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Short Report

Effect of Repeated Electroconvulsive Shock Treatment on a Depression Model, Mouse Forced Swimming

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SUZUKI, M. and MASUDA, Y. *Effect of Repeated Electroconvulsive Shock Treatment on a Depression Model, Mouse Forced Swimming.* Tohoku J. Exp. Med., 1999, **189** (1), 83-86 —— Mouse forced swimming is one of the behavioral depression models and repeated electroconvulsive shock (ECS) treatment has been used to human depression. In order to investigate the mechanism of the anti-depressive effect induced by repeated ECS, we investigated the effect of repeated ECS with the mouse forced swimming model. The 5 times par-day ECS remarkably increased the typical anti-depressive behavior climbing 24 hours after the final treatment. The anti-depressive activity was declined by a dopamine 1 antagonist SCH-23390 at the doses of 1 and 0.1 mg/kg, but not by the other dopamine, serotonin and adrenoceptor antagonists at the dose of 1 mg/kg. The present findings strongly suggest that the late anti-depressive effect of repeated ECS is mediated by the dopamine 1 receptor activity. The present findings will also contribute to the further investigations of the effect of repeat ECS treatments on human depression. ———— electroconvulsive shock; repeated treatment; mouse forced swimming; human depression

Electroconvulsive shock (ECS) treatment has been used for human depression. Although ECS induces acute changes of neuronal functions (Karoum et al. 1986), the anti-depressive effect is found after the repeated treatments and the mechanism of the late effect has not been clear. Mouse forced swimming has been considered one of the depression models. The single supramaxial ECS induces anti-depressive behaviors in the forced swimming test (Porsolt et al. 1977), but the effects of repeated ECS on the model has not been reported. In the present study, we investigated the effects of the repeated ECS with the mouse forced swimming model.

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Materials and Methods

Male ddY mice (Funabashi Co., Funabashi), 8 weeks after birth and weighing 25～28 g, were used. They were housed in a group of five in a plastic cage (338×140×225 mm) with free access to food and water. The animal room was kept at 21-25°C with 50-60% humidity and lighted on from 7 : 00 to 19 : 00. The mice were forced to swim for 6 minutes at least 24 hours before the following experiments (Porsolt et al. 1977). All of the studies were supported by the Ethics Committee for Animal Experiments of Akita University School of Medicine, Japan.

Apparatus to measure the anti-depressive effect in the forced swimming test was the same to the original one (cylinders; 10 cm diameter, 20 cm height: Porsolt et al. 1977), but, the measuring procedure was slightly changed from the original one. Briefly, mice were dropped into the cylinders (containing water of 25°C, 10 cm height) and left there for 6 minutes. The climbing the cylinder wall (an escape-directed behavior) was considered a distinctive anti-depressive behavior (Kitada et al. 1981), and prolonging time of the climbing was counted during the last 3 minutes. As it has been reported that even intact mice show the behavior in the first 3 minutes (Porsolt et al. 1977), the behavior in the last 3 minutes will clearly indicate the anti-depressive effect of ECS. In order to detect whether the climbing is induced by increase of the locomotor activity or not, voluntary running of the mice was measured for 5 minutes (Masuda et al. 1996) just before the measurement of the test.

Supramaxial ECS (100 V, 50Hz, 2 seconds) was given through the probes of an ECS therapy apparatus (Sakai Co., Tokyo) during anesthetization with ether. A group of mice were given ECS or only ether-anesthetization, and another given 5 times par-day ECS or 5 times par-day ether-anesthetization. The voluntary running and the climbing of these 4 groups of mice were measured 24 hours after the final treatment.

In order to detect the neuronal mode of the effect of the repeated ECS, the other 11 groups of mice were given 5 times par-day ECS or 5 times par-day ether-anesthetization. Twenty four hours after the final treatment, these groups of mice were individually injected with each neurotransmitter receptor antagonists, SCH-23390 (dopamine 1), sulpiride (dopamine 2), NAN-190 (serotonin 1A), ketanserin (serotonin 2), LY-278584 (serotonin 3), prazosin (α-1 adrenoceptor), yohimbine (α-2 adrenoceptor) and alprenolol (β-adrenoceptor), or 0.5% carboxymethylcellulose sodium (CMC), and the voluntary running and the climbing were measured 15 minutes after the intraperitoneal injection. All of these drugs were purchased from Funakoshi Co. (Tokyo), and the antagonists were prepared with 0.5% CMC. The dose of these antagonists was 1 mg/kg, but SCH-23390 was injected at 1, 0.1 and 0.01 mg/kg.

Results and Discussion

The voluntary running of the mice treated with ECS or ether-anesthetization was not different and was not dependent on the number of treatment. The climbing time of the mice 5 times-treated with ECS remarkably increased, but that of the mice one time-treated did not (Table 1). The voluntary running of

Table 1. *Effect of electroconvulsive shock or ether-anesthesia on the climbing of mouse in the forced swimming test*

	Climbing time (seconds) 24 hours after the final treatment of	
	ECS	Ether-anesthetization
1 treatment	3.0±1.90	0
5 treatments	69.8±3.92*	0

A value in this table indicates the means±S.E. of climbing time of 5 mice.
*$p<0.01$ compared to the 1 treatment (Mann-Whitney's U-test).
ECS, electroconvulsive shock.

Table 2. *Effects of neurotransmitter antagonists on climbing of mice 5 times-treated with electroconvulsive shock or ether-anesthetization*

Antagonist	Dose (mg/kg)	Climbing time (seconds)	
		ECS	Ether-anesthetization
0.5% CMC vehicle (Control)	—	70.2±3.82	0
SCH-23390 (Dopamine 1)	0.01	67.4±4.80	0
	0.1	36.8±5.32*	0
	1	1.0±0.45*	0
Sulpiride (Dopamine 2)	1	71.4±2.32	0
NAN-190 (Serotonin 1A)	1	69.2±3.31	0
Ketanserin (Serotonin 2)	1	72.0±1.58	0
LY-278-584 (Serotonin 3)	1	69.6±3.49	0
Prazosin (α-1)	1	70.0±3.89	0
Yohimbine (α-2)	1	72.6±1.69	0
Alprenolol (β)	1	72.0±3.48	0

A value in this table indicates the mean±S.E. of climbing time of 5 mice.
*$p<0.01$ vs. control using Mann-Whitney's U-test.
ECS, electroconvulsive shock.

the mice treated with 5 times ECS or 5 times ether-anesthetization were not affected by each of the antagonists. The effect of 5 times ECS treatments on the climbing was weakened by SCH-23390 at the doses of 1 and 0.1 mg/kg, but not by the other antagonists (Table 2).

The present results clearly indicate that repeated ECS induces the anti-depressive effect on mouse forced swimming even 24 hours after the final treatment and the late anti-depressive effect is strongly mediated by dopamine 1 receptor activity. Although the relations of dopamine 1 neuron activity and mouse forced swimming has been previously reported (Nikulina et al. 1991), the present results indicate that the acute change of the dopamine 1 activity acutely changed by each ECS treatment does not induce the late effect. These suggest that the mechanism of the late anti-depressive effect must be investigated under the other hypothesis. Previously, we have reported that a common serum substance affects behaviors (Masuda et al. 1997). Now, we are trying to detect an anti-depressive substance induced by repeated ECS.

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