Mapping action potential initiation sites in corneal cold receptors

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Very little is known about the process of sensory activation of thinly myelinated (Aδ) and unmyelinated (C) sensory neurones that supply the majority of tissues in the body. Both these types of sensory neurone form highly branched nerve terminal arbours with many naked nerve endings. In the cornea, which is exclusively innervated by Aδ- and C-fibre sensory neurones, spike shape analysis and pharmacological blockade of Na^+ channels indicates that the most terminal region of the axon branches is able to support regenerative action potentials (APs) (Carr *et al.*, 2002). This finding leaves open the possibility that APs may be initiated in the most distal portions of the axon branches in these neurones. In the present study we used extracellular recording at the surface of the guinea-pig cornea to record AP activity directly from the 'naked' nerve terminals of cold sensitive neurones (Brock *et al.*, 1998). Briefly, the eyes were dissected from guinea pigs killed by an overdose of pentobarbitone sodium (100 mg/kg). The eyes were mounted in a recording chamber and the optic nerve and associated ciliary nerves drawn into a suction-stimulating electrode. Spontaneous and electrically evoked nerve terminal impulses (NTIs) were recorded with glass electrodes (~50 μm tip diameter) applied to the epithelial surface of the cornea. Cold receptors have an ongoing discharge of APs that is decreased and increased by heating and cooling respectively. Temporal mapping by collision of ongoing APs with electrically evoked antidromic APs, reveal that in most receptors spontaneous impulses are initiated at a site located close to site of recording at the nerve terminal. Analysis of NTI shape was used to investigate changes in the configuration of these signals when they were produced by APs initiated close to the site of recording. Most NTIs are diphasic (positive-negative), with the initial positive phase reflecting the discharge of membrane capacitance as the action potential invades the nerve terminal. Therefore most NTIs are generated by action potentials that are initiated at a point that is electrotonically distant from the nerve ending and that propagate antidromically to site of recording. However, in a small proportion of recordings, ongoing NTIs with an initial negative component due to local influx of Na^+ were recorded, indicating APs initiated at a site electrotonically very close to the site of recording. The results suggest that the sensory signal transduction and regenerative process producing APs can lie in parallel within the nerve terminal.

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