EFFECT OF PSYCHOSTIMULANTS ON MEMBRANE PERMEABILITY TO K^{42} IN DIFFERENT PARTS OF THE RAT BRAIN

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The effect of psychostimulants on incorporation of K^{42} into the tissues of different parts of the rat brain was studied. Amphetamine (2.5 mg/kg) and piridrol (12.5 mg/kg) reduce the permeability of the diencephalon and mesencephalon to K^{42}. No effect was found in the cerebral cortex. Caffeine (25 mg/kg) increased incorporation of the isotope into the cortical tissue; the permeability of the diencephalon and mesencephalon was not affected. Amphetamine and caffeine increase, while piridrol does not affect, the permeability of the medulla to K^{42}.

The stimulant effect of amphetamine, piridrol, and caffeine is accompanied by changes in the distribution of K^+ in different parts of the brain as the result of a disturbance of neuron membrane permeability [1, 2]. It has also been shown that the functional state of the CNS is largely dependent on the permeability of the blood-brain barrier to K^+ [4, 9, 17]. The important role of changes in the permeability of the brain to K^{42} in the mechanism of action of certain neurotropic drugs has also been demonstrated [5, 16].

The effect of psychostimulants on the permeability of different parts of the brain to K ions was studied in this investigation.

EXPERIMENTAL METHOD

Psychostimulants were injected intraperitoneally into albino rats in doses causing an increase in motor activity without signs of depression (amphetamine 2.5 mg/kg, piridrol 12.5 mg/kg, caffeine 25 mg/kg). The animals were decapitated at the time of maximal motor excitation, namely, 1.0-1.5 h after injection of the psychostimulants. An intravenous injection of 20 μCi K^{42} was given 10 min before decapitation. The brain was carefully freed from meninges and washed to remove blood. The γ radiation of the isotope in intact tissues of the cerebral cortex, diencephalon, mesencephalon, and medulla and also in the blood plasma was counted on a scintillation counter (type 770, Friesecke und Hoepfner, West Germany). The index of permeability of the blood-brain barrier was the ratio, expressed as a percentage, of the radioactivity of the tissue (pulses/min/g) to the radioactivity of plasma taken at the same time (in pulses/min/ml).

EXPERIMENTAL RESULTS

The highest radioactivity of the isotope 10 min after its injection into the control rats was observed in the diencephalon and mesencephalon, and the lowest in the cerebral cortex. The radioactivity of all parts of the brain investigated was considerably lower than in the plasma (Table 1). Low permeability of the brain to K^{42} has also been described by other workers [7, 9, 10, 12, 15]. This phenomenon is specific for brain tissue, for the peripheral nerves adsorb the isotope readily [7].

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TABLE 1. Effect of Psychostimulants on Tissue Permeability in Various Parts of the Rat Brain to K^{42} (M±m)

Name and dose of drug	Cerebral cortex			Diencephalon and mesencephalon			Medulla			Blood plasma
	radioactivity	tissue permeability		radioactivity	tissue permeability		radioactivity	tissue permeability		radioactivity
		abs.	%		abs.	%		abs.	%	
Amphetamine (2.5 mg/kg):										
control	1222±56	0,318	100	1532±48	0,400	100	1307±134	0,340	100	3842±55
experiment	1116±76	0,246	77	1260±98	0,278	69	1923±50	0,425	125	4525±120
Piridrol (12,5 mg/kg):										
control	1278±63	0,340	100	1870±73	0,490	100	1728±23	0,46	100	3760±75
experiment	1326±99	0,330	97	1292±92	0,324	66	1898±71	0,470	104	4033±55
Caffeine (25 mg/kg):										
control	1140±58	0,288	100	1320±81	0,337	100	1290±75	0,328	100	3924±152
experiment	1350±50	0,413	143	1240±56	0,368	109	1780±111	0,535	163	3362±123

After injection of amphetamine and piridrol a decrease in the permeability of the diencephalon and mesencephalon to K^{42} was observed. In the cerebral cortex neither psychostimulant had virtually any action. Caffeine increased the penetration of K^{42} into the cortex; the permeability of the diencephalon and mesencephalon was unaffected by this drug. Amphetamine and, in particular, caffeine (but not piridrol) increased the permeability of the medulla.

Psychostimulants, increasing motor activity but differing in their chemical structure, thus have an unequal action on the permeability of different parts of the brain. Presumably this factor is one of many responsible for qualitative differences between the stimulant effects of the phenylalkylamines (amphetamine and piridrol) and the purine bases (caffeine). However, even the effect of amphetamine and piridrol, closely similar in their structure, on the penetration of K^{42} into certain parts of the CNS and, in particular, into the medulla, is different. It is interesting to note that the sedative action of barbiturates of similar chemical structure (thiopental and pentobarbital) is also accompanied by different changes in permeability of the brain to K^{42} [16].

According to Cohn [6], the K isotope, once it has penetrated into the brain, is almost completely localized in the cell phase. The results of the present experiment showed that amphetamine and piridrol, which lower the permeability of the brain tissue to K^{42}, at the same time reduce the intracellular K^+ concentration in the brain. Caffeine, however, which increases the penetration of K^{42} into the brain, does not affect the intracellular K^+ [2]. This is evidently because of an increase in the "exchangeable" fraction of K^+ and a decrease in its fraction which is not exchanged for the injected isotope [10, 12]. The stable intracellular K^+ fraction is located in the mitochondria [13]. Caffeine increases the oxygen absorption by the brain mitochondria [3] and can thus lead to the accumulation of K^+ [8, 11]. Caffeine presumably brings about the same redistribution of K^+ between the subcellular fractions as Ca^{++} [14]. The intracellular K^+ content remains unchanged under these circumstances.

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