A study on the brain structures related to conditioned emotional response by means of [14C]2-deoxy-D-glucose method.

Yamadori, T

Sugioka, K

Ishimoto, Y

(Citation)
The Kobe journal of the medical sciences,37(3):111-127

(Issue Date)
1991

(Resource Type)
departmental bulletin paper

(Version)
Version of Record

(URL)
https://hdl.handle.net/20.500.14094/E0034098

Kobe J. Med. Sci. 37, 111/127, June 1991

A STUDY ON THE BRAIN STRUCTURES RELATED TO CONDITIONED EMOTIONAL RESPONSE BY MEANS OF [^{14}C] 2-DEOXY-D-GLUCOSE METHOD

TAKASHI YAMADORI, KOZO SUGIOKA, and YOSHIHIDE ISHIMOTO

First Division, Department of Anatomy,
Kobe University School of Medicine

INDEXING WORDS

conditioned response; 2-DG method; autoradiography; brain structure; rat

SYNOPSIS

Brain structures activated during conditioned emotional response were studied by means of the [^{14}C]2-deoxyglucose method. The experimental (CSE) animals were conditioned with paired 25 25-sec-long flicker sequences (CS) and 1-sec-long 150 V AC electric shocks (US), while the control (CSC) animals were given only 25 CS sequences. Average densities of a unit square (200 μm × 200 μm) of 47 nuclei or cortical areas in the left hemisphere were obtained from an autoradiogram and the optical density ratio (ODR), which is the relative optical density of each structure to that of the corpus callosum, was calculated. Comparison of ODRs of each structure from both groups revealed a significant increased uptake of [^{14}C]2-deoxyglucose ($P<0.05$, Mann-Whitney U-test) in the caudal portion of area 10, area 2, area 18 and the hippocampal formation.

Received for publication: March 22, 1991
Authors' names in Japanese: 山鳥　崇, 杉岡幸三, 石本喜秀

INTRODUCTION

Several structures in the brain, such as the prefrontal lobe, hippocampal formation, cingulate gyrus, amygdaloid body, anterior thalamic nuclear group, mediodorsal thalamic nucleus, mamillary body, etc. have been implicated in memory processing [2,4,8,15,18,25,26,27,29,32]. However, the precise role of each of these structures on mnemonic function is still controversial. Most especially, studies elucidating the areas or structures related to classical conditioning or learning by the [^{14}C]2-deoxyglucose ([^{14}C]2-DG) method are limited[6,7,13], although physiological studies on the neuronal activity of the hippocampal formation and other specific structures which were thought to be related to conditioning have been undertaken[1,3,25,34]. In the present study we aimed to disclose the brain structures related to conditioned emotional response, which are considered to be a fundamental process of memory, by means of the [^{14}C] 2-DG method[36] that is capable of mapping the metabolically active areas of the brain during physiological and psychological stimulation.

MATERIALS AND METHODS

Animals and psychological experiments

Twelve adult male Wistar strain rats weighing 250 to 300 g were used. The animals were divided into an experimental (CSE, n=6) group and a control (CSC, n=6) group. Two days prior to the experiment, a 50 cm (approx.) long polyethylene tube (PE-50, Clay Adams) was inserted into the right external jugular vein of the animal. The other end of the tube was curled and enclosed in a plastic cylinder about 5.0 cm long and 1.3 cm in diameter, which had been sewn to the back of the animal.

For the CSE group, 25 paired 25-sec-long flickers (0.5 sec "on" and 0.5 sec "off" using a 10 W electric lamp on the ceiling of the experimental box) and 1-sec-long 150 volt AC electric shocks through

the grid-floor were administered as the conditioned stimulus (CS) and unconditioned stimulus (US), respectively. The intertrial interval (ITI) was 10 - 70 sec (mean 50 sec) and the interstimulus interval (ISI) was 24 sec, i.e., the US was given at the last sec of the CS presentation. The flickers and electric shocks were controlled by a programmable controller (OMRON, Koken-Rika Co.). The CSC group received only 25 25-sec-long flickers (Fig.1).

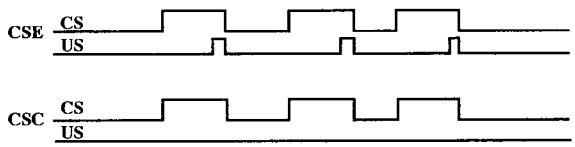

Fig. 1
Schematic representation of CS-US presentation in the CSE and CSC groups.

Two days after conditioning, animals of these 2 groups were given the CS 3 times. At the start of the conditioned emotional response test, 50 μCi of [^{14}C] 2-deoxy-D-glucose (New England Nuclear, Spec. act.: 45-55 mCi/mM) in 0.5 ml saline was pulse injected through the jugular venous catheter from the outside of the box. Then, the first 25-sec-long flickers were administered followed by 15 min ITI. The second CS was administered in the same way. Immediately after the third stimulus, that is, about 35 min after the start of the test, 1 ml of a saturated solution of KCl was injected through the same venous catheter to sacrifice the animal.

A box (410 × 210 × 300 mm in size) was used for the experiment. The walls and ceilings were made of acrylic plate while the floor was made of a copperphosphate grid. An electric current of 150 volts AC through a 250 KOhm resistance could be administered to the floor grid. The walls were also covered with a green, semi-transparent cellophane to blind the animal from the surroundings. A 10 W electric lamp was fixed on the acrylic plate-ceiling which also serves as an access door.

Autoradiography

A slight modification of the method of Sokoloff et al.[36] was used for the autoradiographic analysis, namely, an optic density ratio (ODR) was used instead of local cerebral glucose utilization (LCGU) to compare the incorporation of 2-DG between the 2 groups[6,7,17,38]. Immediately after death, the brain was taken out and the whole brain was frozen in cooled liquid freon (-60℃) and stored for 1-2 days in a deep freezer. Then, serial frontal sections of 20 μm thickness were prepared with a cryostat. Out of every 5 consecutive sections was selected for autoradiography and another one for Nissl staining. The sections for autoradiography were mounted on a glass cover slip, dried on a hot plate at 60℃, serially glued to a cardboard, and exposed for 7 days to a Fuji RX film (Fuji Corp.) in an X-ray cassette. A set of [^{14}C] methyl-methacrylate standards (Amersham), consisting of a series of progressively increasing known [^{14}C] concentrations, was also exposed to the same film. Each autoradiographic film image, which represented a 100 μm interval, was numbered.

Microphotometry

Alternate sections on the autoradiogram, namely, one per every 200 μm in the rostro-caudal direction, were cut out from the developed film and mounted on a glass-slide. Eight pieces of the film representing [^{14}C] standard concentration were also cut out and mounted on a glass-slide.

The density of a unit square (200 μm × 200 μm) was measured with a microphotodensitometer (Sankei, Co.) prepared for this purpose. The stage of the microphotodensitometer was automatically movable at a selective distance in both X and Y directions, so that automatic measurement of the density of the unit square was feasible. The density of the square read by the photo-multiplier was recorded on a NEC 9801 personal computer. Consequently, the density of the unit square was classified into 8 grades according to the [^{14}C] standard and was depicted as a color picture on the CRT

(cathode ray tube). After photometry, the average density of the unit square in 47 structures of the left hemisphere was calculated by a computer using a graphic tablet. The average density of the unit square in each section was divided by the density of the corpus callosum (CC) of the same section to obtain the optical density ratio (ODR) of each structure to the white matter, which showed the lowest and the most constant optical density in the brain. In the rostral or caudal sections where no corpus callosum was observed, the mean density of the corpus callosum of all the CC-containing sections of the brain was used as the denominator to obtain the optical density ratio of each structure. The ratios of the same structure belonging to CSE and CSC groups were analyzed for significance by the Mann-Whitney U-test.

Demarcation of cortical areas

To measure the density of each structure, it was necessary to demarcate the borderline on an enlarged autoradiogram. The Nissl stained sections and Koenig and Klippel's[12] atlas were helpful for the demarcation of various nuclei. In demarcating the nuclei in the brain stem, Pellegrino et al.'s[28] atlas was also used, while the cortical areas were demarcated following Krieg's[14] atlas. The demarcation of cortical areas was performed in a way so as to transfer the dorsal projection drawing of cortical areas in the Krieg atlas onto the dorsal surface of the autoradiographic sections. In this manner, only the density of areas that can be projected on the dorsal surface was measured in each section. The lateral and medial projection drawings of the Krieg atlas, which show the cortical areas in each surface, were not used in the present study to avoid any discrepancies in demarcation. To demarcate the borderline of each cortical area of the autoradiographic section, a line perpendicular to the tangent of the corpus callosum was drawn from the borderline point of the cortical surface in accordance with the direction of cell columns (Fig.2).

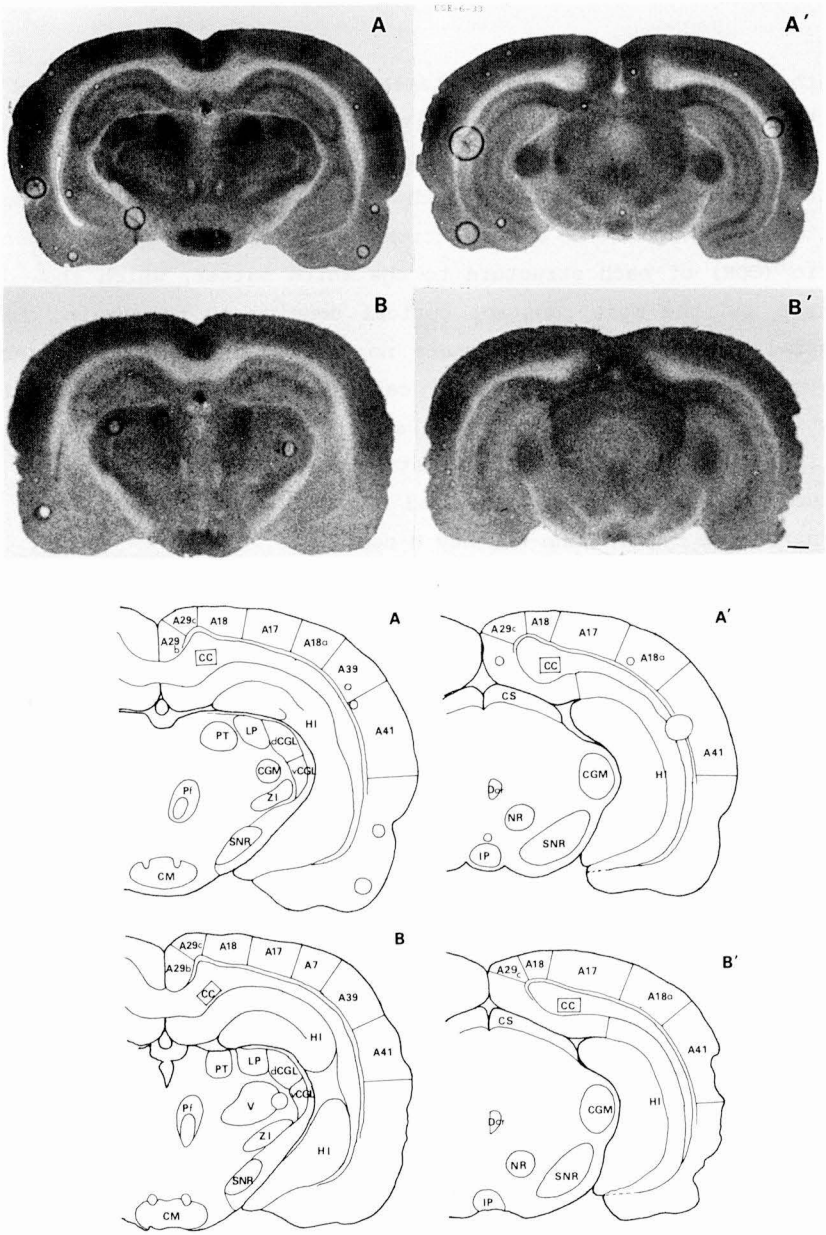

Fig. 2 Sections from autoradiograms of cases CSE-6 (A, A') and CSC-4 (B, B'). "A" is a section at the level of the lateral geniculate body and the mamillary body. The cingulate cortex includes A29c (dorsal) and A29b (ventral). "B" is a section at the same level as "A". "A'" is a section at the level of the interpeduncular nucleus and "B'" is a section at almost the same level as "A'". Medial geniculate body is dense and conspicuous in both "A'" and "B'". Abbreviations in the explanation figures are indicated in the text and tables.
Scale bar: 1 mm

RESULTS

As shown in Table 1, the mean unit-square-density of 16 diencephalic structures was measured and the ODR was calculated. These structures were the anterior thalamic nuclear group (A), paratenial thalamic nucleus (Pt), lateral thalamic nucleus (L), ventral thalamic nucleus (V), medial thalamic nucleus (M), posterior part of the lateral thalamic nucleus (LP), posterior thalamic nucleus (P), reticular thalamic nucleus (R), parafascicular nucleus (Pf), dorsal nucleus of the lateral geniculate body (dCGL), ventral nucleus of the lateral geniculate body (vCGL), medial geniculate body (CGM), habenula (Hb), mamillary body (CM), subthalamic nucleus (SUT), and zona incerta (ZI). Comparison of the ODR of the same structure within the CSE and CSC groups revealed that no nucleus had a significant increase in ODR ($P<0.05$). Although the mamillary body (CM) showed a high density of labeling in each brain, there was no significant difference in ODR between the CSE and CSC groups. In the telencephalon, mesencephalon, and pons the ODR of 11 nuclei was calculated (Table 2). These included the caudate nucleus-putamen (CP), globus pallidus (GP), amygdaloid body (CA), pretectal area (PT), superior colliculus (CS), inferior colliculus (CI), substantia nigra (SNR), red nucleus (NR), Darkschewitsch's nucleus (Dar; and its surrounding area), interpeduncular nucleus (IP) and oculomotor nucleus (NIII). Again, no nucleus showed a significantly higher 2-DG uptake in the CSE group.

The labeling density of 20 cortical areas, including the hippocampal formation, was also measured (Table 3). Comparing the results within the CSE and CSC groups, the caudal portion of area 10, area 2, area 18 and the hippocampal formation (HI), including the dentate gyrus (GD), displayed increased ODR ($P<0.05$) in the CSE group. Although the ODR in the caudal portion of area 10 in the CSE group displayed higher ODR as compared with the CSC group, the reaction of the whole area to the conditioned stimulus remains unclear since the labeling density within the whole area could not be figured out in all cases. Area 2 by the Krieg atlas seems to correspond to Par 1 by Zilles and Wree's[42] atlas into which the

Table 1 ODRs of diencephalic nuclei.

	CSE-group		CSC-group	
	Mean	SD	Mean	SD
A	1.95	0.19	1.79	0.22
Pt	1.85	0.16	1.74	0.22
L	1.83	0.18	1.69	0.16
V	1.88	0.12	1.70	0.19
M	1.88	0.17	1.72	0.19
LP	1.87	0.13	1.69	0.19
P	1.93	0.19	1.79	0.22
R	1.66	0.14	1.51	0.14
Pf	1.88	0.25	1.72	0.23
dCGL	1.85	0.17	1.65	0.18
vCGL	1.72	0.19	1.59	0.10
CGM	1.90	0.18	1.74	0.21
Hb	1.85	0.20	1.68	0.23
CM	2.17	0.17	1.95	0.26
SUT	1.84	0.17	1.73	0.19
ZI	1.88	0.20	1.68	0.20

SD: standard deviation, A: anterior thalamic nuclear group, Pt: paratenial nucleus, L: lateral thalamic nucleus, V: ventral thalamic nucleus, M: medial thalamic nucleus, LP: posterior part of the lateral thalamic nucleus, P: posterior thalamic nucleus, R: reticular thalamic nucleus, Pf: parafascicular nucleus, dCGL: dorsal nucleus of the lateral geniculate body, vCGL: ventral nucleus of the lateral geniculate body, CGM: medial geniculate body, Hb: habenula, CM: mamillary body, SUT: subthalamic nucleus, ZI: zona incerta

Table 2 ODRs of telencephalic, mesencephalic and pontine nuclei.

	CSE-group		CSC-group	
	Mean	SD	Mean	SD
CP	1.69	0.09	1.56	0.13
GP	1.32	0.06	1.26	0.08
CA*	1.62	0.14	1.53	0.09
PT	1.94	0.16	1.76	0.21
CS	1.82	0.19	1.67	0.17
CI	1.91	0.17	1.74	0.25
SNR	1.54	0.10	1.42	0.11
NR	1.78	0.17	1.62	0.18
Dar	2.01	0.18	1.83	0.23
IP	1.99	0.21	1.79	0.20
NIII	2.03	0.28	1.80	0.31

CP: caudate nucleus-putamen, GP: globus pallidus, CA: amygdaloid body, PT: pretectal area, CS: superior colliculus, CI: inferior colliculus, SNR: substantia nigra, NR: red nucleus, Dar: Darkschewitsch's nucleus, IP: interpeduncular nucleus, NIII: oculomotor nucleus, CA*: The density was measured in 5 CSC animals.

sensation from vibrissae, sinus hairs, and trunk and tail are transmitted. In the same way area 18 seems to correspond to area 29D and Oc2M. The hippocampal formation, as well as the dentate gyrus, had been deemed as the structures most relevant to memory or a conditioned emotional response. Measurement of the labeling density of the whole hippocampal formation including the dentate gyrus (HI) was first carried out and it showed an increased ODR ($P<0.05$) in the CSE group.

Table 3 ODRs of cortical areas.

	CSE-group		CSC-group		
	Mean	SD	Mean	SD	
A 1	1.83	0.10	1.69	0.19	
A 2	1.91	0.09	1.75	0.20	*
A 2a	1.95	0.09	1.80	0.24	
A 3	1.84	0.08	1.73	0.19	
A 4	1.88	0.08	1.73	0.19	
A 6	1.88	0.08	1.76	0.21	
A 7	1.90	0.11	1.75	0.21	
(A 10)	1.92	0.11	1.70	0.18	*
A 17	1.96	0.11	1.82	0.22	
A 18	1.86	0.10	1.71	0.18	*
A 18a	1.96	0.14	1.83	0.22	
A 23	2.01	0.15	1.81	1.23	
A 24	1.91	0.13	1.80	0.22	
A 29b	2.01	0.19	1.80	0.24	
A 29c	1.95	0.13	1.74	0.19	
A 36	1.83	0.20	1.76	0.26	
A 39	1.96	0.13	1.85	0.22	
A 40	1.91	0.11	1.80	0.20	
A 41	2.11	0.11	1.80	0.20	
HI	1.55	0.09	1.42	0.11	*

*: $P< 0.05$, Mann-Whitney U-test

A: Area, HI: hippocampal formation, (A10): The density was measured only in the caudal (posterior) portion of area 10 in all CSE animals and in only 5 CSC animals.

Behavior of several rats within both groups was observed during conditioning. At earlier trial stages, rats of the CSE group showed escape behaviors such as jumping or running at the time of shock (US) administration. Conversely, these animals displayed walking and/or rearing during the intertrial interval (ITI). When the conditioned stimulus was administered, however, such locomotion or gross body activities disappeared and animals showed an immobility response (termed "freezing"). This reaction is a species-specific

defense behavior elicited in painful or fearful situations. At later trial stages, rats of the CSE group showed a dominant immobility (freezing) response in the pre-CS period. In the period immediately following CS presentation, rearing and/or walking was observed. The application of an electric shock, however, quickly abolished these behaviors. With the presentation of the US (electric shock), the rats showed escape behavior such as jumping or running, but these behaviors soon subsided. Freezing continued to be observed during most of the post-US period. The appearance of freezing behavior with the presentation of the CS was taken as an evidence for the learning of the CS-US association. The animal of the CSC group, to which only the CS was presented, showed sniffing, face washing and grooming, which were not observable in the animals of the CSE group. In addition, the CSC animals exhibited no behavioral change at any stage.

DISCUSSION

In the present study, we employed the [^{14}C] 2-DG method to map active brain structures which are associated with areas of higher deoxyglucose incorporation. Structures relevant to conditioned emotional response were considered to be those with higher ODR. Our rationale for using ODR is to minimize the influence of individual variations among materials or density variations among sections of the autoradiograph, as recommended by Sharp et al.[35], when local cerebral glucose utilization could not be measured. Sokoloff et al.[36] indicated that the experimental period can be limited to 30 min, but the [^{14}C]deoxyglucose-6-phosphate concentrations in the tissue rise continuously and by 45 min are responsible for most of the ^{14}C in the tissues. However, according to our experimental schedule, we sacrificed the animal 35 min after the [^{14}C]2-DG application. This interval was thought to be within the permissible period of survival.

It is interesting to note that the caudal portion of area 10 showed an increased 2-DG uptake in the CSE group as compared with the CSC group. As it had been initially planned in the present study

to examine the structures related to conditioned emotional response particularly in the diencephalon and its surrounding structures, the rostral part of the cerebrum was discarded before sectioning. Thus, any assumption that there is a significant increase of 2-DG uptake in whole area 10 is precluded. Regarding the involvement of the prefrontal cortex in conditioned response or in memory processing, several reports should be considered. Fuster and Alexander[5] stated that excitation of neurons in the prefrontal cortex and mediodorsal thalamic nucleus was associated with the performance of a delayed response task in monkeys suggesting a role of frontothalamic circuits in the attentive process involved in short-term memory. Mishkin and Manning[19] reported that the cortex below the principal sulcus in the inferior prefrontal cortex of monkey appeared to be related to non-spatial memory, while the function of the tissue in the principal sulcus itself appeared to be limited to spatial memory. Orona and Gabriel[25] also implicated the prefrontal cortex and mediodorsal thalamic nucleus in learning and memory, while Roland[30], in a cerebral blood flow (CBF)-positron emission tomography (PET) study, demonstrated that the middle portion of the midfrontal area of the cerebral cortex in humans was activated when sensory information that was transformed during a task had been somatosensory in nature or was retrieved from memory. In 1985, Passingham[27] demonstrated memory impairment in a monkey with a prefrontal cortex lesion (involving tissue in the principal sulcus). He proposed that a frontal mechanism operated on information related to working memory. Recently, Lewis[16] commented that the frontal lobes were considered to be involved in the temporal context of memory while the hippocampus might play a more critical role in processing spatial contextual memory.

Area 2 by the Krieg atlas is considered to be the center of somatosensory system into which the sensation from vibrissae, sinus hairs, and trunk and tail are transmitted[39]. The higher uptake of 2-DG in this area can be attributed to conditioning process. Area 18 by the Krieg atlas seems to correspond to Oc2M and 29D by the Zille and Wree atlas. Oc2M is considered to be an association cortex of the Oc1, the primary visual cortex[33], while area 29D is considered as

a part of the agranular retrosplenial cortex[40]. Regarding the cingulate cortex, Piercey et al.[29] reported that the anterior cingulate was related to memory, and Meunier and Destrade[18] suggested that the posterior cingulate cortex, and in particular the cingulum bundle, was involved in both early acquisition and long-term memory processes. It is an interesting observation in the present study that Krieg's[14] area 18 which includes Oc2M and 29D showed significant increase of 2-DG uptake.

In the present study, optical density was not prominent in the hippocampal formation as compared with other structures, but it showed an increased uptake of 2-DG ($P<0.05$) in the CSE group, vis-a-vis the CSC group. It is widely held that the hippocampus or hippocampal formation is relevant to mnemonic function and learning[4,9,11,20,23,29]. The hippocampus is also said to be related to a cognitive, or spatial map of the environment[16,21,22] and some investigators[24,31] even linked this structure to working memory. Winocur[41] concluded that memory loss following thalamic (dorsomedial nucleus) damage was related to a deficit at the early stage of new learning, whereas hippocampal amnesia resulted from impairment at a later, integrative stage in which long-term memories were formed and durably stored. Although the dentate gyrus was implicated in a conditioned emotional response, it was impossible to elucidate clearly the uptake of 2-DG in this structure. Segal et al.[34] reported that neuronal units in the dentate gyrus were different from the hippocampus proper, though both were involved in classical conditioning. Neuronal units in the dentate gyrus responded by augmentation to a conditioned stimulus which led to food and by inhibition to the same stimulus when it preceded electric shock. However, units in the hippocampus proper responded by augmentation in both situations. As the demarcation of the dentate gyrus was not easy to be distinguished in coronal sections, the density of this structure was measured as a part of the hippocampus.

The mediodorsal nucleus of the thalamus, which is functionally associated with the prefrontal cortex, is reportedly related either to a certain process of conditioning and learning[3,25], or to short-term[5] and spatial memory[10]. According to Stokes and Best[37], lesions of

the mediodorsal thalamus in rats may fundamentally compromise memory systems and alter its ability to respond appropriately in a minimally cued environment. However, no specific increased 2-DG uptake was recognized in the medial thalamic nucleus (M) in the present study. The Mann-Whitney U-test also revealed no significant increase in the ODR in the mamillary body (CM) and the anterior thalamic nuclear group (A) in the CSE group vis-a-vis the CSC group, although these structures were reportedly related to spatial learning and memory[8], and to processes relevant to the maintenance and retention of the behavior[25], respectively. In the present study, the structures of the acoustic system showed higher incorporation of 2-DG in both the CSE and CSC groups.

To recapitulate, at the 25-trial stage, the conditioning is thought to be in formation process. Although structures such as the caudal portion of area 10, area 2, area 18 and the hippocampal formation showed an increased 2-DG uptake at the 5 % level of significance (Mann-Whitney U-test), no other structures showed increased uptake at a significance level of 5 %. As mentioned previously, some other structures or nuclei showed increased 2-DG uptake in the CSE group, but the density on the autoradiogram was not so high as to indicate a significant increase of uptake vis-a-vis the CSC group. In the present study, the metabolically activated structures in the process of a conditioned emotional response were disclosed; however, additional experiments are required to further elucidate the areas, which are relevant to aversive conditioning.

ACKNOWLEDGEMENTS

The authors wish to express their thanks to Prof. Dr. Peter J. Hand for reading the manuscript and to Mr. Tomiyoshi Setsu for typewriting.

REFERENCES

1. Berger, T. W. and Thompson, R. F.: Proc. Natl. Acad. Sci. USA. 1978. 75. 1572/1576. Identification of pyramidal cells as the critical elements in hippocampal neuronal plasticity during learning.
2. Brierley, J. B., Corsellis, J. A. N., Hierons, R. and Nevin, S.: Brain. 1960. 83. 357/368. Subacute encephalitis of later adult life.
3. Delacour, J.: Neuroscience. 1984. 13. 705/715. Two neuronal systems are involved in a classical conditioning in the rat.
4. Delay, J., Brion, S., Lemperiere, Th. et Lechevallier, B.: Rev. Neurol. (Paris). 1965. 113. 583/594. Cas anatomo-clinique de syndrome de Korsakoff post-comitial apres corticotherapie pour asthme subintrant.
5. Fuster, J. M. and Alexander, G. E.: Science. 1971. 173. 652/654. Neuron activity related to short-term memory.
6. Gonzalez-Lima, F. and Scheich, H.: Behav. Brain Res. 1984. 14. 213/233. Neural substrates for tone-conditioned bradycardia demonstrated with 2-deoxyglucose. I. Activation of auditory nuclei.
7. Gonzalez-Lima, F. and Scheich, H.: Brain Res. 1986. 20. 281/293. Neural substrates for tone-conditioned bradycardia demonstrated with 2-deoxyglucose. II. Auditory cortex plasticity.
8. Holmes, E. J., Jacobson, S., Stein, B. M. and Butters, N.: Exp. Neurol. 1983. 81. 97/113. Ablations of the mamillary nuclei in monkeys: effects on postoperative memory.
9. Isaacson, R. L. and Wickelgren, W. O.: Science. 1962. 138. 1104/1106. Hippocampal ablation and passive avoidance.
10. Isseroff, A., Rosvold, H. E., Galkin, T. W. and Goldman-Rakic, P. S.: Brain Res. 1982. 232. 97/113. Spatial memory impairments following damage to the mediodorsal nucleus of the thalamus in rhesus monkeys.
11. Kaada, B. R., Rasmussen, E. W. and Kveim, O.: Exp. Neurol. 1961. 3. 333/355. Effects of hippocampal lesions on maze

learning and retention in rats.

12. Koenig, J. F. R. and Klippel, R. A.: The rat brain. A stereotaxic atlas.(Williams and Wilkins, Baltimore). 1963.
13. Kossut, M. and Rose, S. P. R.: Neuroscience. 1984. 12. 971/977. Differential 2-deoxyglucose uptake into chick brain structures during passive avoidance training.
14. Krieg, W. J. S.: J. Comp. Neurol. 1946. 84. 221/275. Connections of the cerebral cortex. I. The albino rat. A. topography of the cortical areas.
15. Leis, T., Pallage, V., Toniolo, G. and Will, B.: Behav. Neural Biol. 1984. 42. 140/157. Working memory theory of hippocampal function needs qualification.
16. Lewis, R. S.: Psychobiology. 1989. 17. 102/107. Remembering and the prefrontal cortex.
17. Maxwell, R. C. and Fink, G.: Neuroscience. 1988. 24. 241/263. The patterns of [^{14}C]2-deoxyglucose uptake in female rat brain produced by electrical stimulation of hypothalamic and limbic brain areas.
18. Meunier, M. and Destrade, C.: Behav. Brain Res. 1988. 27. 161/172. Electrolytic but not ibotenic acid lesions of the posterior cingulate cortex produce transitory facilitation of learning in mice.
19. Mishkin, M. and Manning, F. J. : Brain Res. 1978. 143. 313/323. Non-spatial memory after selective prefrontal lesions in monkeys.
20. Moss, M., Mahut, H. and Zola-Morgan, S.: J. Neurosci. 1981. 1. 227/240. Concurrent discrimination learning of monkeys after hippocampal, entorhinal, or fornix lesions.
21. O'Keefe, J.: Exp. Neurol. 1976. 51. 78/109. Place units in the hippocampus of the freely moving rat.
22. O'Keefe, J. and Conway, D. H.: Exp. Brain Res. 1978. 31. 573/590. Hippocampal place units in the freely moving rat: why they fire, where they fire.
23. Olds, J. and Hirano, T.: Electroencephalogr. Clin. Neurophysiol. 1969. 26. 59/166. Conditioned responses of hippocampal and other neurons.

24. Olton, D. S., Becker, J. T. and Handelmann, G. E.: Behav. Brain Sci. 1979. 2. 313/365. Hippocampus, space, and memory.
25. Orona, E. and Gabriel, M.: Brain Res. 1984. 22. 109/122. Multiple-unit activity of the prefrontal cortex and mediodorsal thalamic nucleus during acquisition of discriminative avoidance behavior in rabbits.
26. Pandya, D. N. and Yeterian, E. H.: Neuropsychologia. 1984. 22. 109/122. Proposed neural circuitry for spatial memory in the primate brain.
27. Passingham, R. E.: Behav. Neurosci. 1985. 99. 3/21. Memory of monkeys (Macaca mulatta) with lesions in prefrontal cortex.
28. Pellegrino, L. J., Pellegrino, A. S. and Cushman, A. J.: A stereotaxic atlas of the rat brain. Second Ed. (Plenum Press, New York and London). 1979.
29. Piercey, M. F., Vogelsang, G. D., Franklin, S. R. and Tang, A. H.: Brain Res. 1987. 424. 1-9. Reversal of scopolamine-induced amnesia and alterations in energy metabolism by the nootropic piracetam: implications regarding identification of brain structures involved in consolidation of memory traces.
30. Roland, P. E.: Trends Neurosci. 1984. 11. 430/435. Metabolic measurements of the working frontal cortex in man.
31. Sahgal, A.: Behav. Brain Res. 1984. 11. 47/58. Hippocampal lesions disrupt recognition memory in pigeons.
32. Sarter, M. and Markowitsch, H. J.: Behav. Neurosci. 1985. 99. 342/380. Involvement of the amygdala in learning and memory: a critical review, with emphasis on anatomical relations.
33. Sefton, A. J. and Dreher, B.: In Paxinos, G. ed., The rat nervous system 1 (Academic Press, New York) 1985. 169/221. Visual system.
34. Segal, M., Disterhoft, J. F. and Olds, J.: Science. 1972. 175. 792/794. Hippocampal unit aversive and appetitive conditioning.
35. Sharp, F. R., Kilduff, T. S., Bzorgchami, S., Heller, H. C. and Ryan, A. F.: Brain Res. 1983. 263. 97/103. The relationship of local cerebral glucose utilization to optical density ratios.
36. Sokoloff, L., Reivich, M., Kennedy, C., De Rosiers, M. H., Patlak, C. S., Pettigrew, K. D., Sakurada, O. and Shinohara,

M.: J. Neurochem. 1977. 28. 897/916. The [^{14}C] deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedure, and normal values in the conscious and anesthetized albino rat.

37. Stokes, K. A. and Best, P. J.: Behav. Neurosci. 1988. 102. 294/300. Mediodorsal thalamic lesions impair radial maze performance in the rat.
38. Sutherland, L. C., Martin, M. J., McQueen, J. K. and Fink, G.: Brain Res. 1983. 271. 101/108. Water deprivation results in increased 2-deoxyglucose uptake by paraventricular neurons as well as pars nervosa in Wistar and Brattleboro rats.
39. Tracey, D. J.: In Paxinos. G. ed., The rat nervous system 2 (Academic Press, New York). 1985. 129/152. Somatosensory system.
40. Vogt, B. A. and Peters, A.: J. Comp. Neurol. 1981. 195. 603/625. Form and distribution of neurons in rat cingulate cortex: areas 32, 24 and 29.
41. Winocur, G.: Behav. Brain Res. 1985. 16. 135/152. The hippocampus and thalamus: their roles in short- and long-term memory and the effects of interference.
42. Zille, K. and Wree, A.: In Paxinos. G. ed., The rat nervous system 1 (Academic Press, New York) 1985. 375/415. Cortex: areal and laminar structure.

ERRATUM

The paper published in the previous issue should be notified as follows:

T. Yamadori, et al.: A Study on the Brain Structures Related to Conditioned Emotional Response by Means of [^{14}C]2-Deoxy-D-Glucose Method. Kobe J. Med. Sci., Vol.37, No.3, pp.111-127, June 1991.

Authors' names in Japanese should be corrected into 山鳥 崇, 杉岡幸三, 石本喜秀.