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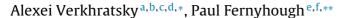
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Review

Calcium signalling in sensory neurones and peripheral glia in the context of diabetic neuropathies



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ABSTRACT

Peripheral sensory nervous system is comprised of neurones with their axons and neuroglia that includes satellite glial cells in sensory ganglia, myelinating, non-myelinating and perisynaptic Schwann cells. Pathogenesis of peripheral diabetic polyneuropathies is associated with aberrant function of both neurones and glia. Deregulated Ca²⁺ homoeostasis and aberrant Ca²⁺ signalling in neuronal and glial elements contributes to many forms of neuropathology and is fundamental to neurodegenerative diseases. In diabetes both neurones and glia experience metabolic stress and mitochondrial dysfunction which lead to deregulation of Ca²⁺ homeostasis and Ca²⁺ signalling, which in their turn lead to pathological cellular reactions contributing to development of diabetic neuropathies. Molecular cascades responsible for Ca²⁺ homeostasis and signalling, therefore, can be regarded as potential therapeutic targets.

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1. Calcium signalling and its deregulation in neuropathology

Calcium signalling is fundamental for information processing in the CNS. Highly localised Ca²⁺ signals regulate neurotransmitter release and synaptic plasticity, whereas global Ca²⁺ signals as intracellular Ca²⁺ waves link excitation with energy production (through mitochondrial Ca²⁺ signalling) and gene expression (through numerous Ca²⁺-dependent transcriptional pathways). In neuroglial cells, which can be defined as principal homeostatic cells of the nervous system, Ca²⁺ signals provide the substrate for excitability and are involved in local and long-range signalling, the latter being mediated by Ca²⁺ waves propagating through the glial syncytium.

Molecular cascades that regulate Ca^{2+} movements between cellular compartments and between cells and the environment have primarily evolved to maintain Ca^{2+} homeostasis, which keeps the concentration of free Ca^{2+} steady and distinct in different cell compartments. The concentration gradients created by active transport underlie signalling function, because regulated changes in permeability of plasmalemma or endomembranes result in Ca^{2+} fluxes that rapidly change free Ca^{2+} concentration; these changes in $[Ca^{2+}]$ are decoded by numerous Ca^{2+} -sensitive enzymes that act as sensors that trigger or discontinue cellular physiological responses. Molecular cascades of Ca^{2+} homeostasis and signalling, which include Ca^{2+} channels (that mediate transmembrane Ca^{2+} diffusion), Ca^{2+} exchangers, ATP-dependent Ca^{2+} transporters and

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