VIII. 3. Evaluation of Cerebral Activity and Autonomic Function during Accompanying with Animal: a PET Study

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Introduction

Nowadays, partnership between human and animal has been well-established, relieving mental stress and anxiety for control our emotions in our busy life. Human-animal bond has been studied in terms of autonomic function and central brain activities. Previous investigators argued that heart rate and blood pressure of human subjects decreased when being together with pet dogs¹, suggesting the presence of relaxing effects¹. Human-animal association possesses substantial impacts on moods and behaviors, which eventually brings psychological well-being. Previous findings suggest that human-animal association promotes psychological well-being in healthy people²-³. Clinical effects of animal-assisted therapy (AAT) has also been studied beforehand. Barker et al showed that AAT reduced state of anxiety levels among hospitalized Schizophrenia patients⁴. Furthermore, AAT provided vast effects on improvement of dementia level of geriatric patients⁵ and prevention of psychological disabilities of abused children⁶. However, the mechanism of these physiological and psychological well-beings among healthy subjects and psychiatric patients has not been studied elaborately.

The aim of the present work was to investigate the effects of being together with accompanying dog on our mood, autonomic activity and regional brain activity. Three dimensional positron emission tomography (3D-PET) and 2-deoxy-2-[¹⁸F]fluoroglucose ([¹⁸F]FDG) were applied to evaluate static regional brain activities in certain static conditions, i.e. with and without accompanying dogs. Subjects’ psychological condition and autonomic activity were assessed using Stress Response Scale (SRS-18) and heart rate
variability analysis (HRV).

**Subjects and Methods**

Fourteen healthy volunteers (men: 2; women: 12), those who are members of Japanese Animal Hospital Association, were assigned for this investigation. They had age range from 25 to 65 years old (mean ± S.D.: 43 ± 10.8 years old), without any psychological disorders. A written informed consent was taken from all subjects before start of the experiment. All the subjects were requested to take adequate rest and sleep during the night before the experiment day and they refrained from eating and drinking for at least 5 h prior to the start of the experiment. The study protocol was approved by the Clinical Committee for Radioisotope Studies of Tohoku University.

**Study design**

Each subject was studied twice as staying with accompanying animal (task) and without any company (control). The order of the conditions was counter-balanced. Subjects were requested to sit on chairs comfortably with eyes open in a dimly lit and quiet room. Then, two chest electrodes, Magnerode, TE-18 (Fukuda Denshi Co., LTD., Tokyo, Japan) were attached on subjects’ chest, over manubrium sternum and apex (left 5th intercostals space, about 1 cm medial to the mid-clavicular line) for evaluation of HRV. A Teflon catheter was inserted into the cutibal veins of right hands for administration of [¹⁸F]FDG. Then the subjects were requested to stay with their accompanying dogs for 35 min, following intravenous injection of [¹⁸F]FDG (74.5 MBq). ECG recordings for all subjects were performed following [¹⁸F]FDG injections for 30 min to evaluate HRV. During ECG monitoring, subjects were requested to keep a relaxed-respiration. ECG recording was obtained by using polar 810i (Polar Electro Oy, Finland). Furthermore, subjects’ psychological conditions were assessed by using Stress Response Scale (SRS-18) to rate their own stresses before PET scan was started. After 35 min of long uptake of [¹⁸F]FDG, all the electrodes were detached and they were requested to micturate before the commencement of PET scan. Figure 1 shows the study design.

In another, the resting control condition referred to subjects remaining in a sitting posture in a dimly lit room for 35 min following [¹⁸F]FDG injection (37.7 MBq). They were studied by maintaining similar study design as task condition without accompanying dogs.
**PET scan protocol**

For each subject, PET scans were conducted twice in a day with 2 hour separation for task (with dog) and resting (control) conditions and the order of the conditions were counterbalanced. In the PET scan procedure, the subjects were asked to lie down in the supine position on a PET table with eyes open following 40 min after \(^{18}\text{F}\)FDG injection. The PET room was kept dimmed and quiet and the scanning was done using PET apparatus (SET 2400 W, Shimadzu, Kyoto, Japan) with an intrinsic spatial resolution of 3.9 mm full width at half maximum (FWHM). The 3-D whole-brain emission scan lasted for 15 min from occipitomeatal line (OM line) to the vertex depending on the subjects’ physique. Transmission scan (post-injection) which continued 10 min, was performed with a \(^{68}\text{Ge}^{68}\text{Ga}\) external rotating line source (370 MBqs at purchase) to correct the tissue attenuation of emission photons (Fig. 1).

**Frequency-domain analysis of HRV**

Frequency-domain analysis of HRV is an important method in evaluating sympathetic and parasympathetic activity of heart among resting controls and task condition (with dog). HRV refers to variation between two consecutive heartbeats, those are assessed from RR intervals. Usually, frequency of peak R wave is taken for evaluating autonomic activity. There are two spectral components mostly known in the HRV spectrum as follows: low frequency (LF: 0.04 to 0.15 Hz) and high frequency (HF: 0.15 to 0.4 Hz) components, accordingly\(^7\). For HRV analysis, the values of spectral components (LF and HF) are obtained for evaluation of autonomic function (sympathetic and parasympathetic activity). Here, LF corresponds to mostly autonomic sympathetic activity and HF corresponds to autonomic parasympathetic activity.

For analysis, we used HRV analytical software (University of Kuopio, Kuopio, Finland)\(^8\). In this analytical procedure, a 30 minute-long ECG record (control and task) was used. Consecutive heart beat intervals (R-R interval) of ECG recording were measured after determining peak QRS complex to obtain HRV spectral components (LF and HF). In another, heart rate (HR) was estimated from consecutive R-R intervals. Power spectral analysis of heart rate variability in frequency domain was performed to determine autonomic sympathetic and parasympathetic parameters (LF and HF) with fast fourier transformation technique (FFT). These LF and HF parameters were distinguished from frequency bands\(^8\). The normalization values of LF and HF (nLF and nHF) were used for final elucidation of HRV data. Hence, normalized LF and HF (nLF and nHF) were
determined according to following formulas (9): nLF = LF / (LF + HF) and nHF = HF / (LF + HF), respectively. Here, (LF + HF) is expressed as total power (TP).

$^{18}$FDG-PET data analysis

The statistical parametric mapping (SPM 5) software$^{10,11}$ was used to identify regional glucose metabolic changes of PET brain images among control and task. First, the PET brain images were spatially normalized to reduce anatomical disparities between subjects. An $^{18}$FDG brain template of Montreal Neurological Institute, McGill University, Canada$^{11}$ was used in this normalization procedure by applying affine and nonlinear transformations. Then, smoothing was performed with a 8-8-8 mm isotropic Gaussian filter kernel for compensation of errors in spatial normalization procedure. Voxel-based statistical analysis was performed on these smoothed images using paired t-test, based on the general linear model to obtain metabolic changes of brain activities between two conditions (control vs task). The statistical threshold for significance was set at $p < 0.001$ without corrections for multiple comparisons. The locations of relatively activated brain regions between two conditions were identified in the x, y and z standard coordinates$^{12}$.

Statistical analysis

Group comparisons of SRS-18 scores between control and task were made by using a non-parametric test (Wilcoxon signed-rank test), and significant differences were set at $P < 0.05$.

Results

Subjects’ Psychological Stress Response Scale scores were shown in Fig. 2. SRS-18 scores were significantly lower ($p < 0.05$) in the task condition (with dog) when compared with control (Fig. 2).

Figure 3 shows the data of autonomic activities (sympathetic and parasympathetic: nLF and nHF) among control and task (with dog). It was found relatively stable nLF and nHF between control and task (with dog), evaluating from FFT analysis (Fig. 3).

In another, brain PET image data analysis revealed the changes of regional brain activations between control and task (with dog) ($p < 0.001$) (Fig. 4). SPM results demonstrated the deactivated brain regions in the left middle frontal gyrus (BA, 8), right fusiform gyrus (BA, 20), left putamen and thalamus during task (with dog) to compare with
control (Fig. 4); however, we did not find any activated brain areas at task (with dog).

**Discussion**

The present investigation evaluated the effects of being together with an accompanying dog on our mood, autonomic activity and regional brain activity by using SRS-18 scores, HRV and [18F]FDG-3-D PET technique. Subjects’ psychological condition such as SRS-18 scores were shown decreased (p<0.05) with accompanying dogs. The significantly reduced SRS-18 scores suggested that animal companionship can improve psychological condition from anxiety and stress. One study relating with changes of mood and physical health of animal pet (dog) owner showed that older people with pet dog owner had minor health problems and significant improvements in psychological well-being following after being a pet owner. Recent findings suggest that human-animal bond may promote psychological well-being. Hence, it is suggested that animal-companionship inducing psychological well-being may improve social behavior. Previous study relating with dog contact postulated that human-dog association increased social behavior and decreased agitated behaviors. This increase in social behavior may improve the quality of life (QOL).

Nowadays, the practice of animal companionship has been accomplished among population with psychiatric patients to improve psychological condition. For example, Barker and Dawson (1998) investigated the effects of animal companionship (pet dogs) on 230 hospitalized psychiatric patients and compared a single 30-minute animal companionship session with a 30-minute therapeutic recreation session. They found that the patients who had animal companionship showed a significant decrease in anxieties with mood disorders, psychotic disorders and other disorders. In the present study, significantly lower SRS-18 scores (p<0.05) suggested that subject’s stress and anxiety were relieved by the situation of staying with their dogs.

Recent findings revealed a relatively stable autonomic activities (nLF and nHF) between control and with dog. The heart function is mediated by autonomic nervous system. Hence, the rhythm of heart beat is controlled by autonomic sympathetic and parasympathetic nervous activities. Any variation in heart rate is referred to irregular balance between sympathetic and parasympathetic components of autonomic nervous system functions. Frequency domain parameters of LF (mostly sympathetic nervous activity) and HF (parasympathetic nervous activity) suggest cardiovascular activity linking with physiological status.
It is acknowledged that dominant parasympathetic activity (nHF) represents relaxation effects; however, our results suggest relatively stable autonomic function, suggesting of synchronized sympathetic and parasympathetic activities. This might bring mild relaxation effects on subjects’ mind with accompanying dogs. Inevitably, this stable autonomic activity suggests, human-animal interactions can persuade coolness and relaxation after harmonizing sympathetic and parasympathetic nerves activities of heart. Therefore, human-animal bond brings relaxation by reducing cardiovascular reactivity to stress and reliefs anxiety in the daily busy life.

As for the brain PET study, our results using SPM analysis (SPM 5) revealed the deactivated brain regions in the left middle frontal gyrus (BA, 8), right fusiform gyrus (BA, 20), left putamen and thalamus at task (with dog) when compared with control (p<0.01). However, we did not find any activated brain areas among subjects accompanying with dog. Since recent application of [18F]FDG-3-D PET technique on human-animal bond research was established as the first imaging study, animal companionship-induced (with dog) regional brain activities were assessed to determine a coordination between mind and brain. Accompanying animal (with dog) might have a stress-relieving effect that was demonstrated by deactivated brain areas. Furthermore, these deactivated brain areas during accompanying with dog support relaxations of subjects’ mind in psychological sense.

**Conclusion**

Present investigation evaluated the effects of being together with accompanying animal (with dog) on our mood, autonomic activity and regional brain responses. Results showed a significantly reduced psychological stress response scale (SRS-18) and some deactivated brain areas with accompanying animal, suggesting of psychological well-being and relaxations. Animal-assisted therapy (AAT) might have a potential application to certain programs for psychological rehabilitation and integrative health care facility. The brain mapping technique such as PET seems to be useful to examine the underlying brain mechanism of AAT in terms of regional brain responses.

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References

Figure 4. Reduction of regional brain activities with an accompanying animal (with dog). Results of PET brain images demonstrated the deactivations (p < 0.001) in the left middle frontal gyrus (BA, 8) (a), right fusiform gyrus (BA, 20) (b) and subcortical structures (left putamen and thalamus) (c) during accompanying with dog compared with control. However, any activated brain areas were not found during accompanying with dog.