EFFECT OF STELAZINE ON THE NUCLEIC ACID CONTENT IN BRAIN TISSUE

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When stelazine was given to albino rats (5 mg/kg daily for 15 days), their DNA and RNA levels in the brain fell. The RNA concentration fell to a greater degree, and after administration of stelazine for 15 days the RNA concentration was only half that in control animals.

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In order to elucidate the mechanism of the therapeutic effect of psychopharmacological agents, it is most important to study biochemical changes taking place in the body and, in particular, in the brain under the influence of these drugs.

The nucleic acids responsible for synthesis of the specific proteins of neurons play an essential role in maintaining brain function. Most probably the therapeutic effect of neurotropic drugs can be attributed to some degree to their action on protein metabolism of nerve tissue.

In this investigation changes in the level of the nucleic acids (DNA and RNA) in the brain tissues were studied during administration of stelazine (trifluperazine), a psychopharmacological agent extensively used in the treatment of various forms of schizophrenia and psychoses [1, 2, 4, 5, 9, 11-15, 18].

EXPERIMENTAL METHOD

Stelazine (5 mg/kg body weight) was given by mouth daily for 15 days to female albino rats weighing 180-200 g. The concentration of nucleic acid in the brain tissue was determined spectrophotometrically by the method of R. G. Tsanev and G. G. Markov [7], 5, 10, and 15 days from the beginning of administration of stelazine and 5, 10, and 15 days after it was discontinued. In parallel experiments the DNA and RNA levels were determined in the brain tissue of control animals, and the water content of the brain tissue of the control and experimental rats was determined in percent.

The experimental results were analyzed by statistical methods.

TABLE 1. Changes in Nucleic Acid Levels in Brain Tissue of Rats Receiving Stelazine

Experimental conditions	Period of investigation (in days)	No. of animals	Concentration of nucleic acid (in mg% phosphorus; $\bar{x} \pm S_{\bar{x}}$)			
			DNA	P	RNA	P
Normal (control)	—	15	7,85±0,55	—	26,12±0,97	—
After daily administration of stelazine, 5 mg./kg	5	6	9,58±0,49	<0,025	22,81±1,13	<0,025
	10	6	7,71±0,36	>0,10	18,38±0,83	<0,001
	15	6	6,26±0,53	>0,20	14,56±1,13	<0,001
After discontinuing stelazine	5	6	5,93±0,33	<0,02	15,06±0,35	<0,002
	10	6	6,31±0,47	>0,10	20,17±0,65	<0,001
	15	6	13,71±0,98	<0,001	29,86±1,36	>0,10

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EXPERIMENTAL RESULTS

Administration of stelazine to the animals in a dose of 5 mg/kg was accompanied by the development of an extrapyramidal syndrome, as many other workers have described [3, 6, 8, 10, 16, 17].

As Table 1 shows, during prolonged administration of stelazine the DNA level in the brain tissue fell slightly, returning quickly to normal after discontinuing stelazine. On the 15th day after discontinuing stelazine the DNA content in the brain in fact exceeded its level in normal rats ($P < 0.001$). More marked changes were observed in the RNA level. After administration of stelazine for 15 days the RNA concentration in the brain tissue was reduced to almost half its initial value. After discontinuing the drug the RNA concentration rose again to its original value.

Under the influence of stelazine no significant changes were observed in the water content of the brain tissue compared with the control, suggesting that the nucleic acid concentrations should be expressed relative to dry weight of tissue.

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