THE EFFECT OF ACETYLCHOLINE-LIKE SUBSTANCES ON SENSORY RECEPTORS

FRITZ BUCHTHAL

Institute of Neurophysiology, University of Copenhagen, Denmark

In relation to the discussion of the possible rôle of acetylcholine in the transmission of sensory impulses I would like to report briefly on some observations which Bing and Skouby (1) and Skouby (2, 3) have made in our laboratory. In these experiments a sensitizing effect of small amounts and an inhibiting effect of large amounts of acetylcholine and acetylcholine-like substances on the threshold of different receptors was demonstrated. Local application by intracutaneous injection or by iontophoresis did not elicit adequate sensations, and acetylcholine cannot be considered the adequate stimulus of the receptors.

The number of cold spots was increased 60 to 120 per cent by the injection of 0.3 to 10 μg acetylbetamethylcholine at the edge of the tested area. Similarly, 1 to 40 μg evoked a decrease in pain threshold while larger amounts (100 to 300 μg) produced a transient increase. Prostigmine injected intracutaneously (10^{-4} to 10^{-2} μg) increased the number of reacting cold spots and decreased the pain threshold. Conversely, atropine sulphate (50 μg) applied intracutaneously caused a significant decrease in the number of reacting cold spots and a small increase in pain threshold.

When histamine was applied intracutaneously in subthreshold amounts (10^{-4} to 1 μg), so that neither itching nor pain was produced, the addition of small amounts of acetylcholine (0.1 to 10 μg) caused a pain sensation of the common sort, *i.e.*, not followed by itching. When larger amounts of acetylcholine (10^{2} to 10^{3} μg) were used together with histamine, pain was no longer evoked. Similarly, subthreshold amounts of potassium combined with small amounts of acetylcholine evoked pain.

d-Tubocurarine and flaxedil acted antagonistically to the pain producing effect of histamine plus acetylcholine. When *d*-tubocurarine (0.1 μg) was added to histamine (1 μg) plus acetylcholine (1 μg), pain responses were no longer elicited. *d*-Tubocurarine not only blocked the sensitizing, but also the inhibiting effect of larger amounts of acetylcholine. Thus, an increase in acetylcholine from 1 μg to 100 μg, otherwise inhibiting pain responses from histamine, elicited pain when combined with *d*-tubocurarine (0.1 μg) and subthreshold amounts of histamine.

Acetylcholine can be replaced by decamethonium and succinylcholine.

Adenosine triphosphate (100 to 10^{4} μg) did not elicit pain nor change the response to acetylcholine plus histamine.

In summary, acetylcholine and acetylcholine-like substances sensitize peripheral sensory endings when applied in small amounts and inhibit in larger amounts. With a chemical pain producing substance it is possible to titrate the amounts of the chemical stimulus required against the amounts of acetylcholine-like substances and their inhibitors.

REFERENCES

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