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Symposium on substance P

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DANICA KOCIĆ-MITROVIĆ

SUBSTANCE P IN PREGNANCY

The localisation of SP in the organism is well known. It is found in extracts of many organs from different animal species, mostly in brain, intestine and retina, though in other organs too, in smaller amounts [Euler and Gaddum (1931), Douglas, Feldberg, Paton and Schachter (1951), Pernow (1953), Duner, Euler and Pernow (1954)]. During the thirty years following its discovery the main outlines of chemical properties and physiological action of SP have been covered in a series of papers. We know that SP exerts, besides from other action, some central effects (Euler and Pernow, 1956); probably it also acts as a transmitter substance between the first and second sensory neurons (Lembeck, 1957), as a motility hormone in the digestive tract (Ohnesorge, 1957), and, finally, it is assumed that SP is a physiological tranquillizer (Stern, 1958). Because of the multiple and important functions attributed to SP it was interesting to investigate its effects in pregnancy, the more so, since analogous investigations have been undertaken earlier with a related polypeptide, synthesized in almost the same regions of the central nervous system as SP, namely oxytocin.

We proceeded first to estimate the concentration of SP in the brain of the pregnant rat. SP was extracted following the method by Zetler and Schlosser (1955). A non-pregnant female from the same litter was used as a control. SP in the extracts was estimated on isolated guinea pig ileum after blocking the ACh, H, and 5-HT receptors by atropine, phenergan and LSD, respectively. The contractions were the characteristic SP-type.

In these experiments we observed a marked decrease of SP concentration in pregnancy with particularly low values in its second half (Fig. 1). This finding gave rise to a new problem: why is SP lost during pregnancy and where does it go? This problem is not only interesting per se, but also in connection with such facts as the increase of histaminase (Marcou et al., 1938) and oxytocinase (Tuppy H., 1960) activity in pregnancy, and in view of the incapability of either cerebrospinal fluid or blood to destroy SP (Gullbring, 1943). The answer to these questions was sought in another series of experiments. A standard SP solution (5 ml; 10^{-3} U./ml) was incubated for 1 hour in

a water bath at 37°C with: (a) two drops of blood serum from a pregnant rat, (b) two drops of non-pregnant rat serum, and (c) without serum (control). After incubation the solutions were tested on isolated guinea pig ileum. These experiments demonstrated a decrease of SP activity after incubation with pregnant serum, but no change after incubation with non-pregnant serum (Fig. 2), and finally that the SP-control during incubation does not change its activity.

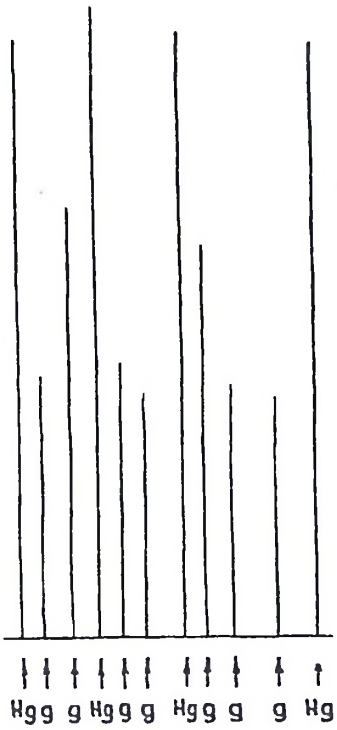

FIG. 1

Concentration of SP in the CNS of pregnant (g) and non-pregnant (Ng) rats.

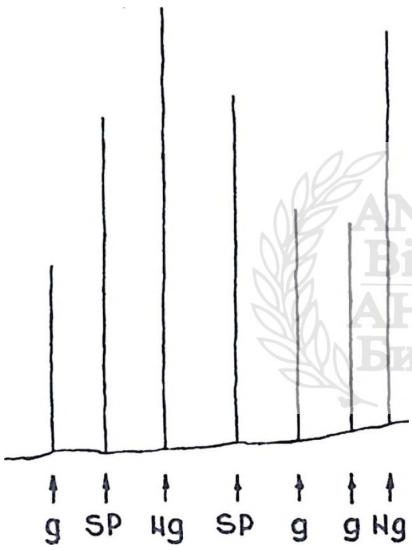

FIG. 2

Concentration of SP incubated with the serum of pregnant (g) and non-pregnant (Ng) rats.

We conclude from these results that, during pregnancy, the SP levels in the CNS of the rat are lowered.

Since SP, according to Lembeck (1956), Holton (1960), and Serafimov (1958), probably takes part in the transmission of sensory impulses we suppose that our results might be interpreted thus, that decreased perception of exogenous stimuli (eventually due to decrease of SP activity) serves to prevent disturbances in the normal course of pregnancy. Our results are in agreement with those of Stern, Gašparević and Kovač (1961) who found that SP is destroyed in human pregnant serum by a factor which is not identical with either diaminoxidase or vasopressinase or oxytocinase.

Summary

(1) The concentration of SP in the brain of the rat decreases during pregnancy.

(2) The pregnant rat serum contains a factor destroying SP, which is different from diaminoxidase, vasopressinase, and oxytocinase.

(3) We assume that our results could be of some importance in a study of the decreased perception to exogenic stimuly in pregnancy.

SP ZA VRIJEME TRUDNOĆE

Koncentracija SP u štakorovom mozgu i maternici opada u toku trudnoće.

Štakorov serum sadrži za vrijeme trudnoće neki faktor koji uništava SP, a razlikuje se od diaminoksidaze, vazopresinaze i oksitocinaze.

Pretpostavlja se da bi ovi rezultati mogli biti od izvjesne važnosti za proučavanje sniženja percepcije egzogenih podražaja za vrijeme trudnoće.

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DISCUSSION

LEMBECK: How many units per gram of SP have been found in the uterus? Furthermore, it should be interesting to refer the SP content of uterus also to the dry weight.

KOCIĆ-MITROVIĆ: I am afraid I cannot answer this, for I have not worked quantitatively.

LISSÁK: May I ask whether you made a control experiment with progesteron injected to pregnant rats?

KOCIĆ-MITROVIĆ: No, I have not.

VOGT: Is it known whether the total SP-content rises or falls in the pregnant uterus.

KOCIĆ-MITROVIĆ: It rises.