RESULTS

Within 24 hours after injection, no rat was dead. After completing the recording experiment, all animals regardless of any treatments survived over 24 hrs until discarded. However, the data from animals with inevitable artifacts and errors were discarded. All data of power spectrum of EEG frequency bands, locomotor activity and stereotyped behaviors at all experimental periods are shown as Table 1.

Power spectrum analysis of Electroencephalogram (EEG)

In the results, a control group of animals with saline injection showed a significant increase of delta band power from baseline activity at 75, 150, 165, and 180 min after the injection (Figure 1). In both of the 0.5 and 1.0 mg/kg BW methamphetamine-treated groups, the power of delta band increased significantly from baseline at 165 and 180 min after drug injection. However, the 2.0 and 4.0 mg/kg BW methamphetamine-treated groups showed no difference from their corresponding baselines.

After comparing the experimental groups with the control group, the delta band of both the 0.5 and 1.0 mg/kg BW methamphetamine-treated groups were not different from the control group while the delta band power of the 2.0 mg/kg BW methamphetamine-treated group was significantly lower than the control group at 75 and 90 min after the injection. The delta band power of the 4.0 mg/kg BW methamphetamine-treated group were significantly different from the control group at 75 min after the injection. No significant difference was observed among delta bands of the experimental groups of methamphetamine treatment.

The control group of animals with saline injection showed a significant increase from baseline of power of theta band during most of the post-injection period, at 75, 90, 120, 135, 150, 165, and 180 min after injection (Figure 2). In the 0.5 mg/kg BW

Table 1. Cortical EEG power of various frequency bands, locomotor activity and stereotyped behavior produced by saline and various doses of methamphetamine. The EEG power band data obtained in successive time blocks of 3-min each were averaged to obtain periods of 15-min each. The locomotor activity and stereotyped behavior data in successive time blocks of 3-min each were summed to obtain periods of 15-min each. The values of the EEG power bands and locomotor activity during four 15-min pre-injection periods were averaged and regarded as the 100% baseline activities and those during the following 3-hr period, in twelve consecutive periods, as the relative activities. Means ± SEM of the data are shown.

	EEG power frequency band							Locomotor	Stereotyped
Time of treatment	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma	Activity	Behavior
-60 - -45 min									
Physiological saline	91.1 ± 3.8	86.2 ± 3.1	89.6 ± 3.7	84.1 ± 3.2	84.6 ± 2.7	100.4 ± 1.6	111.3 ± 2.0	134.1 ± 6.7	0.0 ± 0.0
Methamph. 0.5	95.3 ± 7.4	96.6 ± 4.6	105.1 ± 6.5	91.7 ± 8.8	94.5 ± 5.3	100.2 ± 1.8	103.4 ± 1.8	136.4 ± 10.1	0.0 ± 0.0
Methamph. 1.0	101.4 ± 6.8	91.1 ± 8.6	99.9 ± 6.3	94.0 ± 4.9	94.1 ± 4.2	104.9 ± 2.5	110.3 ± 3.4	127.3 ± 7.0	0.0 ± 0.0
Methamph. 2.0	83.7 ± 4.5	85.0 ± 6.2	88.8 ± 5.6	75.6 ± 4.4	80.7 ± 4.5	101.0 ± 3.0	115.1 ± 2.3	126.6 ± 9.6	0.0 ± 0.0
Methamph. 4.0	103.8 ± 10.3	100.9 ± 12.1	114.9 ± 14.3	99.7 ± 12.5	99.1 ± 12.9	114.3 ± 15.2	124.1 ± 17.8	148.0 ± 6.9	0.0 ± 0.0
-45 - -30 min									
Physiological saline	96.4 ± 3.8	96.5 ± 2.3	93.4 ± 2.2	94.9 ± 2.3	97.9 ± 2.5	99.8 ± 0.9	99.1 ± 1.2	109.8 ± 4.7	0.2 ± 0.2
Methamph. 0.5	99.4 ± 6.3	101.2 ± 5.6	91.1 ± 4.8	108.6 ± 7.8	103.1 ± 4.5	100.2 ± 1.1	98.6 ± 1.6	99.8 ± 7.4	0.0 ± 0.0
Methamph. 1.0	96.3 ± 5.7	92.7 ± 4.7	94.9 ± 3.0	94.6 ± 4.8	94.7 ± 4.2	99.1 ± 1.3	99.5 ± 1.8	109.4 ± 6.2	0.0 ± 0.0
Methamph. 2.0	97.5 ± 4.0	104.9 ± 12.4	93.4 ± 3.6	86.3 ± 5.0	87.8 ± 5.3	93.7 ± 4.8	101.0 ± 7.1	84.4 ± 8.6	0.0 ± 0.0
Methamph. 4.0	106.6 ± 8.4	110.1 ± 12.2	101.5 ± 9.7	108.5 ± 14.1	109.6 ± 14.1	104.5 ± 5.7	110.8 ± 10.1	116.3 ± 4.4	0.1 ± 0.1
-30 - -15 min									
Physiological saline	100.9 ± 3.2	101.9 ± 3.5	102.0 ± 4.0	102.4 ± 4.2	101.6 ± 4.1	98.5 ± 1.41	95.9 ± 1.0	98.1 ± 3.4	0.0 ± 0.0
Methamph. 0.5	97.1 ± 4.5	96.1 ± 4.4	95.1 ± 6.7	95.2 ± 2.6	96.5 ± 3.0	99.4 ± 1.46	101.1 ± 2.1	71.3 ± 10.9	0.0 ± 0.0
Methamph. 1.0	98.0 ± 7.2	101.7 ± 6.9	96.3 ± 5.4	97.1 ± 6.2	100.4 ± 5.2	96.3 ± 2.09	94.0 ± 2.2	75.6 ± 6.0	0.0 ± 0.0
Methamph. 2.0	102.3 ± 6.5	119.9 ± 20.4	100.8 ± 4.8	106.1 ± 5.0	104.1 ± 4.9	101.3 ± 1.9	96.7 ± 2.0	100.9 ± 4.6	0.0 ± 0.0
Mcthamph. 4.0	92.0 ± 7.5	87.4 ± 6.9	81.9 ± 8.5	85.3 ± 11.0	85.5 ± 9.3	89.6 ± 6.9	85.8 ± 7.4	77.6 ± 9.0	0.0 ± 0.0

Table 1. (continued)

Time of treatment	EEG power frequency band							Locomotor Activity	Stereotyped Behavior
	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma		
-15 – 0 min									
Physiological saline	111.3 ± 6.5	115.0 ± 5.2	115.2 ± 3.5	119.1 ± 5.4	116.0 ± 5.1	101.3 ± 1.7	93.5 ± 3.1	57.8 ± 10.1	0.0 ± 0.0
Methamph 0.5	108.0 ± 7.4	105.9 ± 4.6	105.9 ± 4.6	104.4 ± 6.2	105.7 ± 5.7	100.0 ± 0.4	96.7 ± 3.5	92.4 ± 12.2	0.0 ± 0.0
Methamph 1.0	104.1 ± 7.0	108.1 ± 7.5	108.7 ± 8.1	114.2 ± 7.9	110.2 ± 7.1	99.6 ± 2.7	96.0 ± 2.5	87.5 ± 7.5	0.0 ± 0.0
Methamph 2.0	116.3 ± 7.3	133.5 ± 12.5	116.8 ± 5.9	131.9 ± 7.6	127.2 ± 6.2	103.8 ± 1.9	87.0 ± 4.6	87.9 ± 11.2	0.6 ± 0.6
Methamph. 4.0	97.4 ± 7.4	101.5 ± 11.9	101.5 ± 12.1	106.3 ± 11.8	105.5 ± 12.1	91.4 ± 9.5	79.2 ± 9.6	57.8 ± 8.2	0.0 ± 0.0
0 – 15 min									
Physiological saline	87.7 ± 3.2	92.3 ± 3.3	93.1 ± 3.6	94.4 ± 4.4	93.7 ± 3.6	99.9 ± 1.1	103.3 ± 3.5	120.8 ± 10.0	0.0 ± 0.0
Methamph 0.5	75.2 ± 5.8	72.0 ± 4.9	76.7 ± 9.8	59.7 ± 8.9*	62.6 ± 6.6*	85.7 ± 4.6#*	110.2 ± 6.2	120.2 ± 18.6	1.2 ± 0.6*
Methamph 1.0	81.9 ± 9.3	82.6 ± 10.8	76.9 ± 11.0	72.2 ± 9.5*	79.9 ± 10.0	90.6 ± 3.8*	101.7 ± 4.8	145.7 ± 10.2#	3.0 ± 1.1*
Methamph 2.0	75.6 ± 9.1	87.3 ± 12. 5	72.7 ± 2.8	55.6 ± 3.4#*	60.9 ± 3.6#*	86.0 ± 3.1#*	107.1 ± 3.1	184.1 ±20.5#*	4.3 ± 2.0*
Methamph 4.0	83.7 ± 8.0	78.7 ± 6.7	84.4 ± 6.0	65.9 ± 9.3*	70.7 ± 10.3*	90.2 ± 15.1	103.2 ± 18.7*	195.3 ±10.9#*	4.5 ± 1.6*
15 – 30 min									
Physiological saline	110.3 ± 12.0	119.2 ± 11.9	116.7 ± 11.2	123.9 ± 11.2	117.3 ± 9.0	103.2 ± 3.0	95.7 ± 2.7	93.3 ± 16.2	0.0 ± 0.0
Methamph 0.5	82.6 ± 4.0	71.4 ± 6.3*	70.0 ± 8.8*	57.1 ± 7.7*	64.1 ± 7.2*	84.4 ± 4.4#*	105.8 ± 6.2	106.2 ± 22.6	3.8 ± 1.6*
Methamph 1.0	93.2 ± 11.9	73.9 ± 6.7*	86.7 ± 13.0	64.0 ± 7.1*	71.2 ± 8.2*	91.4 ± 3.7*	109.1 ± 4.1	153.2 ± 8.9#*	8.8 ± 1.9*@
Methamph 2.0	82.0 ± 13.1	92.0 ± 14.7	77.9 ± 8.0	51.7 ± 2.9#*	56.9 ± 3.3#*	85.5 ± 4.7#*	104.1 ± 5.6	192.1 ±18.0#*	18.6 ± 3.2*@
Methamph 4.0	127.6 ± 44.0	69.2 ± 10.2*	116.5 ± 16.8	63.1 ± 12.8*	64.0 ± 12.8*	83.3 ± 14.1	98.8 ± 18.6	214.6 ± 8.0#*	19.4 ± 2.6*

Table 1. (continued)

Time of treatment	EEG power frequency band							Locomotor Activity	Stereotyped Behavior
	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma		
30 – 45 min									
Physiological saline	121.2 ± 13.0	117.4 ± 10.9	115.3 ± 9.7	127.1 ± 10.4	119.5 ± 9.31	105.2 ± 2.9	101.4 ± 4.1	81.2 ± 17.0	0.0 ± 0.0
Methamph 0.5	86.6 ± 1.4	76.5 ± 4.9*	81.8 ± 8.1*	67.7 ± 7.4*	72.4 ± 8.43*	88.3 ± 4.9*	106.7 ± 7.4	111.8 ± 21.1	5.4 ± 2.0*
Methamph 1.0	95.4 ± 11.9	77.3 ± 6.8*	80.6 ± 9.2*	70.8 ± 7.9*	69.0 ± 5.3*	90.9 ± 2.75*	103.0 ± 3.7	150.0 ± 24.1#*	11.8 ± 2.5*@
Methamph 2.0	76.2 ± 9.4	92.7 ± 16.3	73.2 ± 6.9*	51.3 ± 3.2#*	56.8 ± 3.7#*	82.7 ± 4.0#*	103.6 ± 6.4	193.8±19.9#*	23.4 ± 3.1*@
Methamph 4.0	106.6 ± 28.9	73.8 ± 12.9*	116.7 ±16.0@	64.1 ± 11.8*	65.7 ± 12.2*	87.2 ± 14.9	105.2 ± 18.6	199.2 ±24.3#*	27.7 ± 3.0*
45 – 60 min									
Physiological saline	118.8 ± 10.7	124.3 ± 10.9	120.6 ± 9.9	132.2 ± 10.4	128.6 ± 9.7	104.0 ± 2.9	96.8 ± 5.4	67.8 ±18.3	0.0 ± 0.0
Methamph 0.5	91.5 ± 3.6	83.0 ± 5.9*	87.4 ± 7.6	76.2 ± 7.9*	81.1 ± 7.6*	90.2 ± 4.5*	99.0 ± 6.1	73.4 ±19.7	3.6 ± 1.9*
Methamph 1.0	89.8 ± 10.8	78.0 ± 8.4*	79.7 ± 10.8*	69.9 ± 7.8*	72.8 ± 6.9*	91.0 ± 3.6*	99.7 ± 4.0	151.6±15.8#*@	9.5 ± 1.9*@
Methamph 2.0	78.4 ± 11.3	95.7 ± 17.1	63.8 ± 6.6#*	52.3 ± 3.3#*	57.4 ± 3.4#*	82.5 ± 4.2#*	104.1 ± 5.9	205.7 25.1#*	20.8 ± 2.8*@
Methamph 4.0	95.1 ± 22.3	73.3 ± 11.6*	110.5 ±16.7@	66.1 ± 13.4*	66.5 ± 12.6*	88.7 ± 15.5	112.1 ±19.1	185.0 ±25.9#*	31.8 ± 3.2*@
60 – 75 min									
Physiological saline	166.1 ± 26.7#	151.3 ± 19.1#	143.4 ± 18.7#	157.5 ± 18.1#	146.0 ±13.1#*	104.7 ± 3.2	91.8 ± 5.6	53.0 ±15.6#	0.0 ± 0.00
Methamph 0.5	99.6 ± 5.5	92.3 ± 4.1*	95.6 ± 7.8	87.2 ± 7.1*	91.3 ± 6.7*	93.3 ± 4.3*	99.3 ± 4.5	73.3 ±18.0	2.2 ± 1.2*
Methamph 1.0	100.7 ± 13.0	79.3 ± 10.8*	80.5 ± 9.1*	70.5 ± 9.4*	77.4 ± 8.9*	90.4 ± 3.0*	100.1 ± 2.8	137.7±13.4#@*	7.0 ± 1.9*@
Methamph 2.0	79.9 ± 10.0*	96.9 ± 15.7*	64.1 ± 7.2#*	56.7 ± 3.2#*	60.9 ± 3.4#*	82.9 ± 3.8#*	103.9 ± 5.3	190.9 ±25.0#*	20.8 ± 3.3*@
Methamph 4.0	92.5 ± 24.0*	78.4 ± 10.8*	107.5 ±17.6	65.3 ± 13.5*	68.0 ± 12.8*	92.9 ± 16.4	115.6 ± 21.8	169.9 ±23.1#*	30.3 ± 3.0*@

Table 1. (continued)

Time of treatment	EEG power frequency band							Locomotor Activity	Stereotyped Behavior
	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma		
75 – 90 min									
Physiological saline	142.8 ± 18.7	140.1 ± 13.1$^{\#}$	131.6 ± 12.2	142.0 ± 11.9	140.6 ±10.8$^{\#*}$	102.8 ± 3.7	90.7 ± 5.6	48.3 ±12.5$^{\#}$	0.0 ± 0.0
Methamph 0.5	134.2 ± 18.3	116.7 ± 10.7	109.2 ± 9.1	108.4 ± 9.1	111.2 ± 9.6	97.2 ± 4.4	92.6 ± 7.5	74.9 ±14.8	0.7 ± 0.4
Methamph 1.0	95.7 ± 13.5	82.7 ± 13.3*	79.2 ± 10.5*	81.7 ± 13.5*	82.1 ± 10.5*	93.3 ± 3.4	97.5 ± 4.4	116.1 ±12.7*	5.7 ± 2.0$^{*@}$
Methamph 2.0	75.3 ± 7.3*	89.2 ± 17.3*	62.0 ± 5.0$^{\#*}$	59.4 ± 4.3$^{\#*}$	66.6 ± 3.9$^{\#*}$	87.2 ± 3.5$^{\#*}$	102.1 ± 5.9	162.0 ±24.1*	16.8 ± 3.7$^{*@}$
Methamph 4.0	87.1 ± 18.7	76.7 ± 9.4*	106.5 ± 19.4$^{@}$	66.1 ± 14.4*	68.8 ± 13.6*	94.1 ± 17.3	116.8 ± 22.0	167.9 ±18.7$^{\#*}$	27.8 ± 3.2$^{*@}$
90 – 105 min									
Physiological saline	119.5 ± 9.1	124.5 ± 8.6	120.7 ± 6.0	135.7 ± 11.4	134.3 ± 9.6	103.8 ± 3.8	95.6 ± 7.0	99.1 ± 10.0$^{\#}$	0.0 ± 0.0
Methamph 0.5	135.6 ± 23.7	116.5 ± 11.3	103.9 ± 5.9	108.2 ± 11.0	110.5 ± 10.5	100.0 ± 6.5	97.2 ± 11.6	98.9 ± 21.8	0.4 ± 0.2
Methamph 1.0	96.3 ± 11.9	84.2 ± 11.4	85.7 ± 10.1*	83.7 ± 10.9*	90.0 ± 9.1*	92.8 ± 3.0	95.8 ± 4.9	105.1±19.8*	3.7 ± 1.6$^{*@}$
Methamph 2.0	81.3 ± 6.2	98.1 ± 19.8	70.2 ± 6.4*	66.8 ± 5.8$^{\#*}$	71.0 ± 5.1$^{\#*}$	90.6 ± 4.0	105.5 ± 7.2	136.6± 26.9*	13.9 ± 3.5*
Methamph 4.0	79.2 ± 16.1	73.9 ± 12.2*	99.5 ± 20.3	66.4 ± 16.3*	67.5 ± 15.1*	91.6 ± 18.9	114.3 ± 24.4	150.3±18.5*	25.9 ± 3.3$^{*@}$
105 – 120 min									
Physiological saline	134.2 ± 18.9	139.2 ± 19.0$^{\#}$	136.3 ± 18.2$^{\#}$	145.6 ± 20.8$^{\#}$	142.6 ±18.8$^{\#*}$	103.5 ± 4.3	96.7 ± 8.5	33.3 ± 11.8$^{\#}$	0.0 ± 0.0
Methamph 0.5	151.8 ± 34.8	135.9 ± 25.2	115.4 ± 12.6	121.6 ± 27.2	124.4 ± 24.9	97.3 ± 5.3	89.4 ± 7.1	53.0 ± 11.1	0.0 ± 0.0
Methamph 1.0	118.9 ± 24.3	105.4 ± 21.8	100.1 ± 12.0	108.7 ± 15.0	112.6 ± 13.6	96.7 ± 3.8	89.5 ± 4.8	75.2 ± 14.7	3.0 ± 1.9$^{*@}$
Methamph 2.0	86.9 ± 10.8	100.9 ± 17.0	74.9 ± 9.2*	77.0 ± 9.1*	80.0 ± 7.8*	93.4 ± 3.5	103.9 ± 7.8	132.5±26.1$^{*@}$	11.0 ± 3.3$^{*@}$
Methamph 4.0	79.4 ± 14.6	77.6 ± 15.3	84.1 ± 16.3	64.3 ± 15.2*	69.0 ±16.3*	95.7 ± 21.4	114.0 ± 24.6	179.0± 24.3$^{\#*}$	19.1 ± 3.1$^{*@}$

Table 1. (continued)

Time of treatment	EEG power frequency band							Locomotor Activity	Stereotyped Behavior
	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma		
120 – 135 min									
Physiological saline	135.5 ± 14.1	139.5 ± 13.7$^{\#}$	142.2 ± 14.2$^{\#}$	155.2 ± 14.6$^{\#}$	147.4 ±13.9$^{\#*}$	104.3 ± 5.0	98.4 ± 10.7	31.3 ± 12.8$^{\#}$	0.0 ± 0.0
Methamph 0.5	151.8 ± 21.2	137.2 ± 14.2	129.4 ± 15.0	143.2 ± 20.1	142.1 ± 17.0	101.0 ± 2.1	83.6 ± 5.6	50.8 ± 17.6	0.0 ± 0.0
Methamph 1.0	161.7 ± 39.3	143.9 ± 32.9	132.6 ± 19.6	142.8 ± 21.9$^{\#}$	141.3 ±18.7$^{\#}$	98.3 ± 3.5	83.7 ± 7.2$^{\#}$	91.3 ± 14.8	2.0 ± 1.3*
Methamph 2.0	85.6 ± 7.8	103.6 ± 18.1	75.3 ± 7.4*	79.6 ± 8.3$^{*@}$	81.6 ± 6.2$^{*@}$	95.1 ± 3.7	102.0 ± 6.2	123.2 ± 32.7*	9.5 ± 3.3$^{*@}$
Methamph 4.0	88.9 ± 16.8	85.5 ± 18.1	79.6 ± 15.9*	76.4 ± 20.7*	81.3 ±21.6*	104.0 ± 23.7	114.4 ± 23.3	170.5 ±23.1$^{\#*}$	15.6 ± 3.2$^{*@}$
135 – 150 min									
Physiological saline	154.0 ± 17.4$^{\#}$	152.4 ± 12.3$^{\#}$	151.7 ± 14.7$^{\#}$	178.1 ± 19.3$^{\#}$	167.0 ±15.6$^{\#*}$	107.0 ± 4.9	89.1 ± 7.7	21.5 ± 8.9$^{\#}$	0.0 ± 0.0
Methamph 0.5	159.0 ± 45.3	138.7 ± 28.4	119.2 ± 17.5	119.3 ± 21.4	126.1 ± 21.7	99.7 ± 3.8	89.8 ± 7.7	30.1 ± 8.5$^{\#}$	0.0 ± 0.0
Methamph 1.0	99.2 ± 11.3	96.9 ± 15.5	95.4 ± 10.6*	108.4 ± 12.1	112.3 ±13.5$^{\#}$	97.0 ± 3.0	94.4 ± 5.6	67.2 ± 14.1$^{*@}$	2.8 ± 1.1$^{*@}$
Methamph 2.0	96.5 ± 8.6	99.2 ± 14.8	103.1 ± 4.8	107.0 ± 15.0	109.6 ± 19.2	113.6 ± 19.8	128.6 ± 19.2	86.7 ± 15.6*	6.9 ± 3.0*
Methamph 4.0	96.0 ± 29.1	96.8 ± 33.5	87.8 ± 26.1*	89.4 ± 33.6*	93.4 ±32.0*	108.1 ± 28.7	110.0 ± 22.1	168.6±14.6$^{\#*@}$	11.4 ± 2.9$^{*@}$
150 – 165 min									
Physiological saline	171.1 ± 20.1$^{\#}$	162.2 ± 15.3$^{\#}$	157.9 ± 15.8$^{\#}$	179.4 ± 21.5$^{\#}$	165.0 ±18.3$^{\#*}$	100.2 ± 5.2	85.3 ± 6.36	20.6 ± 7.5$^{\#}$	0.0 ± 0.0
Methamph 0.5	203.9 ± 42.9$^{\#}$	153.7 ± 26.4$^{\#}$	122.5 ± 6.5	151.0 ± 32.8$^{\#}$	150.4 ±33.2$^{\#}$	101.8 ± 4.2	88.6 ± 14.1	38.1 ± 13.5$^{\#}$	0.0 ± 0.0
Methamph 1.0	178.7 ± 47.3$^{\#}$	152.2 ± 39.3	137.4 ± 28.0	146.2 ± 26.8$^{\#}$	149.9 ±27.1$^{\#}$	100.0 ± 5.7	94.6 ± 10.2	50.6 ± 14.2$^{\#}$	0.6 ± 0.3$^{*@}$
Methamph 2.0	123.8 ± 26.4	125.9 ± 21.3	100.2 ± 14.1	108.5 ± 17.3	105.7 ± 14.9	100.6 ± 3.3	97.6 ± 7.5	64.4 ± 13.6*	6.2 ± 2.9*
Methamph 4.0	133.8 ± 65.0	129.8 ± 62.1	114.3 ± 41.5	128.8 ± 62.3	121.6 ± 48.3	114.3 ± 29.9	108.0 ± 18.3	155.4±17.7$^{\#*@}$	8.8 ± 2.8*

Table 1. (continued)

Time of treatment	EEG power frequency band							Locomotor Activity	Stereotyped Behavior
	Delta	Theta	Alpha-1	Alpha-2	Beta-1	Beta-2	Gamma		
165 – 180 min									
Physiological saline	148.4 ± 17.0$^{\#}$	148.4 ± 13.9$^{\#}$	135.1 ± 10.8	156.1 ± 17.8$^{\#}$	151.1 ±16.4$^{\#*}$	100.7 ± 4.6	90.0 ± 7.82	26.1 ± 8.9$^{\#}$	0.0 ± 0.0
Methamph 0.5	199.3 ± 33.7$^{\#}$	149.6 ± 21.6$^{\#}$	125.2 ± 9.3	155.2 ± 28.8$^{\#}$	161.1 ±32.9$^{\#}$	99.5 ± 6.5	77.6 ± 8.3	49.9 ± 26.6	0.0 ± 0.0
Methamph 1.0	169.9 ± 33.9$^{\#}$	136.9 ± 26.5	130.8 ± 21.2	154.6 ± 20.7$^{\#}$	152.8 ±19.8$^{\#}$	105.7 ± 4.4	89.8 ± 4.3	29.3 ± 11.0$^{\#}$	0.6 ± 0.3
Methamph 2.0	137.9 ± 28.2	170.3 ± 57.3	120.0 ± 20.5	124.4 ± 16.8	120.3 ± 16.2	105.4 ± 4.0	92.0 ± 4.2	51.2 ± 16.3	6.2 ± 2.9*
Methamph 4.0	143.7 ± 49.6	128.3 ± 45.1	111.9 ± 29.9	124.6 ± 35.5	123.2 ± 31.5	117.5 ± 26.7	108.5 ± 24.6	110.2±24.3$^{*@}$	8.8 ± 2.8*

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

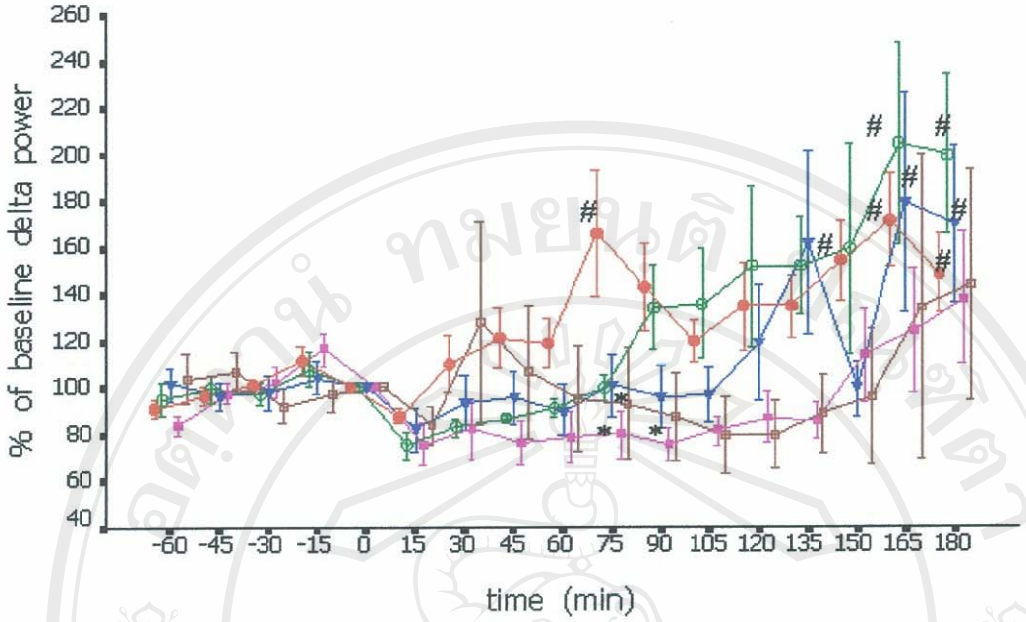

Figure 1. Time-courses of cortical EEG power in the delta band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

#: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

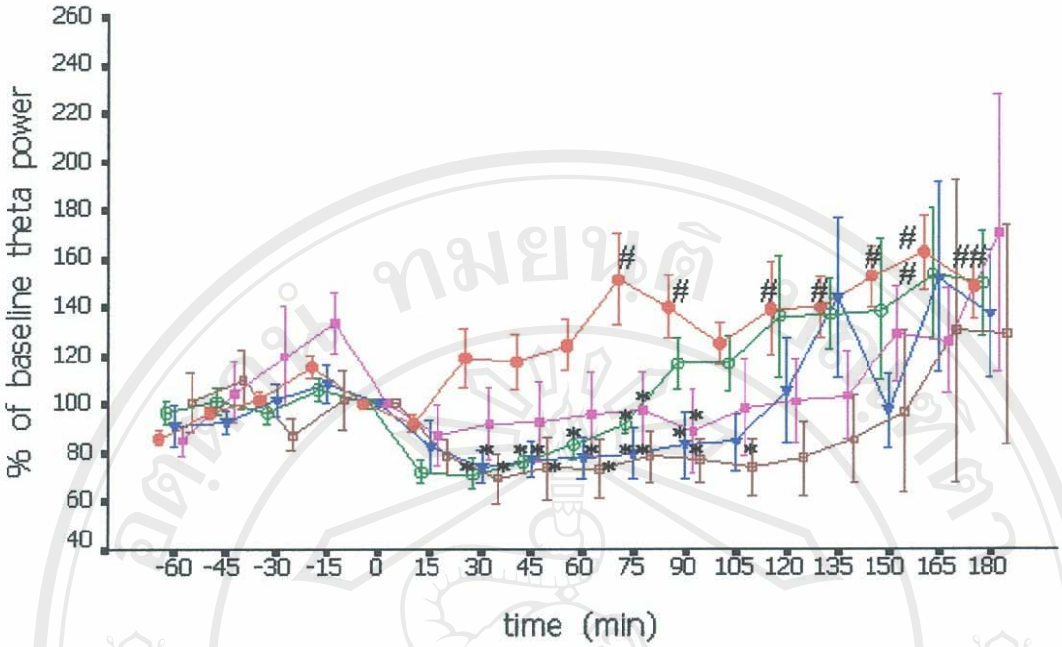

Figure 2. Time-courses of cortical EEG power in the theta band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

methamphetamine-treated group, the power of theta band increased significantly from baseline activity during the brief post-injection period, at only the 165 and 180 min after drug injection. However, the 1.0, 2.0, and 4.0 mg/kg BW methamphetamine-treated groups showed no difference from their corresponding baseline of the power band.

The theta spectrum of 0.5 mg/kg BW methamphetamine-treated group was significantly lower than the control group during the time period from 30 to 75 min after injection. However the spectrum in 1.0 mg/kg BW methamphetamine-treated group was significantly and furtherly lower than the control till 90 min after the injection and the 2.0 mg/kg BW methamphetamine-treated group was observed during the time period from 75 to 90 min after injection while those in the 4.0 mg/kg BW methamphetamine-treated group was observed from 30 to 105 min after injection.

Regarding the over-all theta band spectrum, no significant difference was observed among various experimental groups of different methamphetamine treatment.

The alpha-1 band, in the control group of animals showed a significant increase from baseline activity at 75, 120, 135, 150, and 165 min after injection (Figure 3). The band in 0.5 and 4.0 mg/kg BW methamphetamine-treated groups showed no difference from their baseline activity. The 1.0 mg/kg BW methamphetamine-treated group showed significant difference from baseline at 165 min after injection. The 2.0 mg/kg BW methamphetamine-treated group which showed a significant decrease at 60, 75, and 90 min after injection.

By comparing the alpha-1 spectrum of the control group with the experimental groups, the values in 0.5 mg/kg BW methamphetamine-treated group was significantly lower than the control group during the period from 30 to 45 min after injection while those in the 1.0 mg/kg BW methamphetamine-treated group was significantly lower during the different period, from 45 to 105, and 150 min after injection. In the 2.0 mg/kg BW methamphetamine-treated group, the significantly lower alpha-1 band spectrum was observed, as those in the 1.0 mg/kg BW methamphetamine-treated group except that the lower activity was shown only from 45 to 135 min after the injection. The values in 4.0 mg/kg BW methamphetamine-treated group was significantly lower than the control group from 135 to 150 min after injection. In addition, the alpha-1 band spectrum of 4.0 mg/kg BW methamphetamine-treated group was significantly higher than those from the 2.0

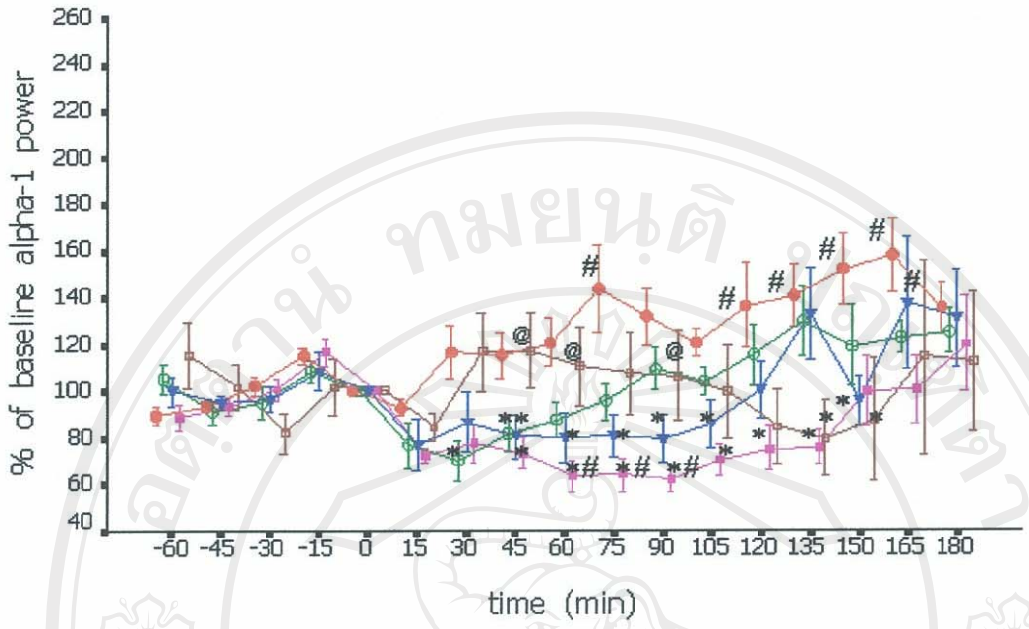

Figure 3. Time-courses of cortical EEG power in the alpha-1 band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

#: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

mg/kg BW methamphetamine-treated group at 45, 60, and 90 min after injection while no significant difference was observed between the 0.5 and 1.0 mg/kg BW methamphetamine-treated groups nor between the 1.0 and 2.0 mg/kg BW methamphetamine-treated groups.

Regarding the alpha-2 power band, the values in the control group of animals with physiological saline injection showed a significant increase from baseline activity at 75, 120, 135, 150, 165, and 180 min after injection (Figure 4) while the values in 0.5 mg/kg BW methamphetamine-treated group showed a significant increase at only 165 and 180 min after injection. This power band in 1.0 mg/kg BW methamphetamine-treated group showed a significant increase at 135, 165, and 180 min after injection. On the otherhand, the power band in 2.0 mg/kg BW methamphetamine-treated group showed a significant decrease from baseline from 15 to 105 min after injection. The power band in 4.0 mg/kg BW methamphetamine-treated group showed no significant difference from baseline.

The alpha-2 power band of 0.5 mg/kg BW methamphetamine-treated group was significantly lower than the control group from 15 to 75 min after injection and those in 1.0 mg/kg BW methamphetamine-treated group was furtherly significant till 105 min after the injection. The power band in both 2.0 mg/kg BW and 4.0 mg/kg BW methamphetamine-treated group was furtherly significantly lower till 135 and 150 min after the injection, respectively.

The power spectrum of alpha-2 band in 2.0 mg/kg BW methamphetamine-treated group was significantly lower from the 1.0 mg/kg BW methamphetamine-treated group at 135 min after injection. No significant difference was observed between the groups of 0.5 and 1.0 mg/kg BW methamphetamine treatment, nor between the groups 2.0 and 4.0 mg/kg BW methamphetamine treatment.

The power of beta-1 band in the control group of animals with physiological saline injection showed a significant increase from baseline activity at 75, 90, 120, 135, 150, 165, and 180 min after injection (Figure 5) while those in the 0.5 mg/kg BW methamphetamine-treated group showed significantly increased values of activity at 165 and 180 min after injection. The animals in the 1.0 mg/kg BW methamphetamine-treated group showed a significant increase of the same band at 135, 150, 165, and 180 min after injection and those in the 2.0 mg/kg BW methamphetamine-treated group showed

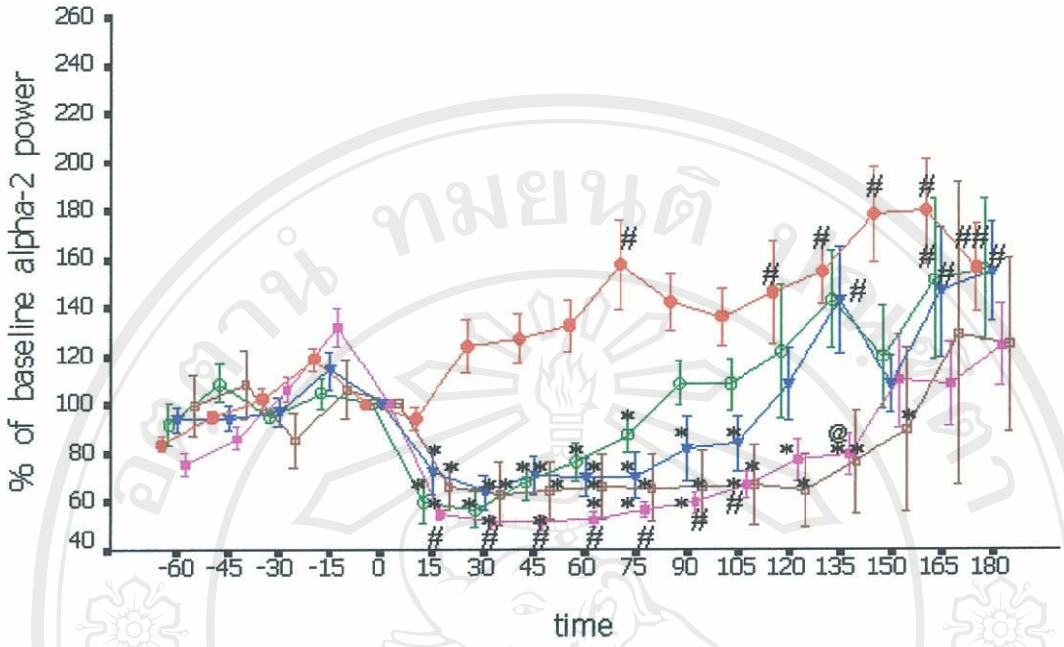

Figure 4. Time-courses of cortical EEG power in the alpha-2 band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

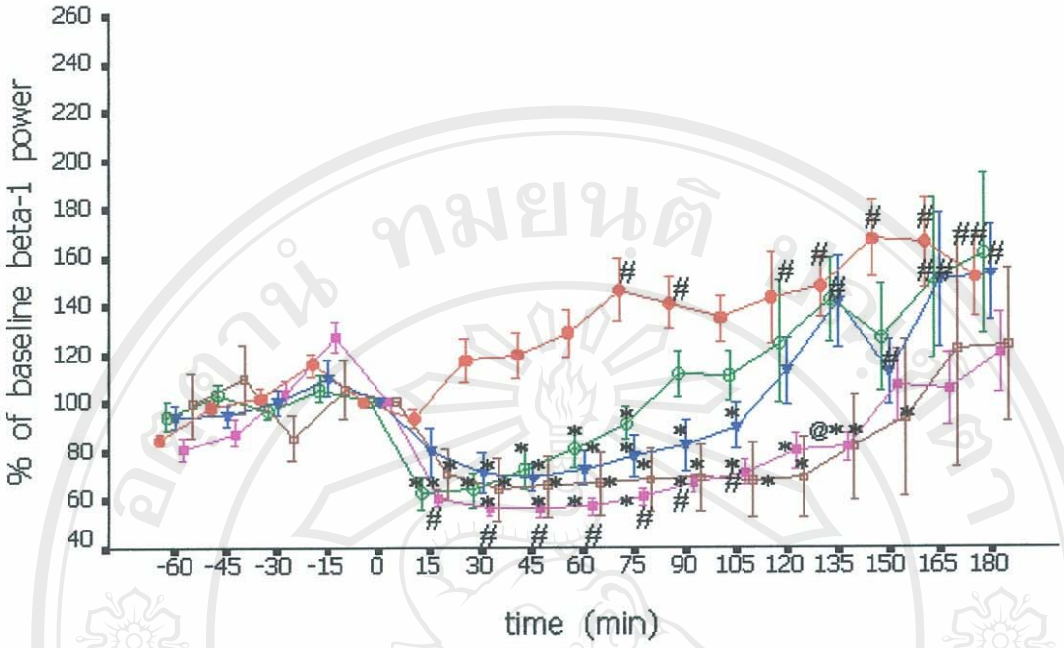

Figure 5. Time-courses of cortical EEG power in the beta-1 band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

decreased activity during the period from 15 to 105 min after injection. The power band of beta-1 in 4.0 mg/kg BW methamphetamine-treated group showed no significant difference from their baseline level.

In comparing the beta-1 power band of different experimental groups with control group, the power band in 0.5 mg/kg BW methamphetamine-treated group was significantly lower than the control group from 15 to 75 min after injection while those in the 1.0 mg/kg BW methamphetamine-treated group was significantly lower than the control group from 30 to 105 min after injection. The value in 2.0 mg/kg BW methamphetamine-treated group was significantly lower than the control group, during different and longer period, from 15 to 135 min after injection. The power band in the 4.0 mg/kg BW methamphetamine-treated group was significantly lower than the control group from 15 to 150 min after the injection.

Among various experimental groups of methamphetamine treatment, the beta-1 band of spectrum of 2.0 mg/kg BW methamphetamine-treated group was significantly lower than the 1.0 mg/kg BW methamphetamine-treated group at 135 min after the injection. No significant difference was observed between the groups of the 0.5 and 1.0 mg/kg BW methamphetamine groups of treatment, nor between the 2.0 and 4.0 mg/kg BW methamphetamine treatment.

The beta-2 power band of the control group of animals showed no significant increase from baseline activity throughout the experiment (Figure 6). The power band in the 0.5 mg/kg BW methamphetamine-treated group showed a significant decrease from baseline from 15 to 30 min after injection. The power band in the 2.0 mg/kg BW methamphetamine-treated group showed a significant decrease from baseline from 15 to 90 min after injection. The activity in both 1.0 and 4.0 mg/kg BW methamphetamine-treated groups showed no significant difference from baseline.

After comparing the power band of beta-2 of different experimental groups with the control group, it was found that both the 0.5 and 1.0 mg/kg BW methamphetamine-treated groups of animals had significant lower activity than the control group from 15 to 75 min after injection while those in the 2.0 mg/kg BW methamphetamine-treated animals were significantly lower than the control group during the period from 15 to 90 min after

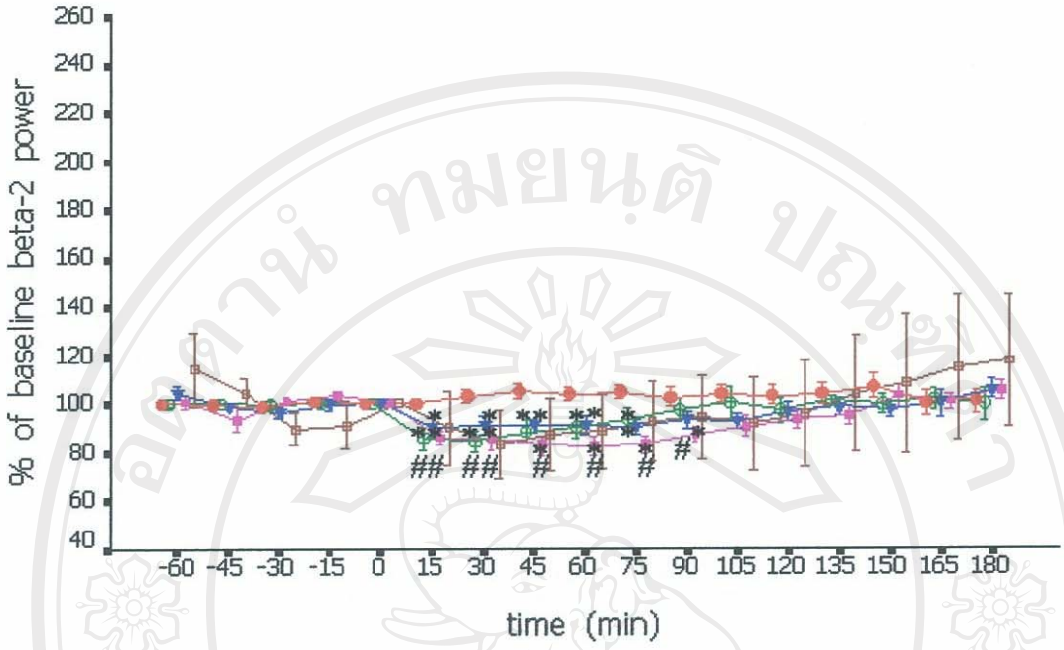

Figure 6. Time-courses of cortical EEG power in the beta-2 band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

the injection. However, the power band in the 4.0 mg/kg BW methamphetamine-treated group showed no significant difference from the control group. No significant difference was observed among the different experimental groups of methamphetamine treatment.

The power band of gamma band of the control group of animals showed no significant increase from baseline activity (Figure 7). Only the gamma band in 1.0 mg/kg BW methamphetamine-treated group showed a significant increase from baseline activity, at 135 min after injection, while, in contrast, the power band in the 0.5, 2.0, and 4.0 mg/kg BW methamphetamine-treated groups showed no significant difference from their baseline activity.

Comparing the gamma power band of experimental groups with the control groups, the power in 0.5, 1.0, and 2.0 mg/kg BW methamphetamine-treated groups was not significant different from the control group while the band in the 4.0 mg/kg BW methamphetamine-treated group was significantly higher than the control group at 15 min after injection.

No significant difference was observed among various experimtntal groups of methamphetamine treatment.

Locomotor Activity

The control group of animals showed the decrease of locomotor activity from baseline during the time period from 75 to 180 min after saline injection (Figure 8). The animals in 0.5 mg/kg BW methamphetamine-treated group showed a significant decrease of the activity from the baseline during a brief period, from 150 to 165 min after injection while those in the 1.0 mg/kg BW methamphetamine-treated group showed, in contrast, a significant increase from the baseline from 15 to 75 min after the injection and a significance decrease from the baseline at 165 and 180 min after injection. The animals in the 2.0 mg/kg BW methamphetamine-treated group showed a significant increase from baseline from 15 to 75 min after injection but those in the 4.0 mg/kg BW methamphetamine-treated group showed a significant increase from the baseline during the two periods, from 15 to 90 and from 120 to 165 min after injection.

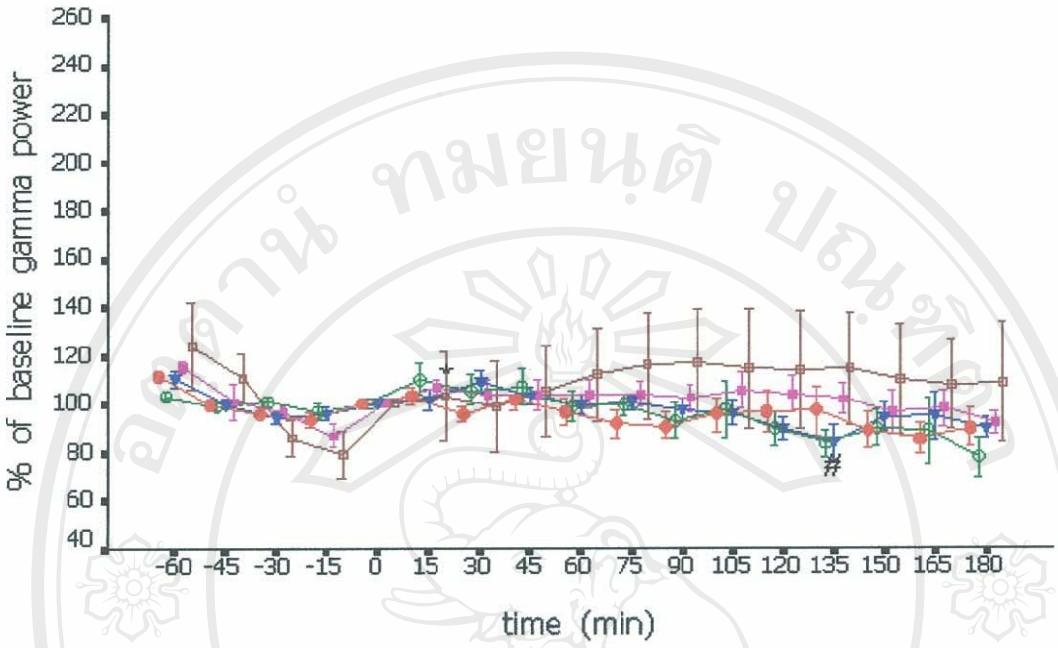

Figure 7. Time-courses of cortical EEG power in the gamma band of frequency spectrum produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of the frequency band was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n= 14.

○: 0.5 mg/kg BW methamphetamine-treated group, n=6.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=9.

■: 2.0 mg/kg BW methamphetamine-treated group, n=8.

□: 4.0 mg/kg BW methamphetamine-treated group, n=7.

: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

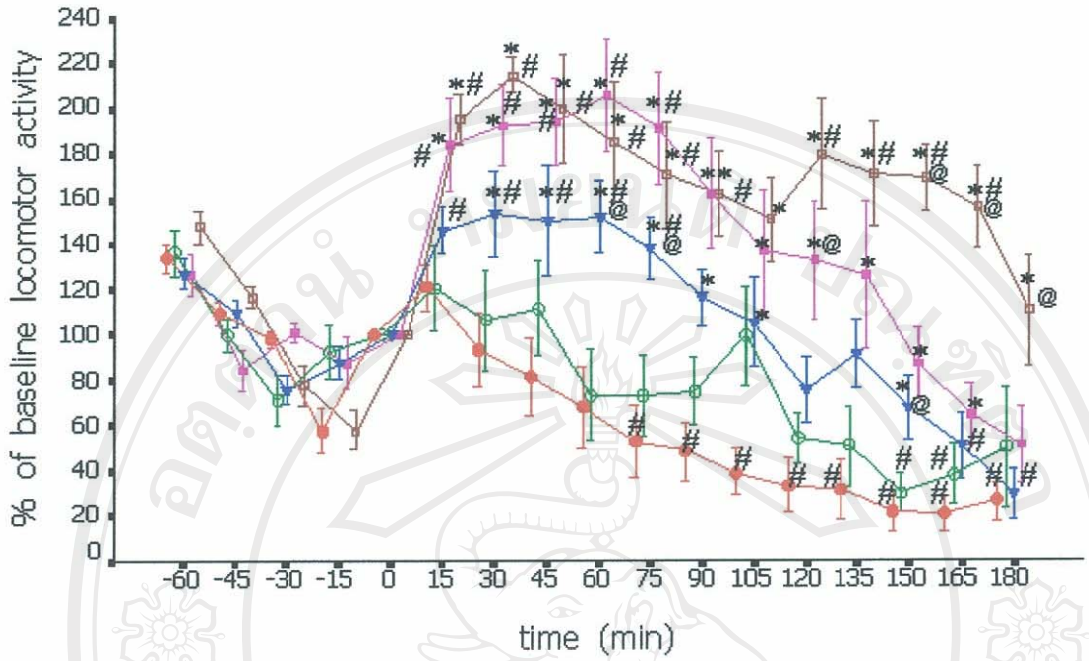

Figure 8. Time-courses of locomotor activity produced by saline and various doses of methamphetamine. The values of the four 15-min pre-injection periods were regarded as the baseline activity of which a value of 100% of locomotor activity was assumed and shown at the time 0. Abscissa: time (min) before and after drug injection, ordinate: percentages of baseline activities. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=11.

○: 0.5 mg/kg BW methamphetamine-treated group, n=11.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=10.

■: 2.0 mg/kg BW methamphetamine-treated group, n=12.

□: 4.0 mg/kg BW methamphetamine-treated group, n=8.

#: Significantly different from baseline, $p < 0.05$.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

By comparing the experimental groups with control group. No significant difference was observed between the 0.5 mg/kg BW methamphetamine-treated group and control group. The locomotor activity of 1.0 mg/kg BW methamphetamine-treated group was significantly higher than the control group from 30 to 105 min after injection and at 150 min after injection. The activity in the 2.0 mg/kg BW methamphetamine-treated group was significantly higher than the control group during the longer post-injection period, from 15 to 165 min. The value in 4.0 mg/kg BW methamphetamine-treated group was multiphasically higher than the control group, from 15 to 180 min after the injection.

Among different doses of methamphetamine treatments, it was observed that higher locomotor activity was produced by higher doses of methamphetamine. The animals in 1.0 mg/kg BW methamphetamine-treated group was significantly higher locomotor activity than the 0.5 mg/kg BW methamphetamine-treated group at 60, 75, and 150 min after injection. The activity in 2.0 mg/kg BW methamphetamine-treated group was additionally higher than those in 1.0 mg/kg BW methamphetamine-treated group at 120 min after injection while those in 4.0 mg/kg BW methamphetamine-treated group was furtherly higher than the 2.0 mg/kg BW methamphetamine-treated group at 150, 165, and 180 min after injection.

Stereotyped Behavior

It was observed that the control group of animals had no stereotyped behavior score throughout the experiments (Figure 9). The behavior score in 0.5 mg/kg BW methamphetamine-treated group was significantly higher than the control group at the time from 15 to 75 min during the post-injection period while the behavior score in 1.0 mg/kg BW methamphetamine-treated group was significantly higher than the control group from 15 min to 165 min. In both 2.0 and 4.0 mg/kg BW methamphetamine-treated groups, in addition, the score was significantly higher than the control group, during all post-injection periods, from 15 min to 180 min after injection.

Among different groups of methamphetamine treatments, the score of stereotyped behavior in 1.0 mg/kg BW methamphetamine-treated group of animals was significantly

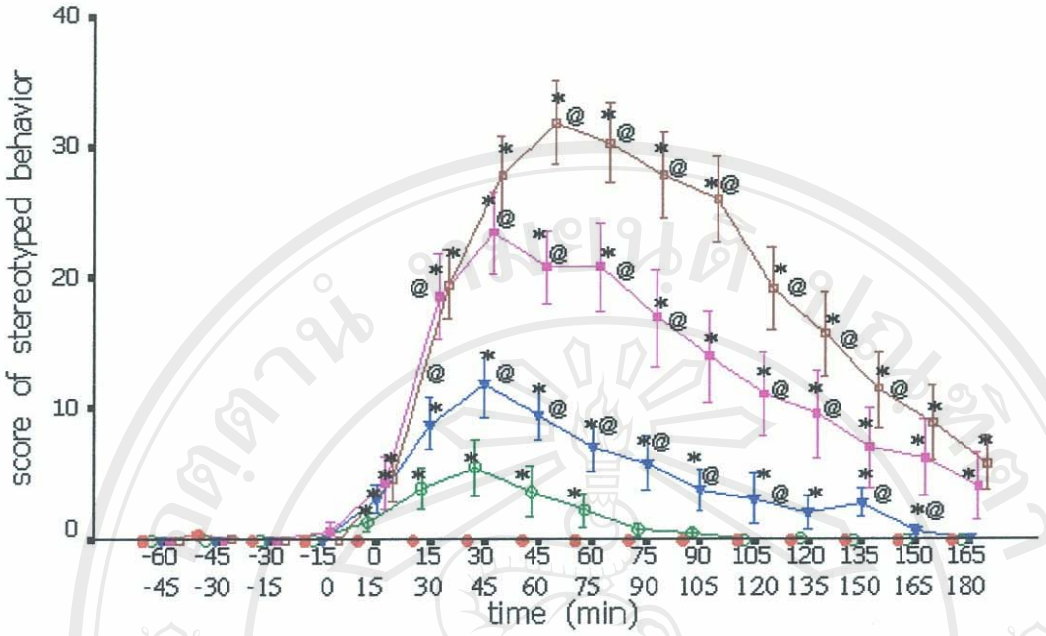

Figure 9. Time-courses of stereotyped behavior produced by saline and various doses of methamphetamine. The summed scores of each 15-min pre- and post-injection periods were shown. Abscissa: time intervals (min) before and after drug injection, ordinate: score of stereotyped behavior. Means ± SEM of the animals in each group are shown.

●: control, physiological saline-treated group, n=21.

○: 0.5 mg/kg BW methamphetamine-treated group, n=22.

▼: 1.0 mg/kg BW methamphetamine-treated group, n=23.

■: 2.0 mg/kg BW methamphetamine-treated group, n=24.

□: 4.0 mg/kg BW methamphetamine-treated group, n=23.

*: Significantly different from control (saline-treated) group, $p < 0.05$.

@: Significantly different from other methamphetamine-treated groups, see text, $p < 0.05$.

higher than the 0.5 mg/kg BW methamphetamine-treated group during most of the post-injection period (at 30, 45, 60, 75, 90, 105, 120, 150, and 165 min after injection). The score of 2.0 mg/kg BW methamphetamine-treated group was higher than the values in 1.0 mg/kg BW methamphetamine-treated group at 30, 45, 60, 75, 90, 120, 135 min after injection. The score of 4.0 mg/kg BW methamphetamine-treated group was significantly higher than the 2.0 mg/kg BW methamphetamine-treated group at 60, 75, 90, 105, 120, 135, and 150 min after injection.

By using all behavioral data at 30 min after injection, the correlation coefficients among EEG, locomotor activity, and stereotyped behavior were calculated across the four dosages of methamphetamine treatment (Table 2). Various degrees of correlations between bands of EEG activity and locomotor activity and stereotyped behavior were obtained. Both locomotor activity and stereotyped behavior correlated with power spectrum of gamma band at -0.8 level but with that of alpha-1 band at 0.8 level. However, there was no statistical significance for all of the above correlation ($p > 0.05$). In contrast, it was observed the correlation level of 1.0 between locomotor activity and stereotyped behavior data and there was statistical significance ($p < 0.001$).

Table 2. Correlation between EEG, locomotor activity, and stereotyped behavior

	Delta	Locomotor Activity	Stereotyped Behavior
Delta	1.0000	.4000 (p=.600)	.4000 (p=.600)
Locomotor Activity	.4000 (p=.600)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	.4000 (p=.600)	1.0000 (p<.001)	1.0000

	Theta	Locomotor Activity	Stereotyped Behavior
Theta	1.0000	-.2000 (p=.800)	-.2000 (p<.800)
Locomotor Activity	-.2000 (p=.800)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	-.2000 (p=.800)	1.0000 (p<.001)	1.0000

	Alpha-1	Locomotor Activity	Stereotyped Behavior
Alpha-1	1.0000	.8000 (p=.200)	.8000 (p=.200)
Locomotor Activity	.8000 (p=.200)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	.8000 (p=.200)	1.0000 (p<.001)	1.0000

	Alpha-2	Locomotor Activity	Stereotyped Behavior
Alpha-2	1.0000	.0000 (p=1.000)	.0000 (p=1.000)
Locomotor Activity	.0000 (p=1.000)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	.0000 (p=1.000)	1.0000 (p<.001)	1.0000

	Beta-1	Locomotor Activity	Stereotyped Behavior
Beta-1	1.0000	-.6000 (p=.400)	-.6000 (p=.400)
Locomotor Activity	-.6000 (p=.400)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	-.6000 (p=.400)	1.0000 (p<.001)	1.0000

	Beta-2	Locomotor Activity	Stereotyped Behavior
Beta-2	1.0000	-.4000 (p=.600)	-.4000 (p=.600)
Locomotor Activity	-.4000 (p=.600)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	-.4000 (p=.600)	1.0000 (p<.001)	1.0000

	Gamma	Locomotor Activity	Stereotyped Behavior
Gamma	1.0000	-.8000 (p=.200)	-.8000 (p=.200)
Locomotor Activity	-.8000 (p=.200)	1.0000	1.0000 (p<.001)
Stereotyped Behavior	-.8000 (p=.200)	1.0000 (p<.001)	1.0000