



Baština Akademije nauka i umjetnosti Bosne i Hercegovine

Symposium on substance P

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1961

Naučno društvo NR Bosne i Hercegovine

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Preuzeto s Baštine Akademije nauka i umjetnosti Bosne i Hercegovine

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CHAIRMAN'S OPENING REMARKS

Thanks to the extraordinary gift of observation of two scientists whose participation confers a particular significance to this gathering there was discovered, thirty years ago, a substance existing in the central nervous system and in the intestine which, though being different from ACh and H (the rôle of 5-HT was not so much as anticipated at that time), produced contractions in the guinea pig ileum and reduced blood pressure in the rabbit. One or two years later this substance was given the name »substance P«. The fact that brain and intestine contain identical or at least similar agents of a polypeptidic character acting like biogenic amines which have a much smaller molecule has brought a fundamentally new concept about factors which can fulfill physiological functions in the central nervous system. Now, after oxytocin, vasopressin and several other centrally acting polypeptides have been found, this concept does not seem to be anything unusual, but thirty years ago it had been a striking novelty.

Von Euler and Gaddum, the discoverers of SP, who also have an outstanding merit for our knowledge about other biogenic amines, have ever since its discovery promoted the studies on SP, but in due course a number of other experimenters also became interested in this field. Almost all of them, it is a pleasure to say, are present here.

At this Symposium we have two basic problems before us: the action of SP in the central nervous system, and its action in the digestive tract. By the way, it is an interesting question in itself why almost every biologically active substance occurring in the digestive tract also occurs in the central nervous system. However, to turn back to the main issue, it is, of course, much easier to study the peripheral effects of SP than its central ones, on the first place because the particular regions of the brain concerned are difficult to approach, and secondly because the responses are complex, and frequently reflect more than one single mechanism.

But the growing importance of central phenomena requires more study of the central effects, and a more favourable balance between papers dealing with peripheral, and such dealing with central effects has been reached at this Symposium.

The remaining important tasks in the SP field to be dealt with are the obtention of more precise knowledge about its distribution, the

finding of specific antagonists, and, possibly, a specific enzyme causing its inactivation. I hope that some of the papers presented here will, in part at least, give answers to these questions and others.

As late as a month ago there seemed to be one problem of great importance — we wanted to put it before this Symposium and even entered it into the programme — namely the question about a standard unit for SP. But an extremely interesting circumstance has made this item unnecessary. Most recently a group of Swiss workers from the Sandoz research laboratories have succeeded in obtaining a SP apparently of absolute purity. This, of course, obviates the need for a conventional standard since absolutely pure SP will serve as a standard in determining the SP-unit.

But this high degree of purity also comprises other implications. It is likely that we shall shortly know the chemical constitution of SP, and it will probably be possible soon to synthesize the compound. So we can tell that we find ourselves at the end of one period in the development of the SP problem, and at the beginning of a new one. The imminent unraveling of the constitution and the possibility to work with a uniform product free from all impurities necessarily imposes the need for a revision of practically all experimental work performed with products obtained by earlier methods of preparation. This, however, does not impair the importance of the papers to be presented at this Symposium because it is very probable that several of the present concepts about the rôles of SP are correct and their validity will remain unchanged.

It will be especially interesting, and the availability of pure preparations will enable us to do so, to elucidate the rôle of impurities masking the real effects of SP. With existing methods it is already possible to see that impurities exert significant component effects. A paper from my laboratory which will be presented at one of the subsequent meetings will show how great the influence of adenosine 5'-monophosphate, for instance, can be with respect to central effects.

One of the concepts mentioned before, which certainly is correct, is that of SP being a transmitting factor in sensory pathways. But, on the other hand, since the distribution of SP has been very thoroughly studied, and its occurrence in various parts of the central nervous system established, it seems unlikely that such a substance may be limited to sensory transmission alone. It would rather seem that the rôle of a transmitting factor can be taken up by SP in other mechanisms of the central nervous system too, as it has been found for the biogenic amines. The practically limitless number of possibilities for the action of already known transmitting substances in the individual synapses of the central nervous system shall by no means be modified with the addition of one more transmitter. And, for the rest, we cannot know whether one or more new transmitters of low or high molecular weight will not be found next.

Now, I find, the time has come to say that this assembly should eventually bestow a new designation, a real name to SP. This, of course, will be the exclusive privilege of the discoverers, professors von Euler and Gaddum.

Finally I want to say a few words more. This is the first Symposium dedicated exclusively to SP and, therefore, this gathering may contribute more than any of those held earlier about polypeptides affecting smooth muscle to the efforts of coordinating our investigations, obtaining better collaboration and more extended exchange of experiences. Small Symposia treating one single topic have great advantages for the development of the topic in question, thus we may expect the same from the present Symposium.

Every physiological and pharmacological analysis, in the last consequence, endeavours to make direct or indirect contributions to the advancement of therapy and not only to extend theoretical knowledge. I therefore also wish to express the hope that thorough understanding of the physiology and pharmacology of SP will surely serve for the benefit of ailing mankind.

ACKNOWLEDGMENT. — *I am indebted to Dr. Seid Huković who acted as a secretary to the Symposium for his invaluable assistance.*

