Some Physiological and Pharmacological Characteristics of the Stimulus Induced Release of Norepinephrine from the Rabbit Superior Cervical Ganglion*

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Summary. The cervical sympathetic nerve stimulated release of norepinephrine (NE) from the rabbit superior cervical ganglion (SCG) was characterized. The quantity of NE released per impulse declined with increasing stimulation frequency over the range of 3/sec to 15/sec. Nerve stimulated NE release was potentiated by 1 micromolar desmethylimipramine and 25 micromolar phenoxybenzamine and inhibited by 1 micromolar bretylium, 25 micromolar methoxamine and 1 micromolar prostaglandin E₂. These results suggest that nerve stimulated NE release in the rabbit SCG occurs from sympathetic fibers which are subject to the same neurosecretory control mechanisms as sympathetic fibers elsewhere in the autonomic nervous system.

Key words: Sympathetic Ganglia Norepinephrine Release.

Supramaximal stimulation of the cervical sympathetic nerve causes the release of norepinephrine (NE) from nerve terminals in the rabbit superior cervical ganglion (SCG) (Noon et al., 1975). This previous study has suggested that NE release in the rabbit SCG occurs from terminals of sympathetic fibers. It was, therefore, of interest to physiologically and pharmacologically characterize the nerve stimulated release of NE in rabbit SCG in order to see if it has characteristics which are similar to those of the nerve stimulated release of NE from sympathetic fibers elsewhere in the sympathetic nervous system.

Concerning the physiological characteristics of NE release, it has been shown previously that a) the release of NE in the rabbit SCG (Noon et al., 1975) and b) neurotransmission elsewhere in the sympathetic...
nervous system (Boullin, 1967; Douglas and Ritchie, 1956) are both dependent on the presence of calcium in the extracellular medium and that both have stimulus threshold levels which are similar to those of C fibers. The present study compares the dependence of NE release on nerve stimulation frequency in the rabbit SCG with the stimulation frequency dependence of NE release in other sympathetically innervated preparations.

There are numerous sympathomimetic and sympatholytic agents which are known to have an effect on the nerve stimulated release of NE from sympathetic endings, by means of their direct action on the release of NE from, or the reuptake of NE into, sympathetic terminals. Examples are the blockade of the release of NE from sympathetic terminals by guanethidine and bretylium and the potentiation of release due to blockade of the reuptake of NE into sympathetic terminals by cocaine, desmethylimipramine etc. (Goodman and Gilman, 1970). The effects of these drugs on the release of NE from several sympathetically innervated tissues have been tested and their respective effects have been shown to be remarkably similar from tissue to tissue.

There are still other sympathomimetic and sympatholytic agents which have also been shown to have an effect on the nerve stimulated release of NE from sympathetic endings. However, the principle activity of this second group of drugs has not been postulated to be a direct action on the NE release, or the NE reuptake process, but, rather, an indirect action by means of their effect on hypothesized neurosecretion regulatory mechanisms. First of all, sympathetic terminals have been postulated to have α-adrenergic receptors which regulate the release of NE (Langer, 1973; Starke, 1973); the evidence on which the postulate is based being the observations that α-adrenergic agonists inhibit, and α-adrenergic antagonists potentiate, nerve stimulated NE release in several sympathetically innervated tissues. Secondly, a presynaptic prostaglandin receptor has been hypothesized to mediate the release of NE (Stjärne, 1973a; Hedqvist, 1974); the principle evidence for this hypothesis being the observation that prostaglandins of the E series block the nerve stimulated release of NE in several sympathetically innervated tissues. The members of this second group of sympathomimetic and sympatholytic drugs have also been shown to have corresponding effects in several different sympathetically innervated tissues.

It was of interest to compare the effects of the above-mentioned sympathomimetic and sympatholytic drugs on the nerve stimulated release of NE from the rabbit SCG with the reported effects of these drugs on the release of NE from other sympathetically innervated tissues. However, since the total number of drugs which have been tested in other tissues is so large, the following representatives of each of the respective classes.