Neuromuscular transmission in arterioles

Key words. Arterioles; sympathetic nerves; prazosin.

Introduction

It is often assumed that superfusion of a smooth muscle organ with the putative transmitter, released by the nerves which innervate that organ, will produce a response identical to that produced by nerve stimulation. Many observations have been made which are in accord

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 synaptic structures, rather they form a diffuse network of varicose fibers. Varicosities, the presumptive sites of transmitter release, often lie up to, and occasionally more, than a micron from the membrane of the smooth muscle cells making up that organ. Such an arrangement could reasonably be expected, like superfusion, to load the extracellular space with transmitter. Indeed the earlier electrophysiological analyses of neuromuscular transmission at smooth muscle organs supported such a view; the membrane potential changes which resulted from nerve stimulation could be modelled only with the assumption that transmitter diffused from its points of release and persisted in the extracellular space for extended periods (for review, see Holman and Hirst). However a number of more recent electrophysiological observations argue against the idea that neural control is exerted in such a 'loose' manner, rather they suggest that control is exerted in an ordered manner not unlike that described for the skeletal neuromuscular junction and for central nervous system synapses. This article aims to summarize the arguments for the latter view with special reference to sympathetic transmission in arterioles. Subsequently the possibility that, if the primary transmitter released by sympathetic nerves innervating systemic arteries is noradrenaline, the functional neural contacts between sympathetic nerves and arterial smooth muscle cells have specialized junctional receptors: (γ-receptors), will be explored.

Most arteries and arterioles are wrapped by sympathetic nerve fibers which, after exposure to formaldehyde when viewed with ultraviolet illumination, show a characteristic fluorescence. The evidence that such nerves store, and can release, noradrenaline has been reviewed. Individual axons usually do not penetrate the muscular wall of either arteries or arterioles, rather they ramify on the adventitial surface. Where distinguishable, single axons running across the surface of an artery have a varicose appearance, the individual varicosities being separated by some 10 μm lengths of fine unmyelinated axon. Similarly the nerve fiber giving rise to the nerve terminals is often varicose. Studies using electron microscopy indicate varicosities contain vesicles, yet have failed to demonstrate the other pre- or post-synaptic specializations which are normally associated with conventional synaptic contacts. Moreover there is a considerable variation in the separation between varicosities and the nearest smooth muscle membrane both between different arteries and between successive varicosities of individual arteries. The smooth muscle cells which make up the muscular wall of an artery or arteriole are individually arranged with their long axes in a circumferential orientation. Individual smooth muscle cells have diameters at their thickest part of about 4 μm and lengths of about 60 μm (see, for example, Hua and Crage). Areas of contact between individual smooth muscle cells have been detected in electron micrographs; these are thought to be the structural units which permit electrical coupling between neighboring smooth muscle cells.

Biophysical aspects of transmission in arterioles

In every artery examined, as with all other smooth muscle organs, electrophysiological studies indicate that individual smooth muscle cells are electrically connected to their neighboring cells to form syncytia. This has been shown by subjecting a portion of an artery to a voltage field, so inducing transmembrane current flow in that portion. Since membrane potential changes can be detected away from the voltage field, the induced current flow must be passively spreading down the artery. Clearly low resistance pathways must exist between the cells in the voltage field and those away from it. A consequence of the syncitial nature of arterial smooth muscle is that when junctional current flows across the membrane of a smooth muscle cell on the adventitial surface, that current will lead to charge displacement on the membranes of the smooth muscles even making up the luminal surface. Whether or not endothelial cells of the lumen are coupled to smooth muscle layers is not known. Electrical coupling between arteriolar smooth muscle cells has also been demonstrated by making paired intracellular recordings from smooth muscle cells separated but within the same arteriolar tree. When current was injected via one electrode a membrane potential change was detected at the second recording point. Current must flow between the individual smooth muscle cells, a proportion leaking across the membrane resistance of each and so producing a voltage change.

Perivascular nerve stimuli applied to all arteries and arterioles examined to date initiates excitatory junction potentials (e.j.ps) in the smooth muscle layer. With the exception of pulmonary arteries (and most veins) which have distinctly slow e.j.ps, e.j.ps recorded across the membrane resistance of each and so producing a voltage change. Perivascular nerve stimuli applied to all arteries and arterioles examined to date initiates excitatory junction potentials (e.j.ps) in the smooth muscle layer. With the exception of pulmonary arteries (and most veins) which have distinctly slow e.j.ps, e.j.ps recorded across the membrane resistance of each and so producing a voltage change.

Figure 1. Comparison between the time courses of an excitatory junction potential and its underlying excitatory junctional current. Recordings from short segment of submucosal arteriole of guinea pig. It can be seen that the duration of current flow is brief when compared with that of the 'unclamped' e.j.p. Note also the small peak amplitude of the excitatory junctional current. Each record is the average of 20 successive stimuli.