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Influence of Electrolytic Lesion of the Midbrain on Rat Amygdala Kindling
(ラット扁桃核Kindling の及ぼす中脳電気破壊の影響)

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〈Introduction〉

It is well known that the development of generalized kindled seizures from a forebrain structure progresses at a markedly accelerated rate if the contralateral, homotopic structure has been kindled previously[3, 8]. This phenomenon that the secondary site (SS) is significantly more easily kindled than the primary site (PS) has been called positive transfer effect (PTE)[3, 10]. In rats, total forebrain bisection prior to amygdala (AM) kindling was reported to have no effect on PTE[6]. In this paper, the effect of midbrain lesion on PTE is investigated in rat AM kindling.

〈Methods〉

Ten male hooded adult rats of the Royal Victoria Hospital strain (weighting 400 – 500g) were used. Each rat was subjected to midbrain electrolytic lesion (lesion group, N = 5) or sham treatment (control group, N = 5). Under pentobarbital anesthesia, bipolar electrodes made of twisted wire (127 μm in diameter) were stereotaxically[7] implanted into the left and right AM in both groups.

In the lesion group, an electrolytic lesion was made by passing 50V of direct electric current (2.5 – 5.0 mA) for 10sec between a stainless steel cannula which was 22G in diameter and insulated except for the tip (the tip coordinates ; 5.8mm posterior and 0.0 mm lateral from the bregma and 9.0mm ventral from the skull) and a needle electrode which was subcutaneously inserted into the caudal back area of the rat. The control group received insertion of the cannula and the subcutaneous needle electrode without passing an electric current.

Two weeks after the operation, PS (left AM) was stimulated sequentially with a 1sec train of constant current 60Hz sine wave beginning at 100 μA with a 100 μA step increase at 10min interstimulus intervals until localized afterdischarges (AD) was induced. The first current intensity to induce AD was designed as the AD threshold (ADT). PS was stimulated hourly (from 9 – 10a. m. to 6 – 7p. m. ; 10times per day) at ADT. The stimulation was repeated until three stage 5 seizures were produced. On the day following the last stage 5 seizures of PS, SS (right AM) kindling began in the same manner as that of PS kindling. If a generalized seizure (stages 4 – 5) did not occur within $\alpha + 3$ stimulations (α ; the number of stimulations to reach stage 5 at PS), SS kindling was stopped, and the animal was assigned a score of $\alpha + 4$ because at least 1 more stimulation would has been required to reach stages 4 – 5. The kindled seizures were classified by a modification of Racine (1972)[8], as follows ; stage 1, rhythmic mouth and facial movements ; stage 2, rhythmic head nodding ; stage 3, unilateral forelimb clonus ; stage 4, bilateral forelimb clonus and rearing ; stage 5, rearing and falling.

Upon the completion of the experiment, the animals were deeply anesthetized and their brain were perfused, serially sectioned (40 μ), and stained by cresyl violet.

〈Results〉

A profile of the kindling is provided in Table 1. There was no significant difference in ADT at PS and SS between the two groups. Kindled seizure of the lesion group was identical to that of the control group. The lesion group reached stages 4 and 5 significantly more slowly than the control group in PS kindling. The lesion group also showed a marked retardation of SS kindling, namely ; (1) all rats did not reach stage 5 ; (2) three of five rats reached stage 4, but showed frequent stage regression from stage 4 to stages 1 – 2 (mean 4.7 times) while the control group did not reveal such regression ; (3) the remaining two rats stayed at stages 1 – 2. According to the scoring criteria described in Methods, the lesion group showed a significantly more number of stimulations to reach stages 4 and 5 than the control group in SS kindling.

In the control group, stages 4 and 5 seizures were significantly more easily induced at SS than at PS. Thus, the control group showed definite PTE. In the lesion group, however, PTE was not observed because SS kindling rate at stages 4 – 5 was not accelerated by PS kindling. There was no significant difference in AD duration (sec)

of stage 4 at PS and SS between the lesioned group (PS ; mean 45.6, range 20 – 56 : SS ; mean 32.0, range 20 – 50) and the control group (PS ; mean 36.2, range 20 – 56 : SS ; mean 27.2, range 11 – 52).

Fig. 1 dipicts the extent of midbrain lesion.

〈 Discussion 〉

In this study, rats with midbrain lesion showed a retardation of AM kindling not only at PS but also at SS. In addition, the lesioned animals did not show PTE. These results suggest that in rat AM kindling the midbrain structure not only regulates the kindling development but also participates in the mechanism of PTE. Studies on the corpus callosum[2] or massa intermedia[4,5] suggest its role in PTE of feline AM kindling. In rat amygdala kindling, however, total forebrain bisection was reported to have no effect on PS and SS kindling[6], which suggest that in rats the interhemispheric pathway achieving PTE is located in the brainstem. The present study is the first to confirm this view.

	ADT (μ A)	Number of stimulations to reach stages 4/5			
		stage 4		stage 5	
P S					
Lesion N = 5	100.0	13.0 (9-18)	*	18.4 (11-23)	*
Control N = 5	100.0	7.2 (5-10)		7.6 (6-10)	
S S					
Lesion N = 5	120.0 (100-200)	14.2 (4-26)	*	22.4 (15-27)	*
Control N = 5	140.0 (100-300)	1.8[a] (1-4)		2.6[a] (1-4)	

Table 1 Kindling profile of the lesion and control groups
Values are means (numbers in parentheses ; range). *, p at least < 0.05 by Mann-Whitney U test ; [a] , p at least < 0.05 as compared with PS of the control (Wilcoxon one sample test).

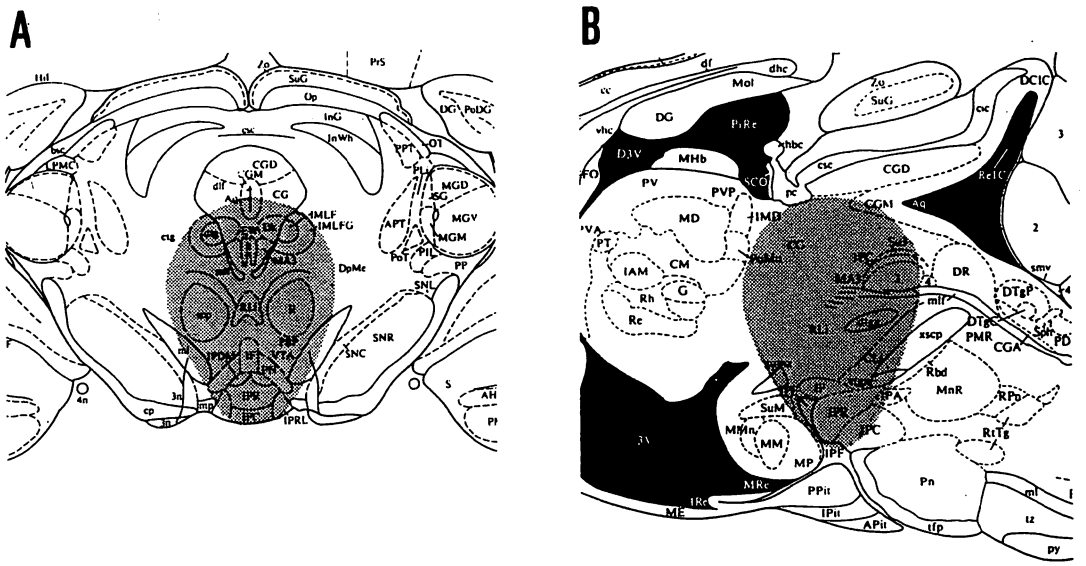

Fig. 1 Schematic reconstruction of the typical extent of electrolytic lesion. The drawings are coronal (A, Bregma −5.80㎜) and sagittal (B, Lateral −0.1㎜) brain sections according to the stereotaxic atlas[7]. Shaded areas represent the lesion area as determined by histological examination.

In our study, the lesioned area was so extensive that the midbrain reticular formation, the interpeduncular nucleus, and other structures were included in this area. In AM kindled cats, unilateral lesion of the midbrain reticular formation raised the generalized seizure-triggering threshold, and reduces susceptibility to pentylenetetrazol challenge[9]. Lesion of the interpeduncular nucleus retarded development of amygdala kindled seizures in rats[1]. No other findings on the significance of the lesioned area for amygdala kindled seizures have been reported. Further study, including lesioning with microinjection of a neurotoxin, will be needed to clarify the specific region that is responsible for PTE in the midbrain.

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