Effects of Aging on Activity of the Prefrontal Cortex and Autonomic Nervous System during Mental Stress Task

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Abstract We evaluated the effect of aging on the prefrontal cortex (PFC) activity and heart rate during the task. Employing near infrared spectroscopy (NIRS), we measured hemoglobin concentration changes in the bilateral PFC during a mental arithmetic task in young and older females. We selected the subjects who exhibited an increase in oxyhemoglobin with a decrease in deoxyhemoglobin during the task. We observed that right PFC activity predominantly modulates sympathetic effects during the task in both groups. However, the changes of oxyhemoglobin and heart rate during the task in older subjects were significantly smaller than those in young subjects. These results indicate that aging affects evoked cerebral blood oxygenation (CBO) response patterns of the PFC during a mental stress task. Aging did not affect the laterality of PFC activity in modulation of ANS function in the subjects who exhibited increases of oxyhemoglobin and deoxyhemoglobin associated with a decrease of deoxyhemoglobin during the task. However, aging reduced the heart rate increase during the task.

1 Introduction

The prefrontal cortex (PFC) plays an important role in mediating behavioral and somatic responses to stress via projections to the autonomic centers [1]. A number of studies have demonstrated that the cerebral regulations of stress responses may be differentially mediated by the right and left PFC [2]. Recently, employing near-infrared spectroscopy (NIRS), we have demonstrated that right dominant PFC activity was associated with a greater increase of heart rate during a mental arithmetic task in young females [3, 4, 5].

NIRS studies demonstrated that elderly subjects showed a significantly lower increase in oxyhemoglobin (oxy-Hb) concentrations in the frontal lobe

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during cognitive tasks compared with young subjects [6]. In addition, older subjects exhibited deactivation (i.e. decreases of oxy-Hb) in the frontal lobe during cognitive tasks [7]. However, it is not yet clear how aging affects the PFC activity and the autonomic nervous system function during mental stress tasks. In the present study, employing NIRS, we measured the cerebral blood oxygenation (CBO) changes in the PFC and heart rate changes during a mental arithmetic task. We compared the CBO changes with heart rate changes in young and elderly subjects.

2 Methods

We studied young ($n = 24$, 21.3 ± 0.9 years) and elderly ($n = 11$, 56.9 ± 4.2 years) females. The subjects were all deemed right-handed according to the laterality quotient questionnaire of the Edinburgh Handedness Inventory. All subjects provided written informed consent as required by the Human Subjects Committee of the Shiseido Life Science Institute.

We employed a mental arithmetic task as a psychological stressor. The subjects were asked to consecutively subtract a two-digit number from a four-digit number (e.g. 1022–13) as quickly as possible for 60 s. In order to assess psychological stress levels, subjects were asked to fill in the State-Trait Anxiety Inventory (STAI) before and after task performance.

CBO was measured in the bilateral PFC with a NIRS monitor (NIRO-300, Hamamatsu Photonics K.K., Hamamatsu, Japan). The NIRO-300 monitor simultaneously measures the concentrations of oxy-Hb, deoxyhemoglobin (deoxy-Hb), and total hemoglobin (total-Hb; oxy-Hb + deoxy-Hb). The hemoglobin concentrations were expressed as changes from baseline concentration (arbitrary units). The NIRS probes were set symmetrically on the forehead with a flexible fixation pad so that the midpoint between the emission and detection probes was 3 cm above the centers of the upper edges of the bilateral orbital sockets; the distance between the emitter and detector was set at 4 cm. This positioning is similar to the midpoint between electrode positions Fp1/Fp3 (left) and Fp2/F4 (right) of the international electroencephalographic 10–20 system. MRI confirmed that the emitter–detector was located over the dorsolateral and frontopolar areas of the PFC.

Heart rate was simultaneously monitored with PFC activity using a photoelectrical sensor (Tsuyama MGF KK, Tokyo, Japan). Instantaneous heart rate was calculated every 10 s from a mean frequency value between 0.05 and 2 Hz by Fourier analysis. ANS function was evaluated by heart rate variability analysis; the low frequency (LF) amplitude (0.04–0.15 Hz) and the high frequency (HF) amplitude (0.15–0.4 Hz) were calculated by power spectral analysis over a 3 min-period at both the start of the task and after task performance.

To analyze PFC activity in response to psychological stress, we calculated changes in oxy-Hb during the task. In order to determine left/right asymmetry of PFC activity, we calculated a laterality index (LI) for the oxy-Hb concentration changes ([right – left]/[right + left]); LI > 0 indicates greater activity of the right PFC, while LI < 0 indicates greater activity of the left PFC [3, 4, 5]. The relationships between PFC activity (LI of oxy-Hb), and heart rate changes were analyzed by calculating Pearson's correlation coefficient.

3 Result

We observed three different patterns of NIRS parameter changes during the task. In both groups, the most common NIRS parameter change was an increase in oxy-Hb and t-Hb associated with a decrease in deoxy-Hb. The frequency of this pattern in the older group (11/20 cases, 55.0%) was considerably lower than in the young group (24/30 cases, 80.0%). The second most common pattern was decreases of oxy-Hb and t-Hb during the task, suggesting a decrease of neuronal activity during the task. This CBO response pattern was more common in the older groups, (5/20 cases, 25%) than the younger group (2/30 cases, 6.7%). The third most common pattern was an increase of deoxy-Hb associated with decreases of oxy-Hb and t-Hb. We observed this pattern in 13.3% (4/30 cases) and 20.0% (4/20 cases) in the young and older groups, respectively. We selected the subjects who exhibited the most common pattern of NIRS parameter changes for the following analysis of the PFC activity.

We evaluated the LI of oxy-Hb concentration changes and heart rate, and found that there were significant positive correlations between heart rate changes and the LI of oxy-Hb in both young ($r = 0.64$, $p = 0.00080$) and older ($r = 0.83$, $p = 0.0016$) subjects (Fig. 1). However, there were significant

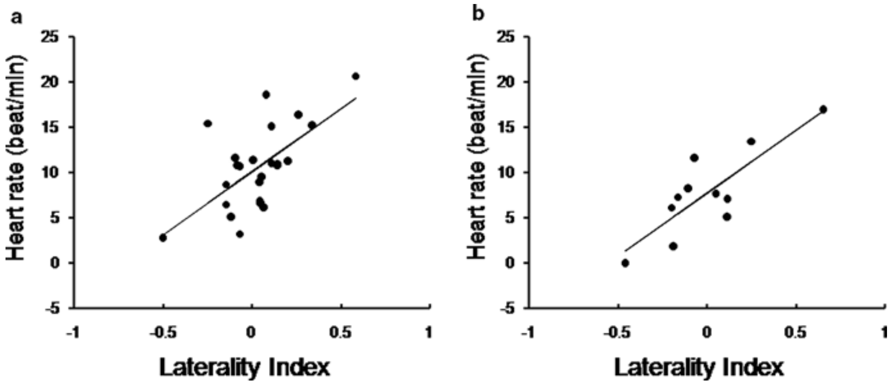

Fig. 1 Relationship between the laterality ratio scores and heart rate changes in young (a) and elder subjects (b). The *vertical and horizontal axes* denote change in heart rate (beat/min) and the laterality index (oxy-Hb), respectively. Significant positive correlations were observed in young ($r = + 0.87$, $p < 0.0001$) and elder subjects ($r = + 0.85$, $p < 0.0001$)

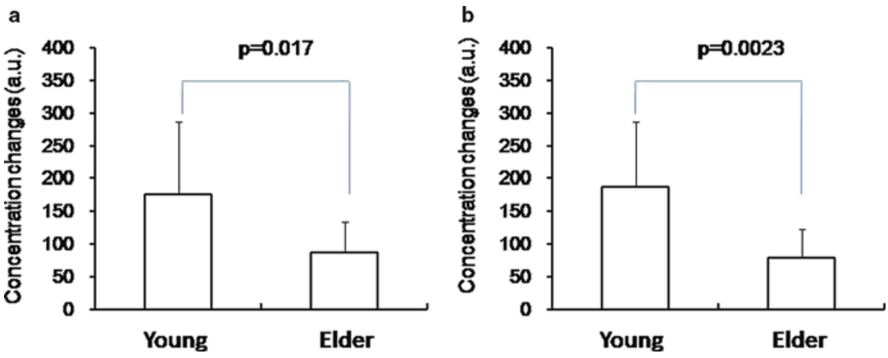

Fig. 2 Differences in oxy-Hb changes during a mental arithmetic task in the *left* (a) and *right* PFC. Note that the changes of oxy-Hb in older subjects were significantly smaller than those in young subjects

differences in changes of oxy-Hb, heart rate and STAI-II between young and older subjects. That is, the changes of oxy-Hb in older subjects were significantly smaller than those in young subjects (Fig. 2). The changes of heart rate in older subjects were significantly smaller than those in young subjects ($p = 0.018$), although there was no significant difference in heart rate at rest between the groups (Fig. 3a). In addition, the changes of STAI-II after the task in older subjects were significantly larger than those in young subjects (Fig. 3b).

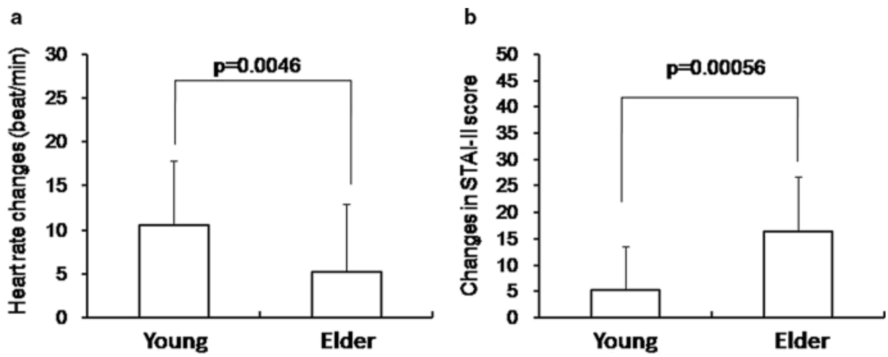

Fig. 3 Differences in changes of heart rate (a) and STAI-II scores (b) during a mental arithmetic task. Note that older subjects showed smaller changes of heart rate and larger changes in STAI-II after the task compared with young subjects

4 Discussion

In the present study, we observed several different patterns of evoked CBO response. The most common pattern of NIRS parameter change was an increase in oxy-Hb and t-Hb associated with a decrease in deoxy-Hb in both the young and older group; this pattern is consistent with the findings of a PET study in normal adults [8]. Interestingly, the frequency of this pattern in the older group was considerably lower than in the young group. In addition, the older subjects exhibited decreases of oxy-Hb and t-Hb more frequently than the young subjects. Such differences in evoked CBO response pattern observed between young and older subjects are consistent with reported NIRS activation studies [6, 7]. These observations may reflect a possible functional reorganization during aging [9].

When we analyzed the subjects who exhibited increases of oxy-Hb and t-Hb associated with a decrease of deoxy-Hb during the task, we observed that right dominance of PFC activity was associated with an increase in heart rate during the mental stress task in both young and older subjects, indicating that the relation between left/right asymmetry of PFC activity and ANS function was not affected by aging. Interestingly, the lateralization of the PFC activity in higher-order cognitive functions tends to be reduced by aging [10]. Therefore, effects of aging on PFC activity depend on characteristics of cognitive tasks.

In the present study, aging reduced the heart rate increase during a mental arithmetic task. However, the effect of aging on ANS response to mental stress remains in dispute. A number of studies have demonstrated that sympathetic nervous system reactivity to stress increases with age in humans [11]. Ng et al., however, demonstrated that older subjects tended to show smaller increases in heart rate during cognitive tasks, including a mental arithmetic task [12]. These results indicate that sympathetic neural hyper-reactivity does not appear to be a fundamental feature of the aging process in humans.

We found that the changes of oxy-Hb in older subjects were significantly smaller than those in younger subjects However, possible changes in optical pathlength during aging could cause such differences. In our preliminary study, we compared the optical pathlength in older and young subjects using time-resolved spectroscopy; however, we found no statistically significant difference between the two groups ($p = 0.28$), which is consistent with the results obtained by Hoshi et al. [13]. These results suggest that aging reduced the neuronal activity in the PFC during a mental arithmetic task.

In summary, aging affects the evoked CBO response patterns of the PFC during a mental stress task. Aging did not affect the laterality of PFC activity in modulation of ANS function in the subjects who exhibited increases of oxy-Hb and deoxy-Hb associated with a decrease of deoxy-Hb during the task. However, aging reduced the heart rate increase during the task.

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