A stainless steel cylinder (diameter, 18 mm) was implanted as a microdrive receptacle at appropriate locations on the skull. A hollow rod (diameter, 15 mm) for head fixation was attached to the skull using dental acrylic. During recording sessions, the head of the animal was fixed rigidly to the frame of the monkey chair using the head holder, and a hydraulic microdrive (MO95-C; Narishige, Tokyo) was attached to the implanted cylinder. Elgiloy electrodes (Suzuki and Azuma 1976) were used for the neuronal recordings. Neuronal activity was recorded from both the banks and lips of the principal sulcus, the inferior convexity and the arcuate areas of the LPFC of both hemispheres of the three monkeys. The action potentials were passed through a window discriminator and converted into square-wave pulses. During the recordings, we changed the task approximately every 50 trials between the outcome-expectancy and spatial-memory tasks, and/or the task version and/or the type of reward. We monitored the position and movement of the eyes of the animals using an infrared eye-camera system (R-21C-A; RMS, Hirosaki, Japan; sampling rate = 4 ms) during the task performance after neuronal recording had been completed.

### Data analysis

Impulse data were displayed as raster displays and frequency histograms. Non-parametric statistics were used for the analysis. Data from the first few trials after changing the task and/or type of reward were omitted from the analysis. Initially, the magnitudes of neuronal activity in relation to the task events (pre-instruction, instruction presentation, delay, go signal, key-press response, reward delivery and omission of reward) were compared with the control activity (2–3 s before the instruction) within the same reward block of trials, separately for reward and no-reward trials in the outcome-expectancy task, and for left and right trials in the spatial-memory task, using the Mann–Whitney *U*-test. The criterion for statistical significance was set at $P < 0.05$ (two-tailed). The magnitude of neuronal activity in relation to each task event was compared between reward and no-reward trials in the outcome-expectancy task and between left and right trials in the spatial-memory task using the *U*-test. Different reward blocks were compared using the Kruskal–Wallis *H*-test. The *U*-test was used for post hoc analysis when a statistically significant difference was observed using the *H*-test. Reaction time (RT) data (that is, the time between the presentation of the go-signal and the key-press response by the monkey) were also examined using non-parametric *U* and *H* tests. In addition, we used the $\chi^2$ and Fisher's exact probability tests to examine the frequency distribution. All of the experiments were conducted in accordance with the NIH Guidelines for the Care and Use of Laboratory Animals (1996) and were approved by the ethics committee of the Tokyo Metropolitan Institute for Neuroscience.

## Results

### Behavioral results

Among the food rewards, preference tests demonstrated that the monkeys consistently preferred cabbage and apple to potato to raisin (> 95% in free-choice tests). There was no significant difference in the preference between cabbage and apple. Among the liquid rewards, the monkeys invariably preferred grape juice, orange juice and isotonic beverage to water, and preferred grape juice to orange juice and isotonic beverage. The RTs were significantly influenced by the reward used in each trial. Details of the RT data are described elsewhere (Watanabe et al. 2001). For all rewards, the RTs were significantly shorter in reward trials than in no-reward trials. The RTs were shorter when a highly preferred reward was used compared with a less preferred reward, in reward and/or no-reward trials. During the neuronal recording sessions, the monkeys performed both tasks with > 98% correct responses for all types of reward.

The eye-movement recordings revealed no significant difference in the frequency of saccadic eye movements between reward and no-reward trials in the outcome-expectancy task, between the left and right trials in the spatial-memory task, or between the different types of reward block. In addition, there was no significant difference between the left and right trials in the time spent looking at the left and right sides of the visual field during the delay period of the spatial-memory task.

### Reward/omission-of-reward expectancy-related and spatial WM-related prefrontal neurons

Some of the findings regarding LPFC neuronal activity within each of the outcome-expectancy and spatial-memory tasks were reported previously (Watanabe 1996; Watanabe et al. 2002). The present report concerns 222 task-related neurons that were examined during both tasks. These showed significant activity changes compared to the control period (2–3 s before the instruction presentation) in relation to one or more task events (pre-instruction, instruction presentation, delay, go signal, key-press response, reward delivery and omission of reward) during at least one version of either task. Of these 222 neurons, we focus here on the 126 that could be examined for the same reward(s) in the same version (visible food, cued food or cued liquid) of both the outcome-expectancy and spatial-memory tasks (Table 1). The majority ($n = 113$; 89.7%) of these 126 task-related neurons showed delay-period activity; that is, they showed significantly higher or lower firing during the delay period compared with the pre-cue control period during both tasks (83 neurons), during the outcome-expectancy task alone (11 neurons) or during the spatial-memory task alone (19 neurons). Most of these 113 delay neurons ($n = 104$; 92.0%) showed differential activity depending on the trial type (reward

**Table 1** Classification of LPFC neurons according to activity on the outcome-expectancy and spatial-memory tasks

| Activity during the outcome-expectancy task | Activity during the spatial-memory task | | | Total |
|---|---|---|---|---|
| | Spatial-WM | Nondirectional-delay | Non-delay | |
| 1 Reward-expectancy | 35 | 11 | 0 | 46 |
| 2 Omission-expectancy | 11 | 11 | 10 | 31 |
| 3 Outcome-unselective delay | 13 | 3 | 1 | 17 |
| 4 Non-delay | 14 | 5 | 13 | 32 |
| Total | 72 | 30 | 24 | 126 |

versus no-reward or left versus right) during both tasks (45 neurons), during the outcome-expectancy task alone (32 neurons) or during the spatial-memory task alone (27 neurons).

During the outcome-expectancy task, 77 of the 126 neurons showed outcome-selective delay activity; that is, they showed *significant* differences in the rate of firing during the delay period between reward and no-reward trials. Among these 77 neurons, 46 showed a significantly higher rate of firing in reward trials and 31 showed a significantly higher rate of firing in no-reward trials; the former were designated as "reward-expectancy" neurons and the latter as "omission-expectancy" neurons. Of the remaining 49 neurons, 17 showed delay-period activity without significant differences in activity between the reward and no-reward trials, and 32 showed no significant delay-period activity in both the reward and no-reward trials; the former, which showed non-differential delay activity, were designated as "outcome-unselective delay" neurons (Table 1).

In the spatial-memory task, 72 of the 126 neurons showed *significant* differences in delay activity between the left and right trials: 32 had a significantly higher rate of firing in the left trials and 40 had a significantly higher rate of firing in the right trials. These spatially differential delay neurons were designated as "spatial-WM" neurons. Of the remaining 54 neurons, 30 showed delay-period activity without significant differences in activity between the left and right trials, and 24 failed to show significant delay-period activity in either the left or the right trials; the former neurons, which showed non-differential delay activity, were designated as "non-directional delay" neurons (Table 1). The Pearson $\chi^2$ -test revealed a significant association between the type of activity observed in the outcome-expectancy task and that observed in the spatial-memory task [$\chi^2 = 32.3$, degrees of freedom ($df$) = 6, $P < 0.001$; Table 1]. We also used the Fisher's exact probability test, which confirmed that the distribution in Table 1 was not a product of chance ($P < 0.001$).

As the activity of the reward/omission-expectancy neurons and the RTs of the monkeys were both related to the presence or absence of a reward, and to the type of reward, we thought that the activity of reward/omission-expectancy neurons might reflect the RT, that is, a larger magnitude of activity change in reward-expectancy neurons might induce a shorter RT in the response of the monkey. However, significant correlations between the magnitude of neuronal activity and the RT were found in most reward/omission-expectancy neurons during certain (for example, cabbage and potato, but not raisin) reward blocks, only when data from the reward and no-reward trials were combined. Regardless of the reward used, when a trial-by-trial correlation coefficient was calculated between the two measures within the reward or no-reward trials, there was no significant correlation ($P > 0.05$) between the two measures, and it was not possible to predict the RT in each trial from the magnitude of the activity in the reward/omission-expectancy neurons. Thus, RT was not directly associated with neuronal activity in the LPFC.

Eye movements were recorded separately from the neuronal data, so direct correlations could not be made between eye movements and LPFC neuronal activity. However, as there were no significant differences in eye movements and position between the different trial types during either the outcome-expectancy or spatial-memory tasks, it appeared that the differential delay activity observed in the LPFC neurons was not directly associated with eye movement or position.

### Activity of reward-expectancy neurons during the spatial-memory task

All of the reward-expectancy neurons ($n = 46$) in the outcome-expectancy task showed delay-period activity during the spatial-memory task, with the majority ($n = 35$) showing spatial-WM activity: 17 neurons had a significantly higher rate of firing in the left trials than in the right trials (Fig. 2a), while 18 had a significantly higher rate of firing in the right trials (Fig. 2b). Twelve of the 35 neurons with both reward-expectancy and spatial-WM activity showed delay-period activity in either the left or right trial alone during the spatial-memory task (Fig. 3a). Of the 46 reward-expectancy neurons, 11 showed the same level of delay-period activity during the spatial-memory task and were non-selective for the remembered locations (Fig. 3b).

### Activity of omission-expectancy neurons during the spatial-memory task

Almost one-third of the 31 omission-expectancy neurons ($n = 10$) showed no delay-period activity change

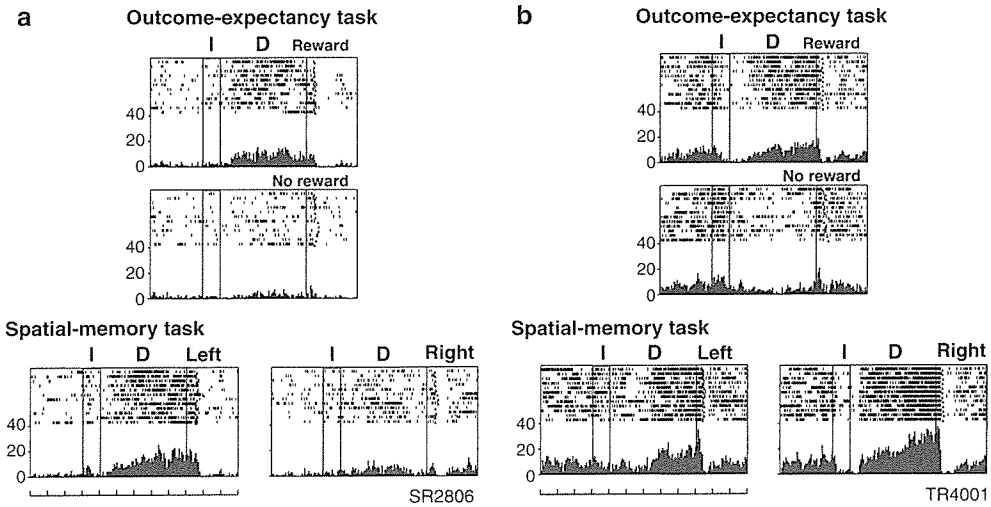


**Fig. 2** Examples of reward-expectancy neurons showing spatial-WM activity during the spatial-memory task. **a** A neuron that was examined in the cued-food version of both types of task with the cabbage reward. This neuron showed reward-expectancy activity by exhibiting significant activations in the reward, but not the no-reward, trials during the outcome-expectancy task. During the spatial-memory task, this neuron showed spatial-WM activity by exhibiting a higher firing rate in the left trials than in the right trials. **b** A neuron that was examined in the visible-food version of both types of task with the cabbage reward. This neuron showed reward-expectancy activity by exhibiting significant activations in the reward, but not the no-reward, trials during the outcome-expectancy task. During the spatial-memory task, this neuron showed spatial-WM activity by exhibiting a higher firing rate in the right trials than in the left trials. For both **a** and **b**, neuronal activity is shown separately for the outcome-expectancy task (*upper part*) and the spatial-memory task (*lower part*) in raster and histogram displays. For the outcome-expectancy task, the *upper* and *lower panels* show neuronal activity for the reward and no-reward trials, respectively. For the spatial-memory task, the *left* and *right displays* show neuronal activity for the left and right trials, respectively. For each display, the first two vertical lines from the *left* indicate the instruction onset and offset, and the *third line* indicates the end of the delay period. *Each row* indicates one trial, and the small upward triangles in the *raster* indicate the time of the key-pressing responses. The *leftmost scales* indicate the number of impulses per second, and the time scale at the *bottom* indicates intervals of 1 s. *I* instruction, *D* delay, *Reward* reward trials, *No reward* no-reward trials, *Left* left trials, *Right* right trials. The *neuron numbers* (SR2806 and TR4001) are indicated on the bottom right

(Fig. 4a), and a similar number ($n=11$) showed non-directional delay activity during the spatial-memory task. Only 10 of the 31 omission-expectancy neurons showed spatial-WM activity during the spatial-memory task: three of these showed a significantly higher rate of firing in the left trials (Fig. 4b), while seven showed a significantly higher rate of firing in the right trials.

## Activity of outcome-unselective delay neurons during the spatial-memory task

Of the 126 neurons that were examined in the outcome-expectancy task, 17 showed outcome-unselective delay activity: the majority of these ($n=13$) showed spatial-WM activity (Fig. 5a), three neurons showed non-directional delay activity (Fig. 5b), and one neuron showed no delay-period activity, during the spatial-memory task.

## Activity of spatial-WM neurons during the outcome-expectancy task

We also examined whether spatial-WM neurons discriminated between reward and no-reward trials during the outcome-expectancy task. Of the 72 spatial-WM neurons, 45 discriminated between them: 35 of these showed reward-expectancy activity (Fig. 2a) and ten showed omission-expectancy activity (Fig. 4b) (Table 1). The remaining 27 neurons did not discriminate between reward and no-reward trials: 13 of these showed outcome-unselective delay activity (Fig. 5a) and 14 showed no delay-period activity.

Of the 30 non-directional delay neurons, 11 showed reward-expectancy activity (Fig. 3b), 11 showed omission-expectancy activity and three showed outcome-unselective delay activity (Fig. 5b) during the outcome-expectancy task (Table 1). Among the 24 neurons that did not show delay-period activity during the spatial-memory task, none showed reward-expectancy activity, ten showed omission-expectancy activity, one showed outcome-unselective delay activity and 13 showed no delay-period activity during the outcome-expectancy task (Table 1).

## Spatial selectivity of delay neurons across the outcome-expectancy and spatial-memory tasks

Each monkey performed the outcome-expectancy and spatial-memory tasks separately. The left and right keys were used simultaneously during the spatial-memory task, while only the center key was used during the

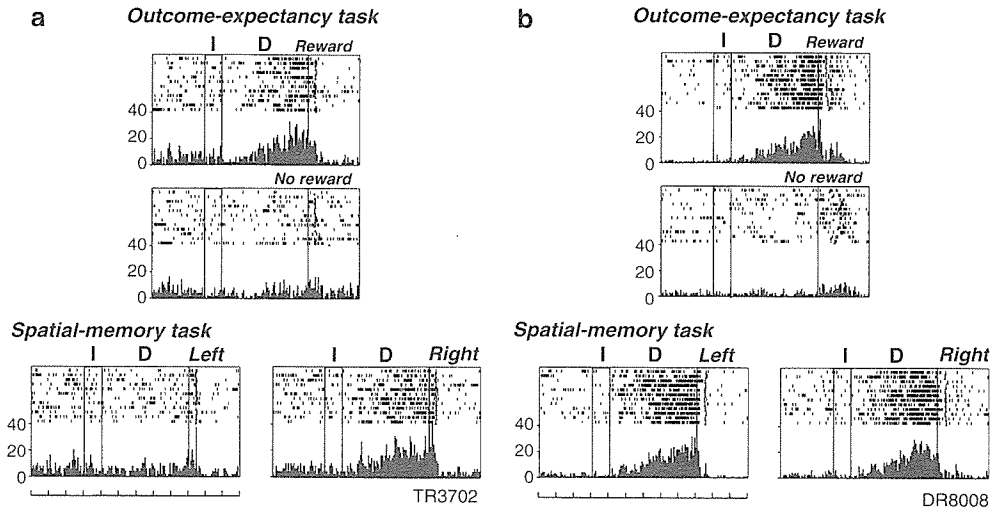


**Fig. 3** Examples of reward-expectancy neurons showing spatial-WM (**a**) and non-directional delay (**b**) activity during the spatial-memory task. **a** A neuron that was examined in the cued-liquid version of both types of task with the water reward. This neuron showed reward-expectancy activity by exhibiting activations during the delay period only in the reward, and not the no-reward, trials during the outcome-expectancy task. During the spatial-memory task, this neuron showed spatial-WM activity by exhibiting activations only in the *right*, and not the *left*, trials. **b** A neuron that was examined in the cued-liquid version of both types of task with the orange juice reward. This neuron showed reward-expectancy activity by exhibiting activations only in the reward, and not the no-reward, trials during the delay period of the outcome-expectancy task. During the spatial-memory task, this neuron showed non-directional delay activity by exhibiting significant activations in both the *left* and the *right* trials, with no significant difference in the magnitude of activation. The other details are as described for Fig. 2

outcome-expectancy task. However, because previous reports have demonstrated that many LPFC delay neurons are involved in spatial mapping (for example, Funahashi et al. 1989), we examined whether there was any relationship between the delay activity observed in the rewarded center key trial in the outcome-expectancy task and that observed in the rewarded left and right trials in the spatial-memory task, using the 72 spatial-WM neurons.

The *H*-test indicated that all of the 72 spatial-WM neurons showed statistically significant differences in delay activity among the right, center and left trials ($P < 0.05$). The post hoc *U*-test demonstrated that in the majority (66 out of 72; 92%) of these neurons, the magnitude of the delay-period firing observed in the center key trials was not significantly larger than the maximum, nor smaller than the minimum, detected between the left and right key trials during the spatial-memory task. In 20 of these 66 neurons, significant differences were observed in the magnitude of delay-period firing both between the center and left key trials, and between the center and right key trials (Fig. 2a). In the remaining 46 neurons, significant differences in the magnitude of delay-period firing were observed either between the center and left key trials or between the center and right key trials (Fig. 3a, 4b). A small number of neurons (6 out of 72; 8%) showed a higher or lower rate of delay-period firing during the outcome-expectancy task than during the spatial-memory task (Fig. 2b, 5a). These neurons showed significant differences in the pre-instruction baseline activity between the outcome-expectancy and spatial-memory tasks.

## Reward–no-reward-discrimination and left–right-discrimination in LPFC delay neurons

Because there were differences in the ability of each LPFC delay neuron to discriminate between the reward and no-reward trials and between the left and right trials, we compared the ability of individual LPFC neurons to discriminate reward/no-reward trials with their ability to discriminate left/right trials. We calculated the "reward–no-reward discrimination index" (RNRDI) of individual neurons using the following formula:

$$\text{RNRDI} = (\text{reward} - \text{no - reward})/(\text{reward} + \text{no - reward})$$

Here, "reward" and "no-reward" indicate the mean discharge rate during the delay period for the reward and no-reward trials in the outcome-expectancy task, respectively. Similarly, we calculated the "left–right discrimination index" (LRDI) of individual neurons using the following formula:

$$\text{LRDI} = (\text{left} - \text{right})/(\text{left} + \text{right})$$

Here, "left" and "right" indicate the mean discharge rate during the delay period for the left and right trials in the spatial-memory task, respectively. Both indices ranged between −1 and 1, with a larger absolute value indicating greater discrimination between the reward and no-reward trials (RNRDI), or greater discrimination between the left and right trials (LRDI). For those neurons that were examined using more than two different types of reward for both tasks, the mean values of

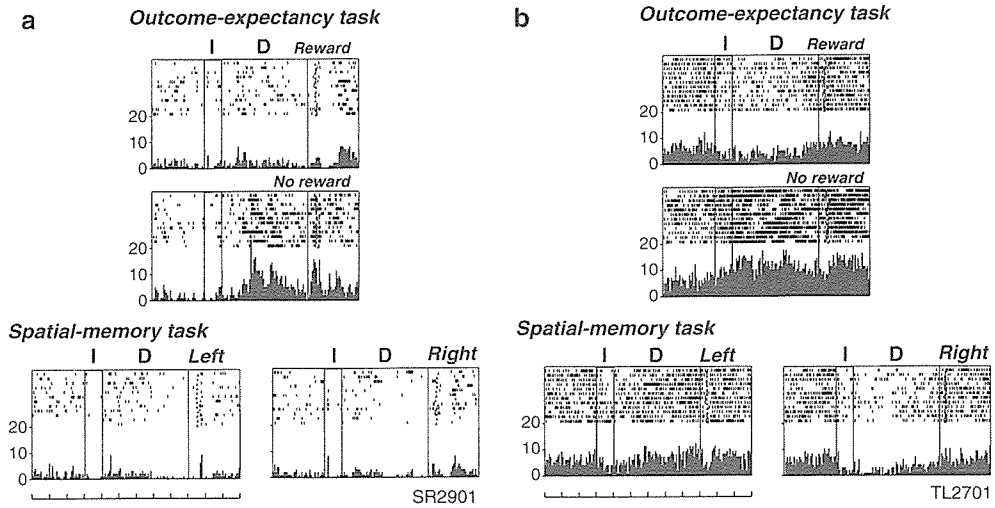


**Fig. 4** Examples of omission-expectancy neurons without (**a**) or with (**b**) spatial-WM activity during the spatial-memory task. **a** A neuron that was examined in the visible-food version of both types of task with the raisin reward. This neuron showed omission-expectancy activity by exhibiting a higher firing rate in the no-reward trials than in the reward trials during the outcome-expectancy task. During the spatial-memory task, this neuron did not show significant delay-period activity. **b** A neuron that was examined in the visible-food version of both types of task with the cabbage reward. This neuron showed omission-expectancy activity by exhibiting a higher firing rate in the no-reward trials than in the reward trials during the delay period of the outcome-expectancy task. During the spatial-memory task, this neuron showed spatial-WM activity by exhibiting a higher firing rate in the *left* trials than in the *right* trials. The other details are as described for Fig. 2

the RNRDI and LRDI were obtained for the different types of reward for each neuron.

The mean (±SD) absolute RNRDI of the 77 (reward-expectancy plus omission-expectancy) neurons was 0.3114 (±0.1651) [0.30 (± 0.16) for the reward-expectancy neurons and −0.33 (±0.16) for the omission-expectancy neurons]. The mean absolute LRDI of the 72 spatial-WM neurons was 0.2833 (±0.1431). There was no significant difference between these two values ($P=0.2711$, two-tailed $t$-test). We also obtained the mean absolute values of the RNRDI and LRDI for the 45 delay neurons that showed both reward-expectancy (or omission-expectancy) and spatial-WM activity. The mean absolute RNRDI and LRDI values of these 45 neurons were 0.2980 (±0.1491) and 0.2547 (±0.1025), respectively. There was no significant difference between these two values ($P=0.115$, two-tailed $t$-test), although there was a weak, but statistically significant, correlation between these two indices ($r=0.4322$, $P<0.01$, two-tailed $t$-test) (Fig. 6). Thus, the greater the discrimination shown by a specific delay neuron between the reward and no-reward trials, the more it tended to discriminate between the left and right trials.

## Comparison of reward discrimination by LPFC delay neurons between the outcome-expectancy and spatial-memory tasks

We reported previously on the ability of individual LPFC delay neurons to discriminate between different types of reward in the outcome-expectancy task (Watanabe et al. 2002). We compared the ability of individual LPFC delay neurons to discriminate between different types of reward during the outcome-expectancy task with that during the spatial-memory task. The "reward difference discrimination index" (RDDI) of individual neurons was calculated separately for reward trials in the outcome-expectancy task, and for combined left and right trials in the spatial-memory task, using the following formula:

$$\text{RDDI} = (\text{preferred} - \text{non-preferred})/(\text{preferred} + \text{non-preferred})$$

Here, "preferred" and "non-preferred" indicate the mean discharge rate during the delay period for the most and least preferred rewards within a task, respectively. This index was calculated using data obtained from 26 neurons that were examined for the most (cabbage or grape juice) and least (raisin or water) preferred rewards in both the outcome-expectancy and spatial-memory tasks. This index also ranged between −1 and 1, with a larger absolute value indicating greater discrimination between the most preferred and least preferred rewards within a task. The mean absolute values of the RDDI were 0.1650 (±0.1041) in the outcome-expectancy task and 0.1478 (±0.1292) in the spatial-memory task. There was no significant difference between these two values ($P=0.6076$, two-tailed $t$-test), although there was a significant correlation between the two values ($r=0.6059$, $P<0.01$, two-tailed $t$-test) (Fig. 7), indicating that reward discrimination by LPFC delay neurons did not differ between the outcome-expectancy and spatial-memory tasks.

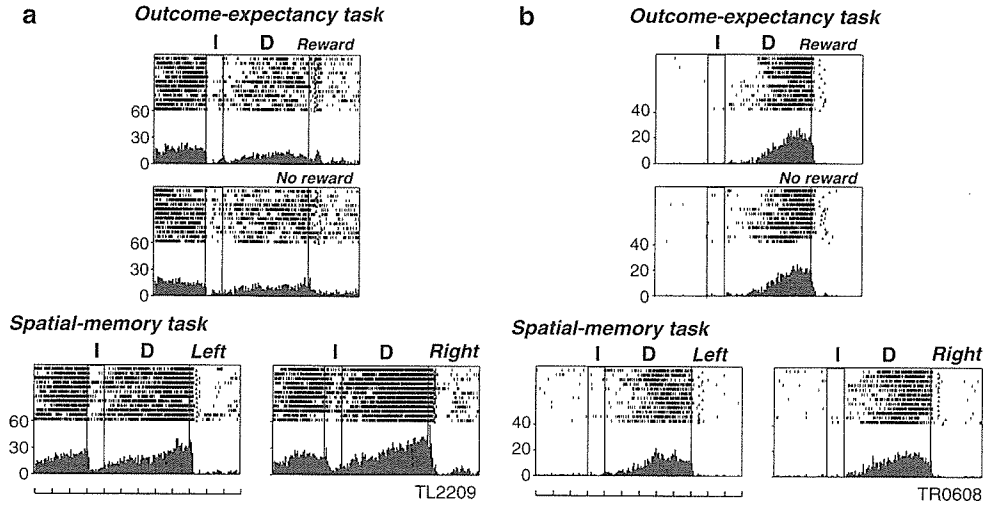


**Fig. 5** Examples of outcome-unselective delay neurons with (**a**) and without (**b**) spatial-WM activity during the spatial-memory task. **a** A neuron that was examined in the visible-food version of both types of task with the potato reward. This neuron showed outcome-unselective delay activity by exhibiting a significant decrease in the firing rate during the delay period of the outcome-expectancy task, with no significant difference in activity between the reward and no-reward trials. During the spatial-memory task, this neuron showed spatial-WM activity by exhibiting a higher firing rate in the right trials than in the left trials. **b** A neuron that was examined in the cued-liquid version of both types of task with the water reward. This neuron showed outcome-unselective delay activity by exhibiting significant activations during the outcome-expectancy task, with no significant difference in activity between the reward and no-reward trials. During the spatial-memory task, this neuron showed non-directional delay activity by exhibiting activations in both the *left* and *right* trials, with no significant difference in activity between the *left* and *right* trials. The other details are as described for Fig. 2

## Modulation of spatial-WM activity by reward-expectancy in LPFC delay neurons

We examined whether there was any enhancement in the ability to discriminate between the left and right trials in spatial-WM neurons when the more preferred reward was used in the spatial-memory task compared with the less preferred reward. We calculated the LRDI for all 21 spatial-WM neurons that were examined using both the most and least preferred rewards. The mean absolute value of the LRDI in these 21 neurons for the most preferred reward was 0.2810 (±0.1270), while that for the least preferred reward was 0.2610 (±0.1132). There was no significant difference in the absolute value of the LRDI between the most and least preferred rewards ($P=0.59$, two-tailed $t$-test). However, more than one-half of these spatial-WM neurons ($n=13$) showed a significantly higher rate of firing throughout the trial

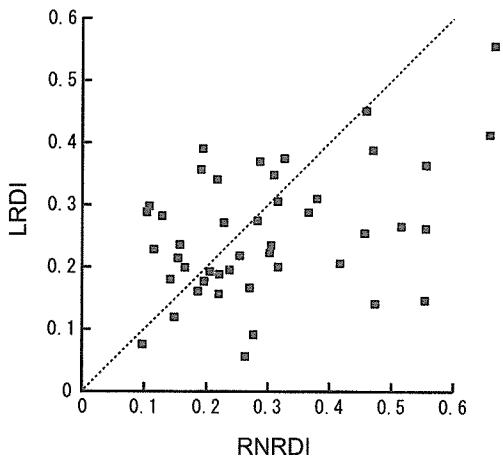


**Fig. 6** Ability of LPFC delay neurons to discriminate between reward and no-reward trials (*RNRDI*) during the outcome-expectancy task, and between left and right trials (*LRDI*) during the spatial-memory task. Absolute values of the left–right discrimination index (*LRDI*) of individual LPFC neurons are plotted against those of the reward–no-reward discrimination index (*RNRDI*). Each filled square represents an individual LPFC neuron. The *dashed line* indicates 45°

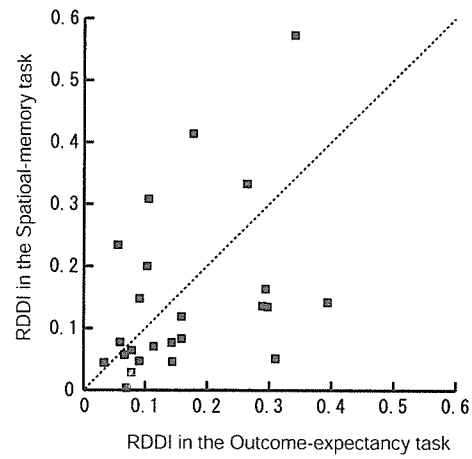


**Fig. 7** Ability of LPFC delay neurons to discriminate between the most and least preferred reward blocks (*RDDI*) in the outcome-expectancy and spatial-memory tasks. Absolute values of RDDI in the spatial-memory task are plotted against those in the outcome-expectancy task. The other details are as described for Fig. 6

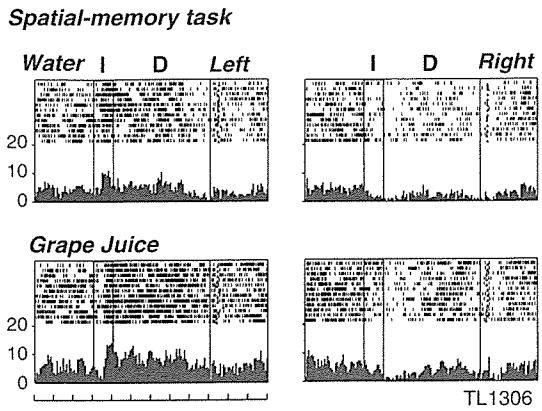


**Fig. 8** An example of a spatial-WM (and reward-expectancy) neuron that discriminated between the most (grape juice) and least (water) preferred rewards. Although this neuron showed a higher rate of firing for the most preferred reward than for the least preferred reward during the delay period, there was no significant difference in left–right discrimination (*LRDI*) between the two different reward trials. The *upper* and *lower panels* correspond to the water and grape juice rewards, respectively. The other details are as described for Fig. 2

when the most preferred reward was used compared with the least preferred reward (Fig. 8). Thus, the use of the more preferred reward often induced an enhancement of the basal neuronal activity, but did not result in an improvement of spatial discrimination by spatial-WM neurons.

## Location of reward/omission-expectancy and spatial-WM neurons in the LPFC

The locations of penetrations of the LPFC neurons examined during both outcome-expectancy and spatial-memory tasks are illustrated in Fig. 9. Both reward-expectancy and omission-expectancy neurons were observed in all of the areas explored (that is, the principalis area including the lips and depths of the principal sulcus, the arcuate area and the inferior convexity area), although no clear localization was observed for either type of neuron. This was also the case for the outcome-unselective delay neurons in the outcome-expectancy task. Spatial-WM and non-directional delay neurons

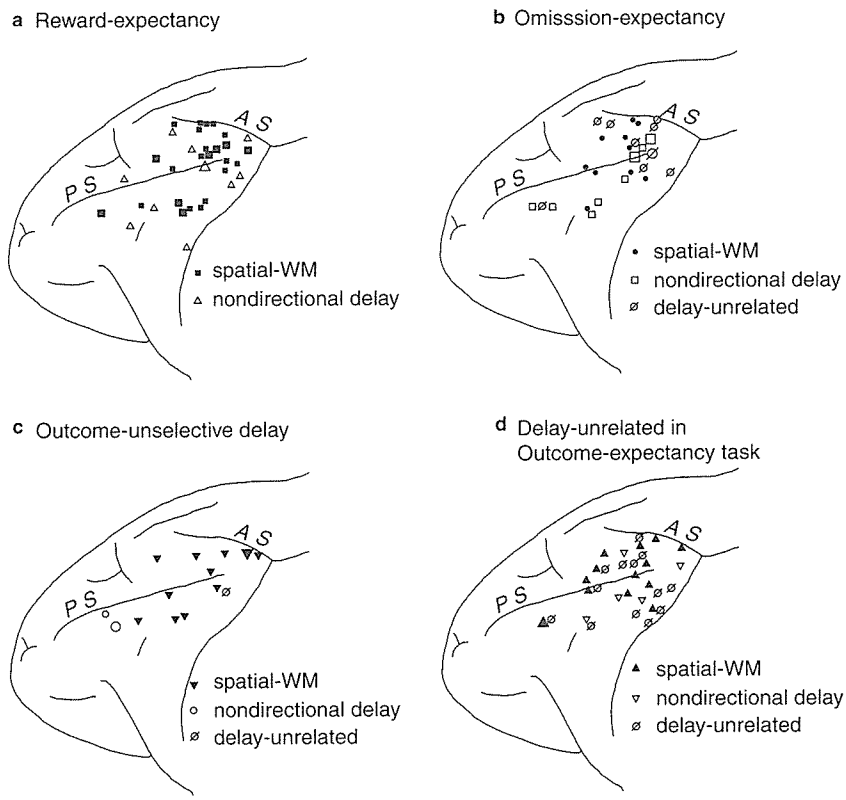


**Fig. 9** Locations of penetrations of the LPFC neurons examined in both the outcome-expectancy and the spatial-memory tasks. Penetrations in the right hemisphere are plotted onto comparable locations in the left hemisphere. **a** Reward-expectancy neurons with spatial-WM (*filled squares*) and non-directional delay (*triangles*) activity during the spatial-memory task. **b** Omission-expectancy neurons with spatial-WM (*filled circles*), non-directional delay (*squares*) and delay-unrelated (*scored circles*) activity during the spatial-memory task. **c** Outcome-unselective delay neurons with spatial-WM (*filled upside-down triangles*), non-directional delay (*circle*) and delay-unrelated (*scored circles*) activity during the spatial-memory task. **d** Neurons that did not show delay-period activity during the outcome-expectancy task with spatial-WM (*filled triangles*), non-directional delay (*upside-down triangles*) and delay-unrelated (*scored circles*) activity during the spatial-memory task. *Large symbols* indicate penetrations in which two or more neurons were found

were also found in the principalis, arcuate and inferior convexity areas.

## Discussion

We examined individual LPFC delay neurons in two different types of task in order to clarify the functional significance of delay-period activity during WM task performance, and particularly the functional relationship between reward/omission-expectancy and spatial-WM activity. LPFC neurons that showed delay-period activity in one task were found to be more likely to show delay-period activity in the other (83 out of 113 neurons; 73.4%). The majority of the delay neurons (104 out of 113; 92.0%) showed differential activity depending on the trial type (reward versus no-reward or left versus right); of these, 43% showed differential activity during both types of task and the remaining 57% showed differential activity during only one type of task (Table 1).

In support of our hypotheses, all of the reward-expectancy neurons showed delay-period activity during the spatial-memory task. Of these, most (35 out of 46; 76.0%) differentiated between the left and right remembered locations. However, only one-third (11 out of 31) of the omission-expectancy neurons discriminated between left and right, and one-third (11 out of 31) of the omission-expectancy neurons failed to show any significant delay-period activity, in the spatial-memory task. Viewed the other way around, neurons showing spatial selectivity during the spatial-memory task were much more likely to be reward-expectancy neurons than omission-expectancy neurons during the outcome-expectancy task.

### Representation of spatial WM and reward/omission-expectancy in LPFC neurons

Spatial-WM activity and reward/omission-expectancy activity were both involved in representing not what was currently being presented, but rather what had been presented previously or would be presented later during the trial; the former was concerned with where the spatial cue was presented or which side the response should be directed to, and is thought to be involved in representing task-relevant cognitive information that guides the monkey in correct task performance in order to attain the reward, whereas the latter was concerned with what type of reward would be delivered. Even omission-expectancy neurons might have been involved in representing the reward, in the sense that although the outcome of the current trial was no-reward, the true reward was moving to a future trial. Reward-expectancy activity in prefrontal neurons has been suggested to represent ";affective WM" (Davidson 2002). However, according to the original and widely accepted definition, WM is the "temporary storage and manipulation of information for complex cognitive tasks" (Baddeley 1986). As reward-expectancy and omission-expectancy neuronal activity is neither a prerequisite nor essential for correct task performance, reward-expectancy and omission-expectancy activities are not considered to constitute neuronal substrates of WM. "Affective WM" might therefore be a misusage of the term "WM".

Recently, the effects of reward on brain activity have been examined in several areas outside of the LPFC. Reward-expectancy and omission-expectancy-related neurons have been identified in the primate orbitofrontal cortex (OFC) (Tremblay and Schultz 1999, 2000; Hikosaka and Watanabe 2000), although WM-related neurons are relatively rare in the OFC (Tremblay and Schultz 2000; Wallis and Miller 2003). Platt and Glimcher (1999) showed that the reward a monkey expects during an oculomotor task modulates the direction-selective activity of neurons in the lateral intraparietal (LIP) area. Similarly, Sugrue et al. (2004) reported that eye-movement-related neurons in the monkey LIP area represent the relative reward value of competing actions. Delay activity of monkey caudate neurons was also modulated by the presence or absence of reward during an oculomotor delayed response task, to the extent that the representation of cognitive information was sometimes overshadowed by the reward information (Kawagoe et al. 1998). The LIP and caudate nucleus are not viewed as areas in which cognitive information initially meets reward information; they might receive task-related cognitive and motivational information from the LPFC (Kawagoe et al. 1998; Platt and Glimcher 1999; Sugrue et al. 2004). Indeed, anatomical studies indicate that the LPFC receives highly processed cognitive information from the posterior-association cortices, as well as highly processed motivational information from the OFC (Barbas 1993). In a recent paper, in which neuronal activity was recorded from both the OFC and LPFC in the same monkey (Wallis and Miller 2003), reward selectivity arose more rapidly in the former than in the latter. Thus, reward information might initially enter the OFC before being passed to the LPFC, where it is integrated with cognitive information. The LPFC could therefore play important roles in modulating eye movement-related neuronal activity in the LIP and caudate nucleus areas by sending integrated cognitive and motivational information.

### Reward and spatial discrimination by LPFC delay neurons

There was a weak, but statistically significant, correlation between the RNRDI and LRDI in individual LPFC delay neurons (Fig. 6). Thus, the more discriminative a certain delay neuron was between the reward and no-reward trials during the outcome-expectancy task, the better it tended to discriminate between the left and right trials during the spatial-memory task. It appears that the ability of LPFC neurons to discriminate between different events is generalized across many dimensions.

The ability of individual LPFC delay neurons to discriminate between different types of reward, as indicated by the RDDI, did not significantly differ between the outcome-expectancy and spatial-memory tasks (Fig. 7). Thus, reward discrimination appears to be consistent across WM and non-WM tasks.

Almost all spatial-WM neurons corresponded to the spatial relationship between the left, center and right keys, although the monkeys were not required to discriminate between the center and left or right keys. Thus, LPFC neurons appeared to be involved in representing the implicit spatial relationship among the three keys.

### Modification of spatial-WM activity by reward-expectancy

Differential outcome effects point towards the importance of reward in controlling the discrimination task performance of an animal (Peterson 1984). Behavioral data also indicate that the RT of an animal is much shorter when a more preferred reward is used, compared with that when a less preferred reward is used (Watanabe et al. 2001). In the present study, many spatial-WM neurons showed enhanced activity when a more preferred reward was used (Fig. 8). LPFC delay neurons also showed enhanced activity when the magnitude of the reward was increased in oculomotor delayed response tasks (Leon and Shadlen 1999; Roesch and Olsen 2003). The enhancement of spatial discrimination was reported in some spatially differential delay neurons when a more preferable outcome was expected, both with respect to the presence or absence of reward (Kobayashi et al. 2002) and different magnitudes of reward (Roesch and Olson 2003).

Neurons in the caudate nucleus also showed both reward-expectancy-related and spatially differential delay activity during an oculomotor delayed response task (Kawagoe et al. 1998). Their delay-period activity, but not their spatial discrimination, was modulated depending on whether the monkey could expect the delivery of a reward.

### Functional significance of the delay-period activity of LPFC neurons for WM task performance

When the bait was omitted from the cue presentation during a delayed response task, the monkeys were reluctant to respond; moreover, when they did respond, the RT became much longer. On such "dry-run" trials, sustained activity in LPFC delay neurons disappeared (Fuster 1973). The disappearance of sustained activity might reflect the absence of a representation of the reward. The characteristics of the activity changes reported in these delay neurons were similar to those of the LPFC neurons in the present experiment, which showed activations in reward, but not in no-reward, trials during the outcome-expectancy task, and showed non-directional delay activity during the spatial-memory task (Fig. 3b). Neurons with such reward/omission-expectancy and non-directional delay activity constituted 19.4% (22 out of 113) of the LPFC delay neurons examined. They do not appear to be concerned with retaining spatial information in WM, and are more likely to be concerned with motivational aspects of WM task performance. Thus, consistent with our hypothesis, a substantial number of delay neurons observed during the spatial-memory task were not directly concerned with the cognitive control of the task performance. Kobayashi et al. (2002) also reported LPFC delay neurons that did not show spatial selectivity, but showed higher or lower firing rates, under reward-present conditions compared with reward-absent conditions during an oculomotor delayed response task.

What, then, is the functional significance of non-directional delay neurons with reward/omission-expectancy activity for the WM task if their activity is not directly concerned with the cognitive control of behavior? Sustained delay activity, and particularly reward-expectancy activity with a magnitude that increases when a more preferred reward is used, might support WM task performance by raising general arousal levels and through attention control, particularly the inhibitory control of internal (perseveration) and/or external (distracting stimulus) interference.

By contrast, spatial-WM neurons without reward/omission-expectancy activity might be involved in representing only cognitive information concerning how the reward can be attained, and could be involved primarily with the cognitive control of the task performance. However, it remains uncertain whether they are concerned exclusively with retaining spatial information in WM. It was recently shown that sustained delay activity in LPFC neurons was more concerned with spatial attention than with spatial WM during a task in which a monkey was required to attend to a certain location while remembering a different location (Lebedev et al. 2004). Moreover, an imaging study reported no activation of the LPFC, but activations in the posterior visual association area, corresponding to the maintenance of object information in WM (Postle et al. 2003). Thus, it is important to note that delay-period activity in the LPFC is not necessarily associated with retaining information in WM, and that some WM tasks can be performed without sustained activity in the LPFC.

### Integration of cognitive and motivational operations in the LPFC

Spatial-WM neurons with reward/omission-expectancy activity might be involved in representing both the reward itself and how it can be attained. In the present study, the enhancement of spatial-WM activity was observed in many such neurons when employing a more preferred reward. Kobayashi et al. (2002) and Roesch and Olson (2003) reported the enhancement of spatial

discrimination in some spatially differential delay neurons when a more preferable outcome could be expected. Thus, reward-expectancy appears to enhance WM activity in LPFC neurons. However, omission-expectancy activity is not thought to be involved in supporting correct task performance. Indeed, spatial-WM neurons were more likely to be associated with reward-expectancy than with omission-expectancy, and only the minority of the omission-expectancy neurons showed spatial-WM activity. Furthermore, it is interesting to note that those neurons that did not show delay-period activity during the spatial-memory task also failed to show reward-expectancy activity during the outcome-expectancy task.

Ablation of the monkey LPFC invariably induces severe impairments in the learning and performance of WM tasks, including delayed response and delayed alternation, although there is no impairment if there is no delay in these tasks (Mishkin 1957; Gross and Weiskranz 1962; Goldman et al. 1971). It has been proposed that delay activity supports WM task performance by "bridging temporal separations between mutually contingent events such as between the cue and motor response (cross-temporal contingency)" (Fuster 1997). During the outcome-expectancy and spatial-memory tasks in the present experiment, several different types of delay-period activity were observed that could bridge the temporal separation between the cue and response, and the LPFC delay activity was not concerned exclusively with retaining task-relevant cognitive information in WM. In fact, some delay neurons were concerned predominantly with reward-expectancy and/or omission-expectancy. These might be involved in attention control during WM task performance. Importantly, we also found many delay neurons that had both spatial-WM and reward/omission-expectancy activities. Employing a more preferred reward induced better task performance in the monkey, as well as enhanced spatial-WM activity in many LPFC delay neurons. This suggests that the LPFC might play a principal role in the integration of cognitive and motivational operations, allowing the monkey to obtain a reward more efficiently.

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# Sleep health, lifestyle and mental health in the Japanese elderly Ensuring sleep to promote a healthy brain and mind

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**Abstract**

The Ministry of Health, Labor and Welfare in Japan proposed a plan called "Health Japan 21," which adopted sleep as one of the specific living habits needing improvement. This has led to increased interest in mental health needs at community public health sites. In addition, it was reported from a recent 2000 survey that one in five Japanese, and one in three elderly Japanese, suffer from insomnia. Insomnia is becoming a serious social problem; so much so that alarm bells are ringing with insomnia listed as one of the refractory diseases of the 21st century. Against this background, in January 2001, Japan began a national project called "Establishing a Science of Sleep."

This article is an overview of sleep and health in the elderly, sleep mechanisms and the characteristics of insomnia among the elderly. At the same time, it introduces the scientific basis for lifestyle guidance that is effective for ensuring comfortable sleep, an essential condition for a healthy, energetic old age, with actual examples from community public health sites. The present authors reported that a short nap (30 min between 1300 and 1500 h) and moderate exercise such as walking in the evening are important in the maintenance and improvement of sleep quality. The study was to examine the effects of short nap and exercise on the sleep quality and mental health of elderly people. "Interventions" by short nap after lunch and exercise with moderate intensity in the evening were carried out for 4 weeks. After the "intervention," wake time after sleep onset significantly decreased and sleep efficiency significantly increased, showing that sleep quality was improved. The frequency of nodding in the evening significantly decreased. As a result, the frequency of nodding before going to sleep decreased, and the quality of nocturnal sleep was improved. Present results demonstrated that the proper awakening maintenance during evening was effective in improving sleep quality. After the "intervention," mental health also improved with improving sleep quality. Furthermore, physical health also improved with improving sleep quality. These results suggest that this "intervention" technique is effective for the quality of life (QOL) and the activity of daily living (ADL) of elderly people.

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*Keywords:* Elderly; Exercise; Intervention; Lifestyle; Nap

## The aging of Japanese society and measures against insomnia

As of 2000, the proportion of elderly people over the age of 65 in Japan had reached 17% of the total population, a proportion that is expected to exceed 22% by 2010 (Ministry of Health, Labor, and Welfare white paper). In the 21st century, we will face a rapidly aging society, and, as seen from the calls for improved quality of life (QOL) rather than simple longevity, there is now a strong desire to achieve longevity with both health and true wellbeing. In June 2000, the World Health Organization (WHO) first published *Healthy Life Expectancy*, which estimates the age to which people can expect to live in health. Of the 191 countries surveyed, Japan was reported to have the longest healthy life expectancy of all, at 74.5 years (males 71.9 years, females 77.2 years; mean lifespan was also the longest in the world at 80.9 years), followed closely by Australia at 73.2 years. The number of elderly people with dementia, on the other hand, is expected to increase 1.8-fold from the current number of about 1.6 million to 2.9 million in 2020. This will also increase the burden and stress placed upon family and caregivers.

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In recent years, it has been reported that sleep is closely related to physical and mental health [1–13], and that one in three Japanese elderly suffer from insomnia [14]. In Japan's aging society, dealing with insomnia among the elderly has become a major social issue. Lack of sleep or sleep disorders in the elderly can lead to social maladjustment, including decreased motivation or depression, and there are physical affects as well with an increased risk for lifestyle-related diseases.

## Approach to comfortable sleep from lifestyle improvements

Ensuring proper sleep is crucial for people to enjoy an energetic, vital old age without becoming senile or bed-ridden. However, if an elderly person does have difficulty sleeping, administration of sleep medication can in many cases be problematic due to low responsiveness to the drug, the risk from combined use with medications for other diseases and regular dose-dependence or side effects from long-term use. To assure proper sleep in the elderly, therefore, lifestyle improvements can play a key role. Sleep science in recent years has shown that regular short daytime naps can help relieve fatigue in the brain and improve nighttime sleep [10,15,16]. Naps are also reported to be effective in lowering the risk of dementia of the Alzheimer's type to one-fifth and in preventing lifestyle-related diseases [17]. These findings strongly suggest that re-examining lifestyles and ensuring high-quality sleep will be effective in greatly reducing the number of elderly with dementia or who are confined to bed. The numbers of such elderly are expected to dramatically increase in the future. Comfortable sleep in old age will not only result in a clear increase in the QOL of elderly people themselves, but will also be important in leading to increased well-being in the family and caregivers of the elderly, and society as a whole.

## Changes with age in sleep architecture and biological rhythms

As a person ages, the time he or she goes to bed, gets up and sleeps tend to become earlier [8] (Fig. 1). In addition, it is reported that sleeping time (time in bed) increases with age for people beyond the age of 60, exceeding 8 h for those older than 80. Thus, there is a marked increase in sleeping time with age.

Fig. 2 shows a model of changes in sleep architecture and biological rhythms. Sleep in the elderly may be characterized in a word as shallow, inefficient sleep. With age there is a considerable decrease in deep sleep (slow-wave sleep, Stages 3–4) and an increase in night awakenings, and thus conspicuous interruptions in sleep. Moreover, there is also an increase in early morning awakening when a person cannot get back to sleep. Another phenomenon is completely sleepless nights, in which a person tries to sleep but cannot, and greets the morning still awake. A considerable number of elderly wake up in a bad mood or low spirits because of poor quality sleep, and so are lethargic throughout the day. The reduction in slow-wave sleep that accompanies age means a less efficient process during sleep of relieving stress or sleep pressure built up during the day. The decrease in slow-wave sleep and increase in night awakenings may be considered signs that the maintenance and control system that manages sleep is aging. As people age, it becomes more difficult to obtain sufficient sleep, as a result of which time in bed inevitably becomes longer. Sleep efficiency is poor (there is not enough sand in the hourglass at night), and so even if a person sleeps for a long time there is a lack of sharpness between sleeping and waking, and the person tends to feel intensely drowsy during the day. Furthermore, age differences in the REM latency (the duration of NREM sleep before the first REM period of the night), with older subjects showing shorter latencies than younger subjects, have been shown in some studies of normal and depressed patients [1,18–20]. The

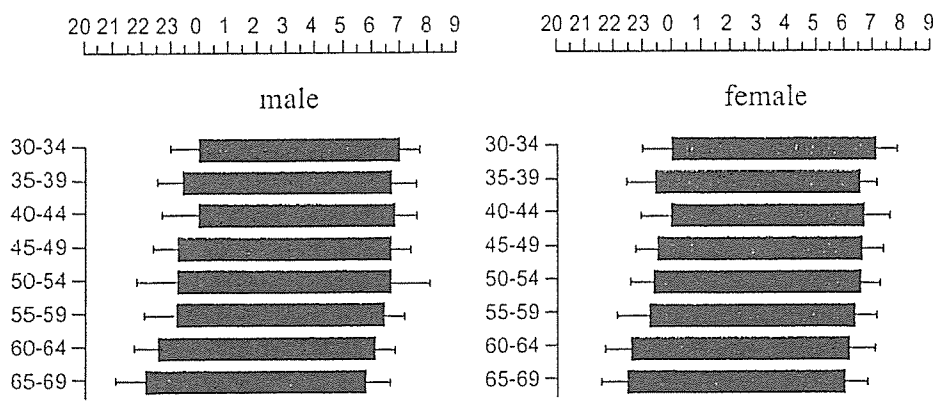


Fig. 1. Changes in sleeping habits from middle age to old age.

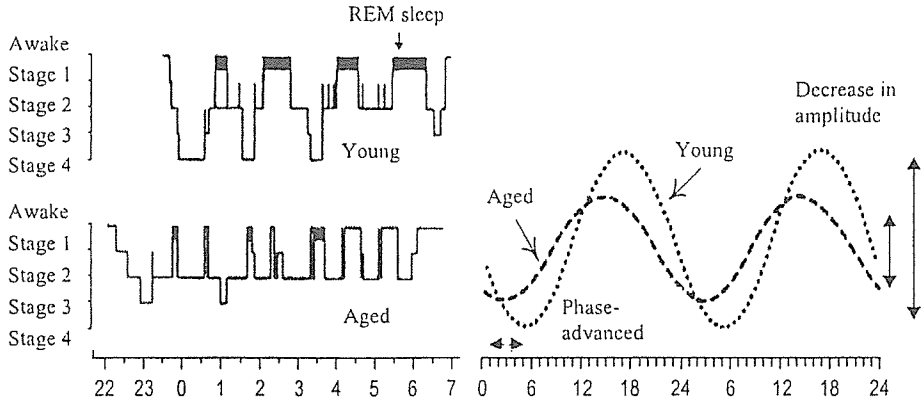


Fig. 2. A model of the deterioration in sleep functions and body rhythm (temperature rhythm) functions due to aging.

results may be a function of the decreased Stages 3 and 4 sleep within that cycle as a function of aging. One additional possibility in explaining short REM latencies in aged individuals is an age-dependent change in the circadian timing system [1].

Elsewhere, deterioration of biological rhythms due to age is seen in various circadian rhythms such as core body temperature, and the core body temperature curve is phase-advanced and a decrease in rhythm amplitude (Fig. 2, right). However, biological rhythms periods are not exactly 24 h but closer to 25 h. Therefore, to match our rhythms to the 24-h day–night rhythms of the outer world, we make a correction in our daily lives of about 1 h each day, through such means as sunlight. With the rise of the sun our eyes catch the sunlight, and the light signal is then carried to a location called the nucleus suprachiasmatic nuclei of the hypothalamus of the brain. The nucleus suprachiasmatic nuclei holds our body clock, and entrains this clock to the 24-h light–dark cycle of a single day. The factor that synchronizes circadian rhythms to the 24-h cycle of the environment is called the entraining agent, and in humans it is known to act in response to bright light, feeding, social contact and exercise. The reduction of occasion to be exposed to entraining agents caused by the transition of living surroundings and/or the deteriorated function of biological clock makes the circadian rhythm ability worse with aging.

## Effects of insufficient or disordered sleep on brain function and physical and mental health: sleep health and mental and physical health

Figs. 3–6 show comparisons of day and night activity, condition of mental health and daytime drowsiness over 1 week between elderly who get poor sleep and those who get good sleep. The gray band is the time in bed at night. The height of the vertical black bars indicates the level of activity, with the parts indicating extremely low activity showing sleeping or dozing. There are a greater number of black bars during the nighttime or time in bed for elderly with poor sleep, and the length of night awakening is nearly 2 h (first night, top row). This shows that activity edges down to an extremely low level during the day, with the person dozing off many times. Thus, elderly with poor

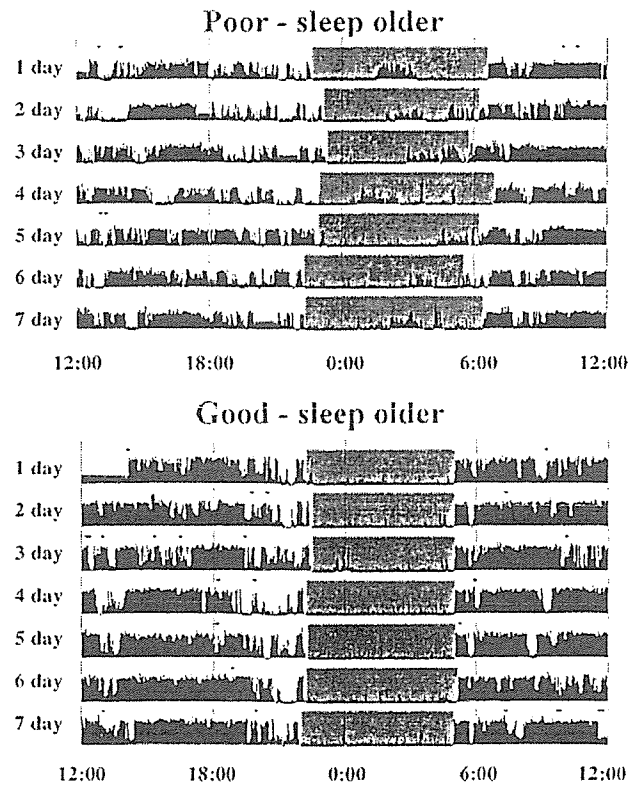


Fig. 3. Comparison of activity levels in elderly people who get good and poor sleep. This figure compares the activity level of elderly people who get poor and good sleep. Subjects wore wristwatch activity meters (actigrams) continuously for 1 week to investigate daytime and nighttime activity. The numeral 0:00 at the midpoint of the vertical axis is 12:00 midnight. The height of the black part shows the activity level (higher equals a greater activity level), and the parts with extremely low activity indicate sleeping or napping.

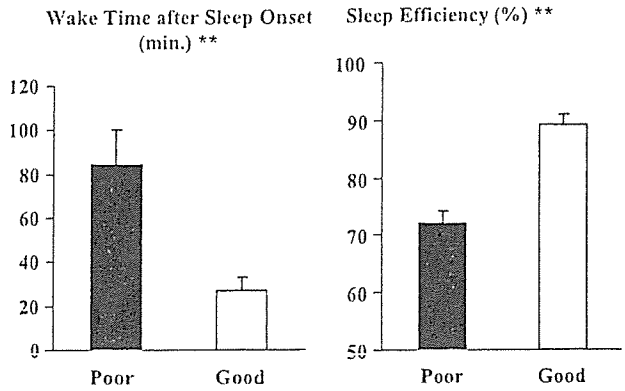


Fig. 4. Comparison of actigraph data between good sleep group and poor sleep group. ** $P<0.01$.

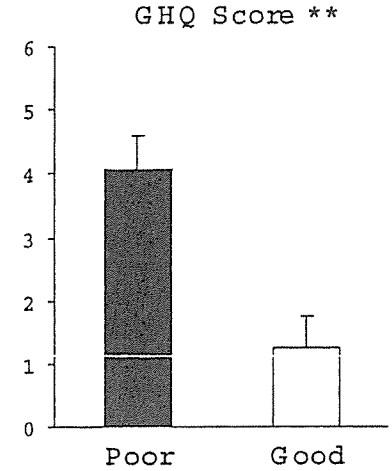


Fig. 6. Comparison of mental health between good sleep group and poor sleep group. ** $P<0.01$.

nighttime sleep doze off many times and have a low level of activity during the day.

Elderly people who get good sleep (Fig. 4), on the other hand, have a high level of activity during the day, are energetic and feel a sharp distinction between sleep and wakefulness. Their subjective feeling of drowsiness during the day is also low (Fig. 5), and they have good mental health (Fig. 6). Elderly people who get good sleep, moreover, are reported to be confident in their own life as well as being confident that they have the trust of others (a high level of social confidence), and to be healthy and volitional [21]. Recently, our studies [10] ($n=467$, 65–94years) have shown that people who get better sleep have higher levels of morale [22] (social adaptability) and satisfaction with regard to their own roles in society, higher levels of activities of daily living (ADLs) (Fig. 7) and fewer illnesses and strong subjective feelings of health. In the above study, a questionnaire based on life habits and sleep health was used. From the questionnaire involving life habits and sleep health [23,24] (Appendix), five sleep-health risk factors were determined by factor analysis, and these were scored as fellows: (1) sleep maintenance problems, (2) parasomnia-like problems, (3) sleep apnea, (4) difficulty waking up and (5) difficulty initiating sleep. Furthermore, the total

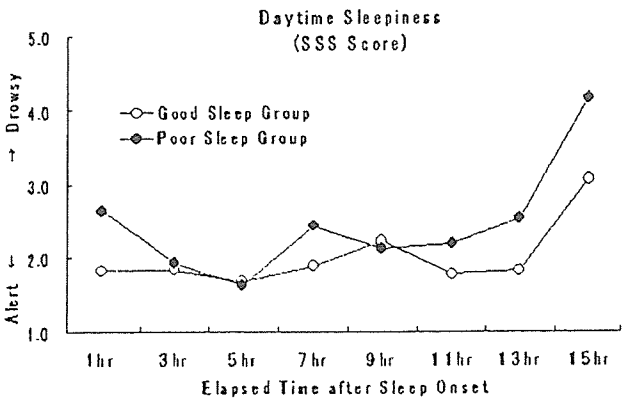


Fig. 5. Comparison of sleepiness between good sleep group and poor sleep group.

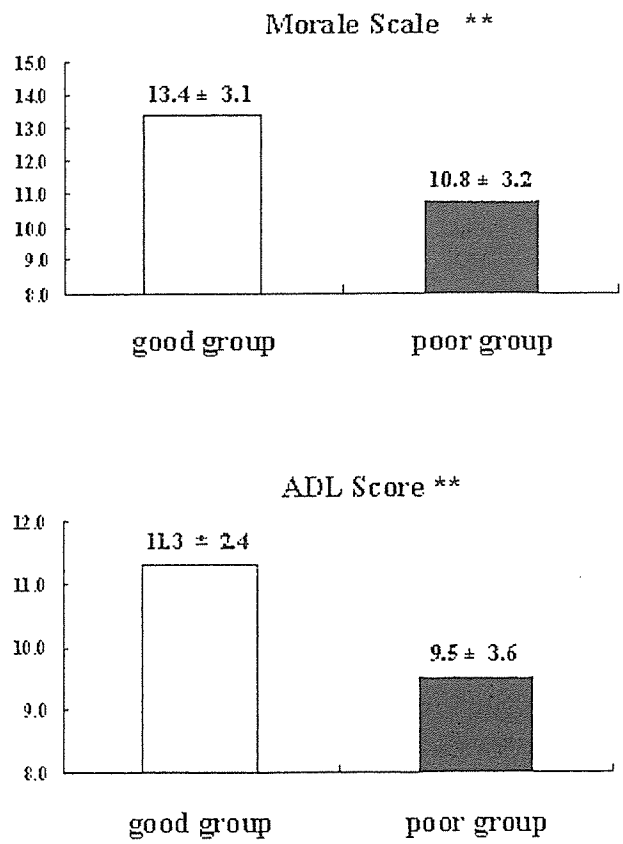


Fig. 7. Comparison of morale and ADL between good sleep group and poor sleep group.

score of each factor score was calculated as the Sleep-Health Risk Index [23,24] (Fig. 8, Appendix A). According to the rank of the Sleep-Health Risk Index, 117 (1/4 higher ranking) subjects were classified in the poor sleep-health group, and 117 (1/4 lower ranking) subjects were classified in the good sleep-health group. The two groups were then compared.

Ensuring good sleep, then, would clearly seem to occupy an important position in maintaining and promoting the mental and physical health of the elderly. The elderly have an increased incidence of various physical diseases, and suffer a corresponding increase in sleep disorders. Sleep has an active role in maintaining the body's functions, and sleep disorders have various affects on the maintenance of life. These can be life-threatening risks for elderly people, whose health is already more fragile than before.

## Effects on the brain, mind and body from sleep lack or disorder

The effects of a lack of sleep or sleep disorder on brain function include decreased memory and learning functions, and lower powers of attention and concentration. Maintaining the powers of attention and concentration is sometimes difficult in the elderly, so that there is an increased risk of accidents such as falls and broken bones. Physically, lack of sleep or sleep disorders can cause decreases in the restorative functions of the body and protective (immune) maintenance functions. Decreased immune function means decreased resistance to infectious diseases, and the elderly in particular have an increased risk of infection. In addition, respiratory disorders during sleep have a great impact on the cardiovascular system, and are known to raise the risk of ischemic heart diseases, hypertension, dementia and other diseases. Known effects on mental health include lower levels of emotional control, motivation and creativity.

## Survey of insomnia among the elderly: characteristics of insomnia in the elderly

Insomnia is an experience of inadequate or poor quality sleep characterized by one or more of the following: (1) difficulty falling asleep (sleep-onset insomnia), (2) difficulty maintaining sleep, (3) waking up too early in the morning (early morning awaking) and (4) nonrefreshing sleep (non-restorative sleep). Insomnia also involves daytime consequences, such as "tiredness, lack of energy, difficulty

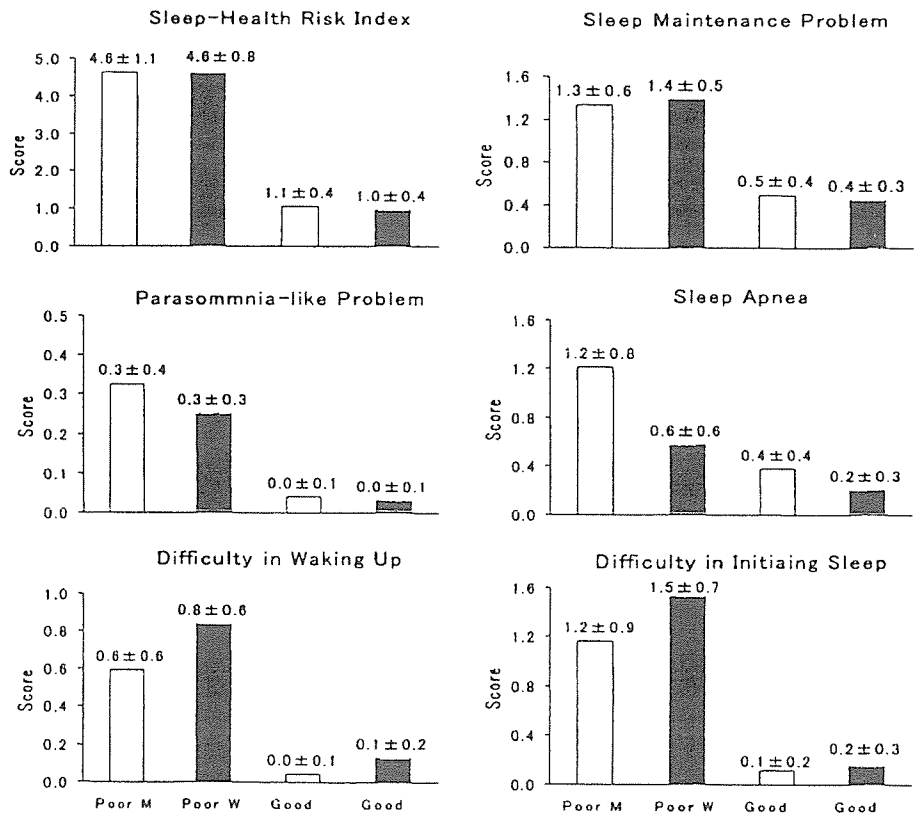


Fig. 8. Comparison of Sleep-Health Risk Index between group and sex difference. ** $P<0.01$.

concentrating, irritability" [4]. A recent national survey [14] of 3030 people aged 20 years or over in Japan found that 21.4% had experienced insomnia within the previous month. Thus, about one in five people today live day-to-day with insufficient or poor quality sleep. By age, the percentages were 18.1% for those aged 20–39 years, 18.9% for those 40–59 years and 29.5% for those 60 years and above. Thus, insomnia increases with age, with about one in three elderly people suffering this condition. About 1 in 10 elderly people are reported to have difficulty falling asleep, 1 in 5 to have night awakenings and 1 in 8 to awake too early in the morning. The causes of insomnia, other than the effects of age, are considered to include lack of exercise and difficulty dealing with stress.

In a survey on sleep disorders in 6466 outpatients (aged 3–99 years) at general hospitals nationwide (1996), the percentages of people reporting the use of sleeping medication or tranquilizers to assist them in falling asleep were 8.2% overall; 11.2% of men and 17.8% of women in their 60s; and 16.3% of men and 20.9% of women in their 70s. Use of such medication was thus shown to be particularly high among elderly women. In addition, people suspected of having restless legs syndrome or periodic limb movement disorder, which tend to be misdiagnosed as sleep-onset disorders or deep sleep disorders, accounted for 1.8% of males and 1.4% of females. Among those 80 years of age or above, they were 4.8% of males and 5.9% of females.

## Reconsidering lifestyles is key to improving sleep: learning from the elderly of the "Longevity Prefecture," Okinawa

To clarify the type of lifestyle and specific measures that strongly impact sleep health, we compared the sleep health and lifestyles in Okinawa, where pre-urbanization lifestyle of Japan is considered to remain and people live unhurried lives, and Japan's largest city of Tokyo. We found an overwhelmingly smaller number of elderly people in Okinawa who were troubled because of sleep, and that elderly people in Okinawa have good sleep health. In terms of lifestyle, many Okinawans took short daytime naps, went out for evening strolls and exercised regularly. It was found in particular that elderly people who took a short nap of less than 30 min between 1300 and 1500 h had good nighttime sleep.

A considerable number of elderly people in Tokyo took naps in the evening or before going to bed, and their poor nighttime sleep was a major cause of deterioration in the proper arousal maintenance function during the day. It was thus found that elderly Okinawans slept well, and that a nonurban lifestyle with daytime naps, evening walks and appropriate exercise played a key role in the maintenance and promotion of sleep health. The elderly of Okinawa, known as the prefecture of long life, is reported to sleep better compared with those in the Tokyo metropolitan area [1]. Factors contributing to this include regular sleeping hours, as well as daily habits such as short naps and light exercise in the evenings [9,23]. In addition, it has been reported [10] that even inside the prefecture as well, there were regional differences in sleep health and lifestyle, furthermore, in ADLs. It thus seems necessary to re-examine the essential human lifestyles of earlier ages that were better for us physically. As may be understood from the foregoing, ensuring comfortable sleep is essential to a healthy, energetic old age.

## Reconsidering naps: short daytime naps are effective in preventing senility and lifestyle-related diseases

Until recently, daytime naps were considered to interfere in falling asleep and the maintenance of sleep at night, and to be a cause of insomnia. In lifestyle guidance for the elderly with sleeping problems, naps were forbidden and enhanced daily activities were emphasized. Recently, however, it has come to be understood that healthy elderly tend to regularly take short daytime naps, and that naps of less than 30 min prevent nighttime insomnia among the elderly. We should therefore re-examine our thinking with regard to napping by the elderly. Moreover, although naps were thought to interfere with nighttime sleep, it is now known that this is only true of long naps of more than 1 h (which have a negative effect because the person goes into deep sleep) that produce sleep inertia (the bad mood and disorientation that a person feels upon waking), and naps close to bedtime.

It has recently been reported [15,16] that short daytime naps inhibit drowsiness and feelings of fatigue, and are effective in improving task results and EEG activity and lowering blood pressure. Short naps, therefore, are beneficial for brain function and relieving fatigue, and effectively prevent lifestyle-related diseases. Moreover, there are further benefits of regular short daytime naps. A habit of taking short daytime naps is known to be a preventive factor for dementia of the Alzheimer type [17]. Short naps of less than 30 min have been shown to reduce the risk of developing dementia to less than one fifth, and daytime naps of between 30 min and 1 h to reduce the risk to less than one half. Naps longer than 1 h, on the other hand, are associated with a twofold increase the risk of dementia of the Alzheimer type. Thus, regular short naps are effective, whereas naps that are too long have the opposite effect. An extremely interesting finding has also been reported that, by taking regular naps of less than 30 min, people with apolipoprotein E4, which is a risk factor for the development of dementia of the Alzheimer type, can greatly reduce the risk of developing the disease. Naps of less than 30 min improve nighttime sleep and alleviate brain fatigue, which is thought to elevate immune function and thereby reduce the risk of developing disease. Comparing the above with

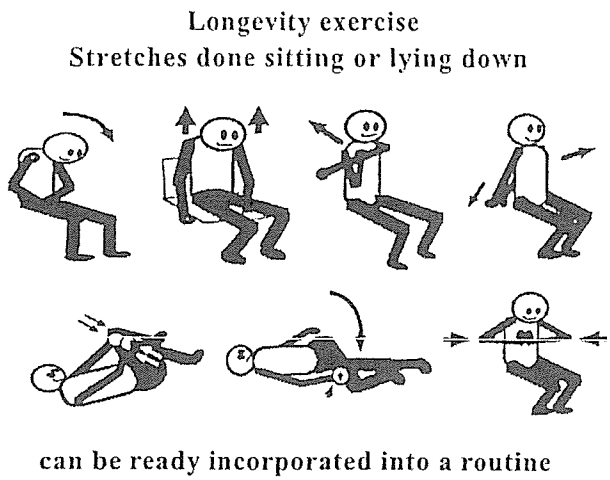


Fig. 9. Longevity exercises.

the fact that many elderly with a motivated lifestyle take regular naps, it would seem possible that short naps at the proper times can delay the advance of aging not only physically but mentally as well.

### Improving effects of short daytime naps and slight exercise in the evening on sleep

Recently, several nonpharmacological treatments have been shown to improve sleep in the elderly [2]: sleep restriction therapy [25], cognitive behavior therapy [26,27], appropriately timed bright light [28], exercise [29,30] and passive body heating [31].

Four years ago, we began a joint university–community project that included a field validation study and sleep-health classes. The aim was to both assist the elderly in obtaining quality sleep and create a lifestyle for an aging society. The subjects were elderly people suffering from insomnia, with whom we conducted a 4-week interventional guidance in short naps after the lunch and light evening exercise (exercises that can be readily incorporated into a routine, such as easy-to-remember light stretches done sitting or lying down and abdominal breathing; Fig. 9, longevity exercises).

The subjects of this study [32] were 11 elderly people (73.8±5.4 years) who gave informed consent for their participation. "Intervention" by a short nap after lunch (30 min between 1300 and 1500 h) and exercise with moderate intensity including stretching and flexibility in the evening (30 min from 1700 h) was carried out for 4 weeks in winter. All subjects were able to lead a normal life at home, and screening tests before the "intervention" were used to exclude those who experienced sleep problem due to illness. Their physical activities were recorded using actigraphs for 1 week pre- and postintervention. Actigraph data were analyzed to determine "sleep" and "wake" periods by applying a Cole's validated algorithm [33] to the portions of the records identified as sleep periods by the combination of sleep logs. Mental health was assessed using the General Health Questionnaire (GHQ) [34]. Furthermore, a questionnaire mainly about their volition and physical health was performed only after intervention.

After the intervention (Figs. 9 and 10), sleep efficiency significantly increased, showing that sleep quality was improved. Furthermore, nodding in the evening significantly decreased after the "intervention." Their GHQ score also significantly decreased, showing that their mental health was also improved. After the "intervention," many elderly answered that volition and physical health also improved (volition: 63.6%; physical health: 90.9% of all subjects).

The key points in the mechanism for improved sleep are maintaining proper wakefulness during the day, and

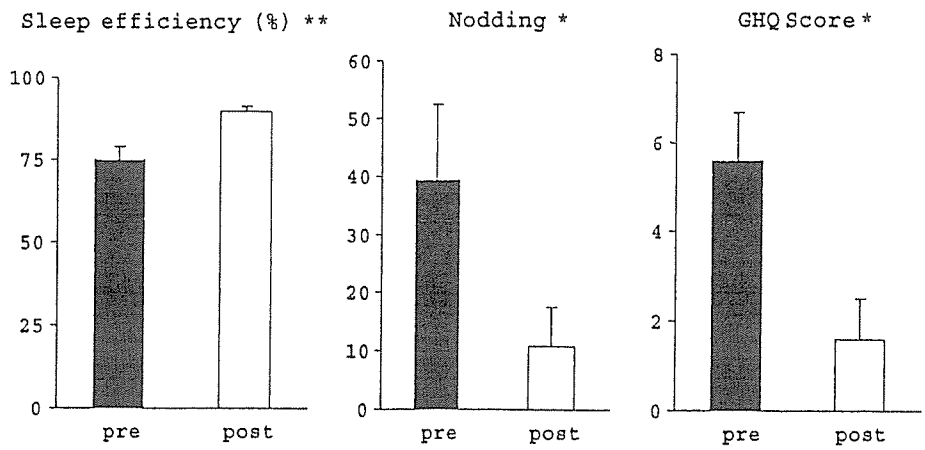


Fig. 10. Comparison of pre- and postintervention results for sleep quality, nodding and mental health in the elderly. * $P<.05$; ** $P<.01$.

preventing dozing off from the late afternoon until bedtime. Present results demonstrated that the proper awakening maintenance during evening was effective in improving sleep quality. Until recently, it was considered that taking a nap has a negative effect on the nocturnal sleep. However, a short nap of 30 min between 1300 and 1500 h has little quantitative effect on nocturnal sleep. Moreover, a short nap is effective for recovery of attention, concentration and brain function [15,23]. The present results reconfirmed that habitually taking a short nap is effective in maintaining sleep quality [14,15,23], and indicated that napping is an effective way for elderly people to maintain the sleep. The body temperature phase of elderly people is advanced 2–3 h ahead of that of young people [35]. Moreover, the existence of a "forbidden zone" was demonstrated [36]. This "forbidden zone" is the time period in the vicinity of the highest value of body temperature, and it corresponds to the peak of muscle and exercise capacity [37]. It is considered that this time zone occurs around 1700 h, and that exercise around this time is effective for improving sleep quality of elderly people. It is also considered that exercise in the evening increases the activity of the arousal system in the "forbidden zone." It is considered that arousal maintenance in the afternoon may be recovered by the short nap, and that the quality of the daytime arousal of the elderly people in this study was improved by exercise in the evening. As a result, the frequency of nodding before going to sleep decreased, and the quality of nocturnal sleep was improved. After the "intervention," mental health also improved with improving sleep quality. Furthermore, volition and physical health also improved with improving sleep quality. A short nap of 30 min and light evening exercise promote good quality sleep at night and a high level of motivation on waking the following day, forming a positive cycle.

## Brain function, physical health and developing the habit of taking short naps and doing longevity exercises

As part of a commissioned survey project on health promotion (Health and Physical Strength Promotion Foundation), in 2001 we conducted a study on establishing lifestyle guidance intervention on field assessment techniques for sleep improvements related to mental and physical health and brain function in the elderly. Elderly people selected on the basis of regular medical checkups and health survey results gathered at a community center, and public health nurses and instructors, with some community health promotion committee members and students of the clinical psychology course at Hiroshima International University, participated as staff. With this group, sleep-health classes were conducted as a health promotion activity and verification study through the cooperation of the university and community (one class consisted of about 20 people, and met 3 days a week for 4 weeks). Health management and guidance, development of habits, interview surveys, measurements, analyses, assessments of effect and feedback were conducted in mutual cooperation. Furthermore, visual detection task and tests of physical strength and fitness (the muscular power of a leg, pliability, balance, etc.) were performed pre- and postintervention.

The subjects of this study were 15 elderly people (73.1±5.2 years) who gave informed consent for their participation. "Intervention" by a short nap after lunch (30 min between 1300 and 1500) and exercise with moderate intensity including stretching and flexibility in the evening (30 min from 1700) were carried out for 4 weeks in winter. All subjects were able to lead a normal life at home, and screening tests before the "intervention" were used to exclude those who experienced sleep problem due to illness. Their physical activities were recorded using actigraphs for 1 week pre- and postintervention.

After the intervention, wake time after sleep onset significantly decreased, showing that sleep quality was improved. Their GHQ score also significantly decreased, showing that their mental health also improved.

After the intervention, in addition to improvements in sleep, the elderly participants were found to have significantly better results on a computer cognitive task as well as improved brain function (Fig. 11). The results of visual detection task were also improved after the "intervention." After the intervention, there was a significant reduction in evening naps and drowsiness and the classes were recognized to be effective in ensuring the maintenance of proper wakefulness before bedtime, including during the day. The reduction in daytime drowsiness is thought to have contributed to improved brain function. As for tests of physical strength and fitness, the muscular power of a leg, pliability, the sense of balance significantly increased. Improvements were also seen in measurements of physical strength (Fig. 12). Alertness, motivation, physical fatigue, concentration ability, appetite, level of confidence and other parameters (Table 1) also showed significant

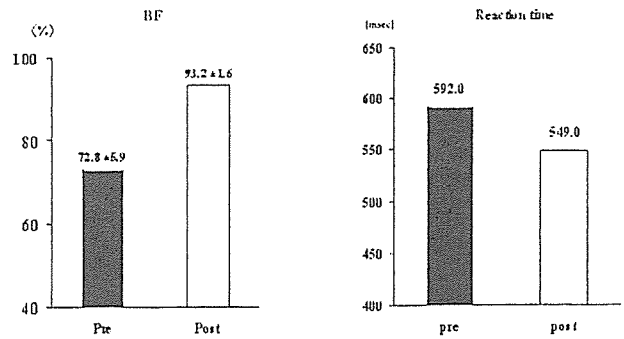


Fig. 11. Comparison of pre- and postintervention results for brain function. ** $P<0.01$.

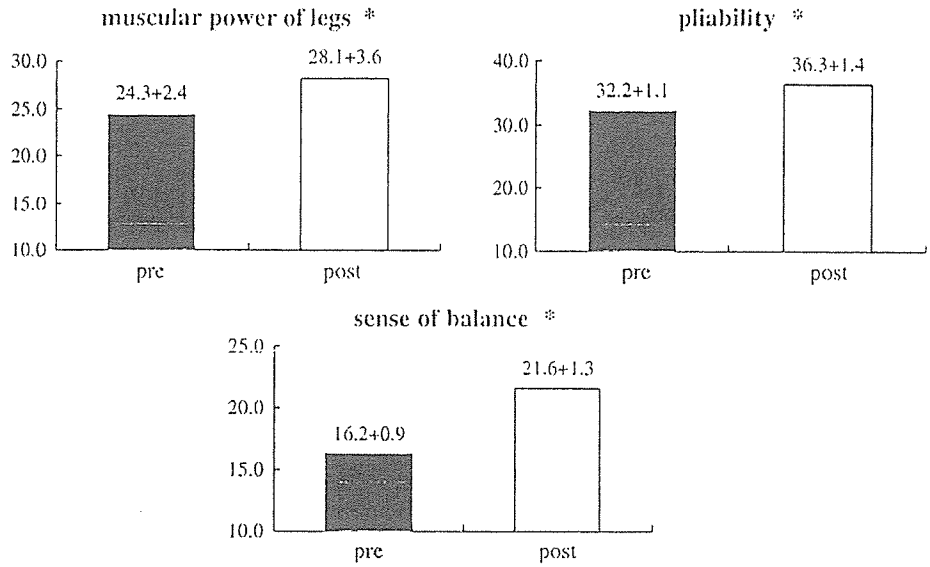


Fig. 12. Comparison of pre- and postintervention results for physical strength measurements.

improvements. After the "intervention," many elderly answered that mental, physical health were also improved.

To evaluate and confirm the effects of the health guidance classes, we developed a subjective mental and physical state assessment sheet to be used mainly on-site by the public health nurses, and investigated the distribution of degree of improvement in health and sleep status (Table 2). About 80% of the elderly reported improvements in state of sleep and falling asleep (Fig. 13). The majority of subjects also reported improvements in their general physical condition and motivation, and felt that food tasted better. These results demonstrated that developing the habits of taking short daytime naps and doing longevity exercises as a result of lifestyle guidance led to improvements in sleep and physical condition and increased motivation. Thus, on both the subjective mental and physical condition assessment sheet and in postinstruction objective indicators such as actigram and physical strength measurements and computer tasks improvements were seen in sleep, motivation, daytime mood and physical condition. Effective field activities are promising as simple evaluation methods in the future. To help establish the habits of taking short daytime naps and doing longevity exercises, regular sleep-health classes are now being held as one means to create a lifestyle for an aged society and prevent dementia and bed confinement. One very interesting result has appeared: in towns that have energetically launched health education and health promotion activities for the elderly, medical fees that were running about 1,000,000 yen per elderly resident 4 years ago have currently been reduced to less than 700,000 yen. In short, the cost of medical care has been reduced to 70%.

Table 1
Psychological improvements (using the visual analogue scale) by intervention

| | Pre | Post | $t$ | $P$ |
|---|---|---|---|---|
| Alertness | 48.0 (14.6) | 78.4 (19.9) | 4.38 | <.01 |
| Motivation | 50.1 (12.3) | 76.5 (24.4) | 3.43 | <.01 |
| Fatigue recovery | 45.4 (10.9) | 77.3 (21.6) | 4.09 | <.01 |
| Concentration | 46.1 (11.1) | 65.8 (20.0) | 2.69 | <.05 |
| Appetite | 52.4 (16.5) | 77.5 (20.3) | 3.79 | <.01 |

Values are expressed as mean (S.E.).

Table 2
Questionnaire of subjective appraisal of mental and physical health

Please respond to the following questions about your state of mental and physical health over the past several weeks

| | | | |
|---|---|---|---|
| 1) How is your overall condition? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 2) How are your shoulders/neck? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 3) Your waist/ lower back? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 4) Your knees? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 5) Sleep? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 6) Falling asleep? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 7) Waking up? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 8) Motivation/drive? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 9) Going out, meeting people (activeness)? | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |
| 10) Taste of meal | 1. Much better | 2. A little better | 3. Unchanged |
| | 4. A little worse | 5. Much worse | |