ACETYLCHOLINE AND TRANSMISSION AT CHEMORECEPTORS

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The evidence at present available favouring the participation of acetylcholine in the transmission of nervous impulses in chemoreceptors of the carotid body is based entirely on a pharmacological study involving the use of nicotine-like drugs, ganglionic blocking agents and drugs capable of protecting the destruction of acetylcholine by inhibition of cholinesterase. The following points concerning the action of these drugs and the interpretation of their effects on the carotid body were discussed.

1. Acetylcholine and nicotine stimulate a variety of sensory end organs, e.g. receptors in the skin and mesentery and baroreceptors in the carotid sinus. The increased discharge in nerve fibres from such receptors produced by injection of these drugs is abolished by hexamethonium and by *d*-tubocurarine although the normal physiological response of the end-organs is unaffected. The impulses probably arise through direct chemical stimulation of part of the terminations of the sensory nerves (1). Douglas (5) showed that the carotid body chemoreceptors behave in a similar way in that hexamethonium, in doses of 15–35 mg./kg., abolished the response to acetylcholine and nicotine but left unaffected that to oxygen lack.

Relatively much larger doses of hexamethonium or d-tubocurarine as well as atropine reduce or abolish the increased chemoreceptor potentials set up by oxygen lack (10, 11). This could be interpreted as evidence that acetylcholine is formed within the glomus cell and possibly acts on an intracellular endplate (2). If so, then it would appear that the concentration of drugs required to block the resqonse to oxygen lack is greater than that to block the response of nicotine-like drugs. Evidence from histological studies indicating that there are two types of cell in the carotid body (8) and that non-specific cholinesterase is scattered irregularly throughout this structure (9) raises the question as to whether oxygen lack and nicotine-like drugs act on the same type of receptor. Since one nerve fibre can supply both types of cell (8), it would not appear possible to differentiate between these two types of response by the electrophysiological techniques which have so far been applied to the investigation of carotid body mechanisms.

2. The doses of drugs required to block the chemoreceptor discharge produced by oxygen lack are 0.5–2.0 mg. for hexamethonium and 1–3 mg. for atropine injected into the common carotid artery. It has been pointed out (10), however, that, on the basis of carotid body blood flow measurements (3), only about $\frac{1}{200}$ part of the drug reaches the carotid body. Calculations based on the volume and rate of injection of the drug (10) and on the carotid artery blood flow indicate that the concentration of the drug in the region of the carotid sinus, and presumably in the carotid body, is of the order of 1 in 1000. It may be that such large concentrations as this are required to penetrate the cell membrane; evidence suggesting that this is so for hexamethonium has been provided by Paton and

Zaimis (12). Atropine in these concentrations may have a local anaesthetic action, and although an attempt was made to rule out this factor, the evidence was based on experiments made by local application on the frog's tongue (10).

3. The chemoreceptor impulse activity in the carotid sinus nerve during oxygen- or air-breathing or during inhalation of gas-mixtures of low oxygen content may be enhanced by close arterial injection of a number of drugs having the properties of anticholinesterases (10, 11). The view has been taken that this action is one on the chemoreceptors of the carotid body. An alternative interpretation of these results concerns the possible role of the sympathetic innervation of the carotid body in these responses. Floyd and Neil (7) showed that increased sympathetic activity led to an increase in the chemoreceptor discharge in fibres of the carotid sinus nerve. By making direct measurements of carotid body blood flow, Daly, Lambertsen and Schweitzer (4) found that stimulation of the cervical sympathetic nerve caused a reduction in the carotid body blood flow due to local vasoconstriction of sufficient magnitude to possibly lead to a local anoxaemia. Since drugs injected into the common carotid artery reach the superior cervical ganglion, may not the increased chemoreceptor discharge in the carotid sinus nerve following the injection of anticholinesterases to be due to potentiation of the sympathetic nervous effects by an action on the ganglion rather than to a direct action on the carotid body? Although eserine injected into the superior cervical ganglion will potentiate the effector response to cervical sympathetic nerve stimulation only under certain conditions (6), this ought to be regarded at least as a potential mechanism which, so far as I am aware, has not been ruled out.

It is felt that the evidence at present available favouring the view that acetylcholine plays a role in the transmission of nervous effects in chemoreceptors of the carotid body is still equivocal.

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