Symposium on substance P

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RADMILA PRŽIĆ

THE INFLUENCE OF SUBSTANCE P ON ATTACK AGAINST THE »WRITHING SYNDROME« IN THE MOUSE

Stern and Huković (1960) have made a comparison between central and peripheral effects of SP using both a crude (5 U./mg) and a highly purified (270 U./mg) preparation. They concluded that periphereal effects change parallelly to the purity of the preparation but central effects do not. Zetler (1956) has reported several central effects of SP using crude preparations of a similar potency as that used in the present work. He found, inter alia, that SP protects the mouse from strychnine convulsions, lengthens the duration of hexobarbital narcosis and antagonizes the analgetic effect of morphine (Mo). Moreover, animals receiving SP are much more quiet than controls. These results are interpreted by Zetler on basis of the assumption that SP acts not only as a transmitter in sensory neurons as it was assumed by Lembeck (1953), but also in the neurons of inhibiting systems. For such reasons Stern and coll. were led to the conclusion that there exists a synergism between SP and central depressants (Mephenesin and Meprobamate), whereas no synergism exists between SP and autonomic depressants (Stern, Dobrić and Mitrović-Kocić, 1957).

Stern and Huković (1960) could not observe a potentiation of central effects by using a more purified preparation, at least not in all cases. Purified SP, e. g., does not protect the mouse against strychnine convulsions; on the contrary, the latter are enhanced. Likewise, there is no effect on hexobarbital narcosis. With respect to its antianalgesic action, however, crude SP shows almost equal effects as the purified preparation and antagonized Mo analgesia as reported by Zetler (1956). We have considered that the examination of the antianalgesic effect of SP by a different method would be useful in deciding whether this effect is an accidental one, or not. It is fully justified to put such a question since Fleisch (1953) has demonstrated before that an analgetic acts with different intensity, depending on the method for testing the sensation of pain. We were well aware, of course, that already Stern and Huković (1960) used a method different from that of Zetler. We have chosen the writhing of the mouse as a criterion, because the corresponding method produces visceral pain (Eckhardt, Cheplovitz,

Lipo and Govier, 1958). Apart form SP we have examined the effect of adenosine 5'-monophosphate (AMP) by the »writhing« method, because Laszlo (1960) has shown that AMP inhibits the periphereal effects of SP, and we wanted to see whether the same action could be observed with respect to the antianalgesic action. A further paper from our laboratory has established the fact that AMP protects against strychnine convulsions and lengthens the duration of hexobarbital narcosis, as well as analgesia produced by Mo (Huković, Košak and Stern, 1961).

Method

The method applied was that by Eckhardt and coll. (1958). Mice of both sexes, weighing 18 to 20 mg, were given a dose of 10—12 mg per animal SP i. p. (1 mg SP = 5 units), 1 mg/kg Mo s. c. and 100 mg/kg AMP s. c. Pain was provoked by 10 mg/kg HCl i. p. or, in some instances, by the histamine liberator L 1935, 2.5 mg/kg.

	SP	AMP*	
HCl	0/10	0,10	Remark
Mo-HCl	0/10	10/10	The quotient denotes the number of treated animals protected from pain vs. the number of treated animals
L 1935	0/10	0,10	
Mo-L 1935	0/10	10/10	

* AMP itself partly lowers the sense of pain.

Table I shows that SP is an antianalgesic antagonizing Mo with the method employed. In the controls HCl produced intense writhing and rubbing of the abdomen against the bottom of the cage. The application of Mo completely eliminated these symptoms. AMP could not break through Mo analgesia but reduced the pain due to HCl, in accordance with the findings of Huković, Košak and Stern (1961). So the antianalgesic effect observed with the SP preparation is an individual effect of SP itself. Consequently SP shows a marked central action, although it is unable to protect against strychnine convulsions or to lengthen hexobarbital narcosis. From another paper it will be seen that SP antagonizes harmine-induced tremor, an effect noticed already by Zetler, whilst AMP does not. Recalling Lembeck's (1953) finding much higher levels of SP in dorsal than in ventral roots, his subsequent work with the rabbit auricle, that by Holton (1960) and Serafimov (1959), and comparing with our own results about the antianalgesic effect of SP we may tell that all of this supports Lembeck's assumption that SP takes part in the transmission of sensory impulses. Further confirmation which is to be seen in the influence which light and darkness exert on the amount of SP in the retina (Stern and Kocić-Mitrović, 1958) and in the potentiation of strychnine convulsions by purified SP (Stern and Huković, 1960). It would seem that the rôle of SP as a transmitter in neurons of inhibitive systems is

less marked. It must be noted, however, that Stern and Huković (1961) observed an extraordinarily quieting effect of SP, purified over an alumina column and completely free from AMP, in mice. Thus a central sedative effect undoubtedly exists. It is most difficult, for the time being, to discuss the physiological significance of the anti-analgesic effect of SP. We do not know as yet, e. g., whether the same antagonism exists against other analgesics outside the Mo group. Pain, as a physiological phenomenon, is a defensive mechanism. So we can consider the potentiation of the sensation of pain, and the simultaneous potentation of reflex capacity (strengthening of strychnine convulsions), as serving the defense reactions of the organism.

In conclusion we can say that AMP is not responsible for the antianalgesic effect of SP preparations, and that this effect is reproducible by various methods.

Summary

SP is considered to act as the transmitting substance in sensory neurons. The antianalgetic effect of SP against morphine has been examined in the mouse writhing test as a specific test for sensation of visceral pain. Adenosine-5'-monophosphate has been examined in the same test in order to see whether it is capable to inhibit the central effect of SP as it was shown earlier to inhibit the peripheral effects of SP. Only SP acted as an antagonist to morphine analgesia, adenosine-5'-monophosphate did not act the same way. Hence, SP has a marked central effect.

UTJECAJ SUPSTANCIJE P NA NAPADAJ PROTIV »WRITHING« SINDROMA KOD MIŠA

Smatra se da SP djeluje kao transmitorna supstancija senzibilnih neurona. Ispitan je antianalgetski efekat SP u odnosu na morfin metodom svijanja miša kao specijalnim testom za osjet visceralnog bola. Istim testom ispitan je i efekat adenozin-5'-monofosfata (AMP) radi utvrdivanja eventualnih smetnji centralnog efekta SP, budući da je već ranije dokazano da AMP sprečava njene periferne efekte. Pokazalo se da samo SP djeluje antagonistički u odnosu na analgeziju izazvanu djelovanjem morfina, dok AMP ne djeluje na efekat morfina. SP, dakle, ima izrazit centralni efekt.

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REFERENCES

ECKHARDT E., F. CHEPLOVITZ, M. LIPO AND M. GOVIER (1958) — Proc. Soc. exp. Biol. N. Y. 98, 186.
FLEISCH A. AND M. DOLIVO (1953) — Helv. physiol. pharmacol. Acta 11, 305—322.
HOLTON PAMELA (1960) — Pergamon Press, Oxford, London, New York, Paris.
HUKOVIĆ S., R. KOŠAK AND P. STERN (1961) — This Symposium, p. 15.
LASZLO I. (1960) — Cit. from J. Physiol. 153, 69 P.
LEMBECK F. (1953) — Arch. exp. Path. Pharmakol. 219, 197—213.
SERAFIMOV N. (1959) — IIIrd Conference of the Yugoslav physiologists, Skoplje.
STERN P., V. DOBRIĆ AND D. KOCIĆ-MITROVIĆ (1957) — Arch. int. Pharmacodyn. 112, 102—107.

STERN P. AND D. KOCIĆ-MITROVIĆ (1958) — Naturwissenschaften 45, 213.
STERN P. AND S. HUKOVIĆ S. (1961) — Unpublished.
STERN P. AND S. HUKOVIĆ (1960) — Med. exp. 2, 1—7.
ZETLER G. (1956) — Arh. exp. Path. Pharmakol. 228, 513—538.

DISCUSSION

KRIVOY: Drug-houses use the writhing method to test for antiemetics.

PRŽIĆ: The main point of this study is that SP antagonizes morphine.

ZETLER: How can one produce the writhing syndrom?

PRŽIĆ: By means of HCl histamine liberator L 1935, or with benzoquinone.