Regulation of Middle Meningeal Artery Diameter by ATP-sensitive potassium channels
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The cellular mechanisms contributing to migraine headache are poorly understood, but may involve prolonged dilation of cranial arteries, specifically the middle meningeal artery (MMA). Agonist-induced activation of ATP-sensitive potassium (K\textsubscript{ATP}) channels is known to play an important role in the modulation of arterial diameter in a number of vascular beds. The objective of the current study was to determine if a tonic vasodilator influence resulting from basal K\textsubscript{ATP} channel activity is present in isolated, pressurized rat MMA. At an intravascular pressure of 40 mmHg, arteries developed pressure-induced constriction (i.e. myogenic tone) representing an approximate 40 % decrease in diameter. Treatment of arteries with either of the K\textsubscript{ATP} channel inhibitors glibenclamide (10 µM) or PNU37883 (10 µM) induced a further decrease in diameter of ≈ 20 %. Also consistent with basal K\textsubscript{ATP} activity, glibenclamide induced a membrane potential depolarization of ≈ 14 mV in MMA segments at an intravascular pressure of 40 mmHg. Further, in MMA loaded with the ratiometric calcium indicator, Fura-2-AM, glibenclamide-induced MMA constriction was correlated with a simultaneous increase in the ratio of 340 nm/380 nm excited fura-2 fluorescence, consistent with an increase in intracellular calcium. Interestingly, the PKA inhibitor, H89 (1 µM), abolished glibenclamide-induced MMA constriction suggesting that PKA activity may underlie tonic K\textsubscript{ATP} channel activation. Glibenclamide or PNU37883 did not alter the diameter of isolated cerebral arteries. Together these results suggest that tonic K\textsubscript{ATP} channel activity plays a key role in regulation of MMA, but not cerebral artery, diameter and may represent a potential target in the development of treatments for migraine headache. Supported by NIH P01 HL095488, P30 RR032135, P30 GM 103498 Totman Medical Research Trust and the Peter Martin Fund.