## Non-L-type calcium channels contribute to cerebrovascular function

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Antagonists of L-type voltage dependent calcium channels (VDCCs) are widely used in the treatment of vasospasm following subarachnoid haemorrhage, however their effectiveness in improving patient outcome is questionable. Our aim was to determine whether non-L-type calcium currents contribute to cerebrovascular function, and to determine the selectivity of T-type VDCC antagonists. Quantitative PCR, immunohistochemistry and immunoelectronmicroscopy were used to define the subtypes and location of voltage-dependent calcium channels expressed in cerebral arteries. Patch clamp electrophysiology, pressure myography and pharmacology were used to classify calcium currents in isolated cerebrovascular SMCs and responses of cerebral arteries. Messenger RNA and protein for L- ($Ca_V1.2$) and T-type channels ($Ca_V$ 3.1, $Ca_V$ 3.2) were detected in cerebral arteries. In isolated SMCs, a high voltage-activated calcium current with L-type VDCC kinetics and sensitivity to the dihydropyridines, nifedipine and nimodipine, comprised 75% of the current, while the residual current had kinetics typical of T-type currents. Both the dihydropyridine-sensitive and insensitive components could be blocked by T-type blockers, but only the sensitive component was blocked by diltiazem. This component was larger in SMCs from smaller arteries. In large pressurised arteries, voltage-dependent constriction was abolished by L-type antagonists, while in smaller arteries, this required both L- and T-type antagonists. However, considerable overlap in the action of these antagonists was found. We suggest that a heterogeneous population of L-type and high voltage-activated T-type VDCCs contribute to vascular tone in resistance sized cerebral arteries, providing a novel therapeutic target for therapy-resistant vasospasm.