ity in the cVN (n=7). When the Bötzinger complex (BötC) was removed all expiratory activity was abolished and could not be reinstated by hypercapnia and/or hypoxia. Suppression of the RTN/vlPF (isoguvacine microinjections, 60 nL, 20 mM) attenuated resting post-I activity from AB (-69±14 %, n=5, P<0.05) and cVN (-68±12 %, n=5, P<0.05), which partially recovered during hypercapnia. Suppression of the RTN/vlPF region abolished late-E AB bursts evoked by hypercapnia. The most potent inhibition of expiratory motor outflow as obtained from microinjections in the caudal half of RTN/vlPF.

We conclude that the integrity of RTN/vlPF is required for regeneration late-E AB bursts during hypercapnia. The BötC is essential for generation of expiratory activity on a 2-phase rhythm. The pons provides essential tonic excitatory drive to post-I cell populations in the brainstem with RTN/vlPF contributing to this drive.

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC41

Attenuation of stretch-activated discharge of rat muscle spindle afferents by ENaC channel inhibitors

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Mechanotransduction is similar in a wide variety of primary mechanosensory nerve endings, with shear stress or membrane stretch opening mechanically gated cationic channels (Guharay & Sachs, 1984). However, the channel types involved are less clear. In mammals, mechanical gating of N- and L-type Ca^{2+} channels (Calabrese *et al*., 2002) and/or amiloride-sensitive epithelial Na^{+} channels (Achard *et al*., 1996) has been suggested. The brain sodium channel 1 (BNC1/BNaC1), from the degenerin/epithelial Na channel (DEG/ENaC) superfamily, is important in rapidly and slowly adapting mechanosensory organs (Price *et al*., 2000). However, little is known about the channels of many mammalian proprioceptors, including muscle spindles. Therefore, we investigated the effect of ENaC mechanosensitive channel inhibitors in rat muscle spindles by examining their sensitivity to amiloride and two homologues, benzamil and 5-(N-Ethyl-N-isopropyl) amiloride (EIPA).

Adult Sprague-Dawley rats (male, 350-620g) were killed by Schedule 1 methods (Animal (Scientific Procedures) Act, 1986), both 4th lumbrical nerve-muscle preparations excised and placed in gassed (95%O_2-5%CO_2) Liley`s saline at room temperature. Spindle discharges in the nerve were recorded en passant with Ag wire electrodes, and spikes in the first 0.5 s of the "hold" phase of 1 mm stretch-and-hold cycles were counted. Data are expressed as mean frequency ± SE. Differences between the pre-drug control and with-drug mean firing frequencies were evaluated by paired t-test, with a significance threshold of $P < 0.05$.

After pre-drug control recording, increasing concentrations of amiloride (n = 14), benzamil (n = 12) or EIPA (n = 13) were applied (1, 10, 100μM and 1mM). All three drugs progressively lowered the spike frequency (Fig. 1), producing significant inhibition at 1 μM (P<0.03 for each). 1 mM drugs produced the most robust block, although none totally abolished firing (14.2%, 11.4% and 9.8% of controls for amiloride, benzamil & EIPA, respectively). No-drug control muscles showed no decrease in firing over the same time scale. These data indicate members of the degenerin/ENaC channel superfamily play a role in spindle mechanotransduction. In guinea pig airway low-threshold vagal afferents, benzamil is a more potent inhibitor than amiloride (Carr *et al*., 2001). In spindles, we find each drug is equipotent but inhibit at 100x lower (1 μM) concentrations. In conclusion, as in some other mammalian mechanosensitive endings, amiloride and its analogues inhibit afferent discharge in muscle spindles. However, spindle endings had much greater sensitivity and did not distinguish between the amiloride analogues.

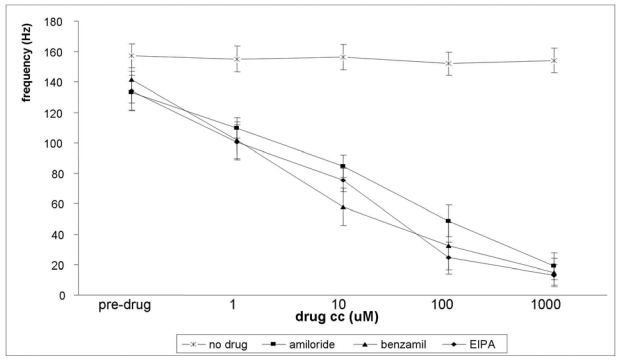

Figure 1 The effects of amiloride or its analogues on the firing rates of muscle-spindles in isolated preparations of lumbrical muscles of the rat.

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PC42

Carotid body and ventilatory responses to acute hypoxia in the anaesthetised adult rat following prenatal hypoxia

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The ventilatory response to hypoxia matures postnatally in mammals due partly to resetting of the carotid bodies (Koch & Wendel, 1968). In the adult, the carotid bodies respond to a