al., 1982; Johannsen et al., 1991; Imeri et al., 1997; Pabst et al., 1999). Since bacterial growth in the colon is influenced by intestinal motility (Yoshimatsu et al., 2002), it is possible that bowel habits also play a role in sleep health.

To date, there have been a few reports studying the relationship between bowel habits and sleep health. For example, it has been shown that poor sleep leads to higher gastrointestinal symptoms on the following day among women with irritable bowel syndrome (IBS) which is a common gastrointestinal disorder producing abdominal pain, bloating and disturbed defecation (Jarrett et al., 2000). Also, Kumar et al. (1992) reported that patients with IBS have markedly increased rapid eye movement sleep and their sleep patterns are abnormal. Although these reports suggest a relationship between IBS and sleep health, they are not enough to determine whether bowel habits are related to sleep health. Recently, we have epidemiologically investigated the relationship between bowel habits including functional constipation (FC) and IBS and sleep health in adult women living in the Tokyo metropolitan area (age 20–65 years, n=1397) using a self-reported questionnaire (Ono et al., 2004, 2005). These reports have demonstrated that sleep health in FC and IBS subjects are worse than that in control subjects,
suggesting that there may be a relationship between bowel habits and sleep health. However, our previous works were based on only subjective parameters in the assessment of sleep health and bowel habits. Objective parameters could help to elucidate the relationship more precisely.

The aim of this study is to investigate the relationship between bowel habits such as FC and sleep health using objective parameters that assess sleep health and bowel habits. Sleep health in FC and control subjects was assessed by actigraphy that monitors activity-based sleep and bowel habits by fecal flora analysis. Although actigraphy cannot assess sleep stages as polysomnography (PSG) does, its use is easy and it can continuously measure sleep-wake schedules and sleep quality in a subject’s natural sleeping environment throughout long periods (American Sleep Disorders Association, 1995; Rotem et al., 2003). Therefore, actigraphy is useful as a tool of sleep assessment.

Methods

Subjects

FC and control candidates were first recruited from evaluated respondents in our previous study that examined the relationship between bowel habits including FC and IBS and sleep health in middle-aged Japanese women (Ono et al., 2004). In the previous study, we used a self-reported questionnaire including five sleep-health risk factors (Tanaka and Shirakawa, 2004): (1) sleep maintenance problems, (2) parasomnia-like problems, (3) sleep apnea, (4) difficulty waking up and (5) difficulty initiating sleep. The sum of each score of these risk factors was calculated as the Sleep-Health Risk Index and it was used as a primary evaluating item of sleep health (for details, see Tanaka and Shirakawa, 2004). The Sleep-Health Risk Index indicates that the higher the score, the worse the sleep health. Therefore, FC candidates were recruited in order of high score on the Sleep-Health Risk Index, and control candidates in order of low score. After recruiting, the present bowel habits and sleep health of candidates were reexamined using the self-reported questionnaire which was employed in our previous study (Ono et al., 2004). When the candidates had different bowel habits or sleep health from those examined previously, they were excluded from the candidates.

Bowel habits were defined by the Rome diagnostic criteria for functional gastrointestinal disorder (Rome II) (Thompson et al., 1999). Control candidates had good daily defecation habits and reported no gastrointestinal symptoms either in the past or at the time of recruitment.

Women receiving medication for any disease, through not including self-medication for FC, were excluded from the candidates. Moreover, women having a daily drinking habit were also excluded from candidates, as drinking is well known to affect and impair normal gastrointestinal motility (Bouchoucha et al., 1991; Persson et al., 1991; Papa et al., 1998).

Table 1  Subjects’ profiles

<table>
<thead>
<tr>
<th></th>
<th>FC (n=10)</th>
<th>control (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>49.2±2.9</td>
<td>50.5±4.1</td>
</tr>
<tr>
<td>BNI</td>
<td>22.7±3.9</td>
<td>22.9±2.4</td>
</tr>
</tbody>
</table>

FC: functional constipation, BMI: body mass index. The values are mean±SD.

When recruited candidates gave informed consent to participate in this study, they were selected as subjects. Eventually, ten FC and ten control subjects participated in this study. The subjects’ profiles are presented in Table 1. The experimental design was approved by the Ethics Committee of Kao Corporation.

Experimental protocol

This study consisted of an actigraphy measurement period of 7 days and, after that, a fecal collection period of 14 days.

Actigraphy measurement

All subjects wore an actigraph (A.M.I., USA), a watch-size device placed on their non-dominant wrist. The actigraph was programmed to run for 7 consecutive days and to record for 24 h. Activity measured by the actigraph was distinguished, according to the algorithm of Cole et al. (1992), into ‘sleep’ or ‘wake’. Sleep onset time was defined as the time when ‘sleep’ continuing for more than 10 min began after 22:00, and sleep offset time as the time when ‘wake’ stably continuing for more than 10 min began before 10:00 the next morning. Sleep period time (SPT) is the time from sleep onset time to sleep offset time. When subjects were involved in intense exercise such as playing tennis, as well as during bathing, the device was removed. All subjects were encouraged to maintain a regular schedule of activity during the actigraphy measurement period. Data analysis was performed for 5 nights during ordinary weekdays because, in many cases, life habits are different at the weekend. The analyzed items are as follows: wake time after sleep onset (WASO), total sleep time (TST) [TST=SPT-WASO], WASO during the first half of the sleep period, WASO during the second half of the sleep period, WASO (%) (WASO/TST multiplied by 100), WASO (%) during the first half of the sleep period, WASO (%) during the second half of the sleep period, average activity during the sleep period, average activity during the first half of the sleep period, average activity during the second half of the sleep period, sleep time during the awake period from sleep offset time to 12:00 and sleep time during the awake period from 12:00 to sleep onset time. The data for each subject was calculated as the mean of values of the 5 nights.

Fecal flora analysis

After the actigraphy measurement period, feces from all subjects were collected once during the fecal collection period of 14 days. Collected feces were kept at 4°C and anaerobically...
transported to an ‘intestinal flora laboratory’ (Calpis co., Ltd., Kanagawa, Japan) which undertakes consignment analysis of intestinal flora, and the fecal flora was analyzed according to the method of Mitsuoka et al. (1976). Analyzed intestinal bacterial species are as follows: Enterobacteriaceae, Streptococcus, Staphylococcus, Lactobacillus, Bifidobacterium, Eubacterium, Bacteroidaceae, Clostridium and Vellonella. Bacterial cell counts per gram of wet feces were calculated and converted into a common logarithmic equivalent. Also, the proportion of each type of bacterium in the total bacterial cell counts was evaluated.

Statistics
The data are expressed as mean±SD. The differences in the data were evaluated by Student’s t-test. P values of less than 0.05 were taken as statistically significant.

Results

Actigraphy
In FC subjects, sleep onset time and sleep offset time were 0:10±1:13 and 6:48±0:35, respectively. In control subjects, sleep onset time and sleep offset time were 23:45±0:54 and 6:10±0:29, respectively. There were no significant differences in sleep onset time and sleep offset time between FC and control subjects. WASO in FC subjects was significantly longer than that in control subjects (FC: 16.78±10.39 min, control: 5.25±4.78 min, p<0.01, Fig. 1A). WASO (%) in FC subjects was also significantly greater than that in control subjects (FC: 3.9±2.1%, control: 1.3±1.2%, p<0.01, Fig. 1B). WASO and WASO (%) during the first half of the sleep period in FC subjects were significantly longer and greater than those in control subjects, respectively (FC: 11.30±7.10 min, 5.0±2.9%; control: 1.70±1.50 min, 0.9±0.8%; p<0.001, Fig. 2). There were no significant differences in WASO and WASO (%) during the second half of the sleep period between FC and control subjects (data not shown). Average activities during the sleep period and during the first half of the sleep period in FC subjects were significantly higher than those in control subjects (during the sleep period, FC: 9.26±1.61, control: 6.88±2.00, p<0.01; during the first half of the sleep period, FC: 10.06±4.10, control: 5.96±1.86, p<0.001). There was no significant difference in average activity during the second half of the sleep period between FC and control subjects (data not shown). FC had no effect on TST (FC: 396.8±50.5 min, control: 385.3±42.0 min). Sleep time during the awake period from sleep offset time to 12:00 in FC subjects tended to be longer than that in control subjects (FC: 147

Fig. 1 WASO and WASO (%) in FC and control subjects. WASO (A) and WASO (%) (B) in FC subjects were significantly longer and greater than those in control subjects, respectively. WASO: wake after sleep onset, FC: functional constipation. The values are mean±SD. **p<0.01, significantly different from the control.

Fig. 2 WASO and WASO (%) during the first half of the sleep period in FC and control subjects. WASO (A) and WASO (%) (B) during the first half of the sleep period in FC subjects were significantly longer and greater than those in control subjects, respectively. WASO: wake after sleep onset, FC: functional constipation. The values are mean±SD. ***p<0.001, significantly different from the control.
17.7±24.4 min, control: 3.2±2.5 min, p=0.078). There was no significant difference in sleep time during the awake period from 12:00 to sleep onset time between FC and control subjects (data not shown).

**Fecal flora**

Table 2 shows fecal flora in FC and control subjects. *Bifidobacterium* counts per gram of wet feces (in log_{10}) in FC subjects were significantly lower than those in control subjects (p<0.05). There were no significant differences in bacterial counts of species other than *Bifidobacterium* between FC and control subjects. The *Bifidobacterium* proportion in total bacterial cell counts in FC subjects was significantly lower than that in control subjects ( FC: 16.5±14.5%, control: 35.8±20.7%, p<0.05, Fig. 3). In contrast, the *Bacteroidaceae* proportion in total bacterial cell counts in FC subjects was significantly higher than that in control subjects (FC: 62.6±23.4%, control: 37.4±20.5%, p<0.05, Fig. 3).

**Discussion**

This study investigated the relationship between bowel habits such as FC and sleep health using actigraphy measurement and fecal flora analysis. In the present study, we showed that WASO and WASO (%) in FC subjects were longer and greater than those in control subjects, respectively, suggesting that sleep health in FC subjects may be worse than that in control subjects. Moreover, counts and proportions of *Bifidobacterium*, which is broadly accepted to be a useful bacterium for human health and one of the indices showing that the intestinal environment is in a desirable condition, were significantly lower in FC subjects than those in control subjects, indicating that bowel habit in FC subjects may be worse than that in control subjects. Our previous studies have reported that there may be a relationship between bowel habits, including FC and IBS, and sleep health using a self-reported questionnaire (Ono et al., 2004, 2005). The results in the present study are in agreement with our previous finding. Therefore, this study seems to support the concept that there may be a relationship between bowel habits and sleep health. Together with our previous reports, it is suggested that bowel habits such as FC might be a risk factor for sleep disorders. In other words, bowel habits, namely intestinal motility, might be a factor participating in sleep regulation.

Our previous studies using subjective parameters have reported that the score of ‘sleep maintenance problems’ in FC subjects is higher than that in control subjects (Ono et al., 2004, 2005). A high score with regard to ‘sleep maintenance problems’ implies that sleep maintenance is wrong. In

![Fig. 3 Proportions of each bacterial species in total bacteria cell counts. The *Bifidobacterium* proportion in FC subjects was significantly lower than that in control subjects. The *Bacteroidaceae* proportion in FC subjects was significantly higher than that in control subjects. FC: functional constipation. The values are mean. *p<0.05, significantly different from the control.](image-url)
addition, in our previous studies, it has been reported that there are no statistical differences in subjective SPT, sleep onset time, and sleep offset time between FC and control subjects (Ono et al., 2004, 2005). On the other hand, in the present study, sleep in FC subjects was more fragmented compared with that in control subjects because WASO and WASO (%) in FC subjects were longer and greater than those in control subjects, respectively. This result suggests that sleep maintenance in FC subjects may be impaired. Moreover, FC had no effects on TST, sleep onset time, or sleep offset time assessed by actigraphy, which will be because social life is restricted by numerous social systems and standards. These observations are also in agreement with our previous findings. In the present study, sleep time during the awake period from sleep offset time to 12:00, but not sleep time during the awake period from 12:00 to the sleep onset time, in FC subjects tended to be longer than that in control subjects, suggesting that in FC subjects there might be substantial, compensatory daytime nap in the morning. If so, this also appears to support the notion that sleep in FC subjects may be worse than that in control subjects. Consistent with the results of WASO and WASO (%), average activities during the sleep period and during the first half of the sleep period in FC subjects were significantly higher than those in control subjects. It is suggested that the depth of sleep in FC subjects might be lighter, in particular during the first half of the sleep period, than that in control subjects; FC subjects might have a little SWS during the first half of the sleep period when SWS primarily appears.

It is well known that growth hormone (GH) secretion is elicited by onset of SWS immediately after sleep onset (Van Cauter et al., 1998). Although GH is required for normal growth and metabolic homeostasis in children, GH secretion occurs throughout life and is known to have profound effects on anabolism, lipolysis, and carbohydrate metabolism. Thus, GH secretion is important not only for children but also for adults. It has been found that GH secretion is inhibited by sleep fragmentation (Van Cauter et al., 1992; Spath-Schwalbe et al., 1995), indicating that awakenings interrupting sleep are an inhibitory factor of GH secretion. In the present study, we showed that sleep in FC subjects may be fragmented. Furthermore, WASO and WASO (%) during the first half, but not during the second half of the sleep period in FC subjects were significantly longer and greater than those in control subjects, respectively. It is suggested that in FC subjects the first half of the sleep period, which corresponds to the timing of GH secretion, may have greater sleep fragmentation. As mentioned above, we also suggest that FC subjects might have a little SWS during the first half of the sleep period. Therefore, GH secretion during sleep in FC subjects might be impaired. Obstructive sleep apnea (OSA) is characterized by sleep fragmentation due to repetitive arousal from sleep in the adult patient (Sullivan and Issa, 1985) and Gianotti et al. (2002) have reported that OSA causes impairment of GH secretion and sensitivity. The question of whether the ability of GH secretion in FC subjects is impaired is a very interesting one for future study.

Muramyl peptides act as a somnogenic substance and it is thought that they are derived from the cell walls of intestinal bacteria, peptidoglycan, via the digestive action of macrophages (Krueger and Majde, 1994; Pabst et al., 1999). It has been reported that muramyl peptides are produced from gram-positive bacteria such as Bacillus subtilis (Vermeulen and Gray, 1984) and Staphylococcus aureus (Johannsen et al., 1991) by macrophage digestion. In the present study, counts and proportion of Bifidobacterium gram-positive bacteria in FC subjects were significantly lower than those in control subjects who are good sleepers. Therefore, Bifidobacterium might supply muramyl peptides under normal conditions and participate in normal sleep throughout the production of muramyl peptides. At present, whether Bifidobacterium can produce muramyl peptides to induce sleep is unclear. However, it has been reported that peptidoglycan including muramyl peptide fragments, prepared from Bifidobacterium thermophilum, has an immunopotentiation effect (Sasaki et al., 1987, 1994), demonstrating that it has physiological activity.

It is found that muramyl peptides have a close association with the appearance of SWS (Krueger et al., 1982; Johannsen et al., 1991; Imeri et al., 1997; Pabst et al., 1999), and that SWS mainly appears during the first half of the sleep period. In the present study, we showed that there may be a relationship between bowel habits and sleep health, and that SWS in FC subjects might be impaired. Therefore, the sleep character expressed by muramyl peptides might explain why FC subjects had greater WASO during the first half of the sleep period; WASO during the first half of the sleep period might be increased due to the impairment of SWS induced by muramyl peptides in FC subjects.

Finally, this study has a number of limitations. We investigated the relationship between FC and the sleep health of middle-aged women in the present study. It has been reported that climacteric disorder profoundly related to menopausal status, in particular severe hot flashes, is associated with insomnia (Ohayon, 2006). In the present study, we did not take the influence of climacteric disorder on sleep health into consideration. Because subjects receiving medication for any disease were excluded from this study, it appears likely that subjects having severe climacteric disorder are not included in this study. Thus, it is possible that the influence of climacteric disorder on this study is small. However, it seems that we cannot completely rule out the influence of climacteric disorder on sleep health, because the possibility remains that subjects with mild and moderate climacteric disorder are included in this study. In addition, the present results should be considered preliminary because this study is limited by its small sample size. Therefore, in order to understand the precise participation of bowel habits in sleep health, further studies, including intervention studies, will be needed.

In conclusion, this study suggests that (1) corresponding to
low *Bifidobacterium* counts and proportion, sleep assessed by actigraphy in FC subjects may be worse than that in control subjects; (2) FC subjects may have greater sleep fragmentation compared with control subjects; (3) there may be a relationship between bowel habits and sleep health; and (4) bowel habits such as FC might be risk factors for sleep disorders.

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