037P AIRWAYS HYPERREACTIVITY TO BRADYKININ IN LUNG PARENCHYMAL STRIPS FROM ACTIVELY SENSITISED BROWN NORWAY RATS CHALLENGED WITH ALLERGEN

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The bronchoconstrictor response to bradykinin (BK) is potentiated 24 h after ovalbumin (OA) challenge in actively sensitised Brown Norway (BN) rats *in vivo* (Ellis *et al*., 2002) Pharmacological analysis implicates a major role for cholinergic nerves in the augmented response, but not mast cells, leukotrienes, tachykinins, or products of cyclooxygenase. The aim of the present study was to determine whether airways hyperreactivity to BK can be detected *in vitro* following OA challenge.

Male BN rats (250-300g) were actively sensitised and challenged with OA or saline 24 h prior to death by exposure to carbon dioxide (Hannon *et al*., 2001). Lungs were perfused *in situ* prior to parenchymal strips being cut from the major lobe. Strips were mounted in 20 ml organ baths containing Krebs' solution at 37°C, bubbled with 95% O_2/5% CO_2. Resting tension was maintained at 1 g. Concentration-response curves were constructed for BK (0.1-3 μM), methacholine (10 nM-0.1 mM) and 5-HT (100 nM-0.1 mM).

BK induced concentration-dependent contractions which were significantly greater in OA-challenged animals than controls (Figure 1A). Responses to methacholine were also slightly, but highly significantly, enhanced in OA-challenged animals (Figure 1B). The enhanced BK response was entirely B_2 receptor mediated, since HOE 140 (10 nM) abolished the response. Atropine (10 nM) and methysergide (30 nM) abolished the responses to methacholine and 5-HT, respectively, but both failed to inhibit responses to BK, thus excluding a role for cholinergic nerves and mast cells.

Indomethacin, 10 and 100 nM, blocked the BK (1 μM) response by 37 and 90% (n=4), respectively, but also inhibited the 5-HT response by 32 and 93% (n=4), respectively. Indomethacin (100 nM) also blocked the methacholine response by 65% (n=4).

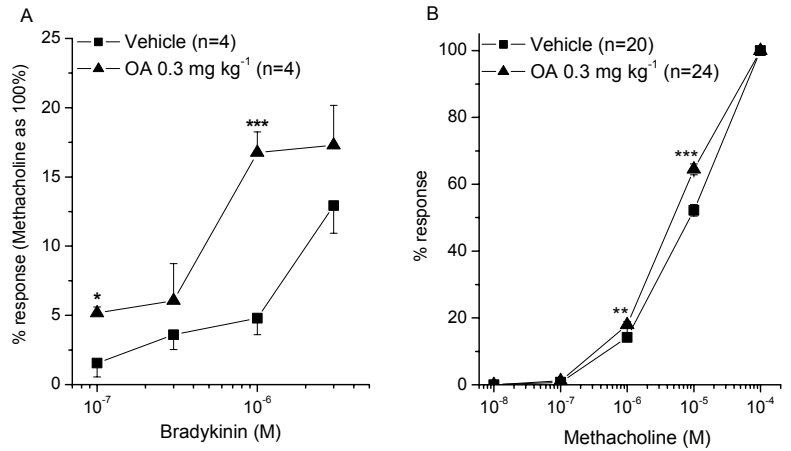

Figure 1: Concentration response curves to BK (A) and methacholine (B) in lung parenchymal strips from OA- and vehicle-challenged BN rats. **P*<0.05, ***P*<0.01, ****P*<0.001 indicates significant difference between OA- and vehicle-challenged animals using Student's *t* test for unpaired data assuming unequal variances.

Thus, the BK contractile response on parenchymal strips is significantly enhanced in tissues taken from actively sensitised OA-challenged BN rats, mirroring the *in vivo* findings. However, in contrast to the *in vivo* findings, the contractile response has no cholinergic component, but a component involving products of cyclooxygenase is implicated.

Ellis, K.M. *et al*., (2002). *Br. J. Pharmacol*., 137, 33P
Hannon, J.P. *et al*., (2001). *Br. J. Pharmacol*., 132, 1509-1523