Characterisation Of Opioid Receptors In Epididymal Human Vas Deferens

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Human vas deferens have been extensively investigated as a model to study sympathetic neurotransmission. There is however little known about opioid receptor expression and pharmacology within human vas deferens in comparison to other species such as mouse and rat.

In this study we have investigated the effects of several standard opioid receptor agonists and antagonists using traditional tissue bath pharmacology assays. Epididymal segments of human vas deferens were obtained with consent from male donors undergoing elective vasectomy and longitudinal muscle strips were mounted in 5ml tissue baths. Electrical field stimulation (efs) was applied to the tissue and standard opioid compounds were added to the baths in a cumulative manner to assess for effects on contractions induced. In the case of an antagonist study, compounds were added to the bath and left to incubate for 30 minutes prior to a cumulative concentration response curve with the corresponding agonist. The MOP receptor agonists DAMGO (IC$_{50}$ 61.01 (35.02-108.04) nM, n=4), Loperamide (IC$_{50}$ 29.92 (25.13-35.82) nM, n=3) and Compound A (IC$_{50}$ 12.18 (5.82-24.83) nM, n=3) all produced a concentration dependent inhibition of efs within epididymal human vas deferens. Pre-incubation with a MOP receptor antagonist, 3µM CTAP, rendered DAMGO inactive up to the highest concentration tested, 10µM (n=3) and resulted in a rightward shift in the IC$_{50}$ of Compound A (IC$_{50}$ 30.19 (1.44-63.44) nM, n=3). The DOP receptor agonists DPDPE (IC$_{50}$ 0.62 (0.36-1.05) nM, n=4), SNC-80 (IC$_{50}$ 80.43 (38.86-106.45) nM, n=3) and Compound B (IC$_{50}$ 0.94 (0.31-2.87) nM, n=5), all produced a concentration dependent inhibition of efs within epididymal human vas deferens. The inhibition of efs by Compound B was insurmountably inhibited by pre-incubation of the DOP receptor antagonist, 3nM Naltrindole (IC$_{50}$ 47.09 (13.24-168.58) nM, n=3) and 10nM Naltrindole (IC$_{50}$ 227.28 (137.78-379.14) nM, n=3). The inhibition of DPDPE was insurmountably inhibited by 10nM Naltrindole (IC$_{50}$ 66.42 (29.16-151.30) nM, n=3). U-50488, a KOP receptor agonist had no effect up to the highest concentration tested, 10µM (n=4) on the contractions induced by efs within the epididymal human vas deferens.

In conclusion, DOP and MOP receptors are present and functional in epididymal human vas deferens. Characterisation was further confirmed by the effects of selective DOP and MOP receptor antagonists within this assay. The selective KOP receptor agonist, U-504888 caused no effect, confirming the absence of KOP receptors in this preparation.