

A COMPARISON BETWEEN THE RECEPTOR REGULATION OF 5-HT NEURONAL FIRING IN THE MEDIAN AND THE DORSAL RAPHE NUCLEUS

Sarah J Judge, Richard McQuade & Sarah E Gartside (A K Daly) Psychobiology Research Group, The Medical School, University of Newcastle, NE2 4HH, UK.

The median raphe nucleus (MRN) and dorsal raphe nucleus (DRN) contain the cell bodies of 5-HT neurones which innervate the forebrain. Although the regulation of 5-HT neurones in the DRN is well established (Innis *et al.*, 1988; Judge *et al.*, 2004) relatively little is known of the regulation of MRN 5-HT neurones. Here we compared the sensitivity of MRN and DRN 5-HT neurones to 5-HT_{1A} receptor-mediated inhibition and α_1 -adrenoceptor-mediated excitation using *in vitro* electrophysiology.

Brain slices (400 μ m thick) containing the DRN and MRN were prepared from male hooded Lister rats (200-400 g). Slices were perfused with oxygenated artificial cerebrospinal fluid (aCSF) containing the α_1 -adrenoceptor agonist phenylephrine (PE, 1 μ M) at 36°C. Extracellular recordings were made from presumed 5-HT neurones in the DRN and MRN. Drugs were applied via the perfusion medium.

Putative 5-HT neurones (83 neurones from 25 animals) were identified on the basis of their location, slow and regular firing, and inhibitory response to 5-HT (10-50 μ M). In the continuous presence of PE (1 μ M), the basal firing rate was markedly lower in MRN neurones than in DRN neurones (0.52 ± 0.03 Hz; range 0.09 – 1.0 Hz; n = 41 vs 1.21 ± 0.07 Hz; range 0.3 – 2.34 Hz; n = 42; $p < 0.001$, unpaired t-test). Brief (2 min) application of higher concentrations of PE (3, 6 and 10 μ M) caused concentration-dependent excitation in both nuclei but the responses were strikingly smaller in the MRN than in the DRN. Thus, two-way ANOVA revealed a main effect of location ($F_{1,13} = 15$ $p < 0.005$) and [PE] ($F_{2,26} = 43.1$ $p < 0.001$) and a [PE]*location interaction ($F_{2,26} = 6.8$ $p < 0.05$). Brief (2 min) application of 5-HT (10, 25 and 50 μ M) caused a concentration-dependent inhibition in both nuclei. In all neurones tested the response to 5-HT was blocked by the 5-HT_{1A} receptor antagonist WAY 100635 (100 nM) (MRN n = 10; $p < 0.001$; DRN (n = 9; $p < 0.001$, paired t-test). The response to 5-HT in the MRN was not significantly different from that in the DRN when expressed as a percentage decrease. Thus, two-way ANOVA revealed a main effect of [5-HT] ($F_{2,54} = 101.7$ $p < 0.001$) but not location ($F_{1,27} = 2.8$ $p = 0.11$). However, when expressed as the number of spikes suppressed, the response to 5-HT in the MRN was significantly smaller than in the DRN. Two-way ANOVA revealed a main effect of location ($F_{1,27} = 9.6$ $p < 0.005$) and [5-HT] ($F_{2,54} = 76.9$ $p < 0.001$) and a [5-HT] *location interaction ($F_{2,54} = 21.5$ $p < 0.001$). To examine whether the basal firing rate might have influenced the 5-HT response, the responses of individual MRN neurones to 5-HT (10 μ M) were tested under conditions of low basal firing rate (0.51 ± 0.09 Hz in presence of 1 μ M PE) and high basal firing rate (1.08 ± 0.1 Hz in presence of 30 μ M α_1 -adrenoceptor agonist norepinephrine). The response expressed as *spikes suppressed* was not different between the low and high firing rate conditions (n = 8; $p = 0.31$, paired t-test).

The data indicate that 5-HT neurones in the MRN are less sensitive to α_1 -adrenoceptor excitation than those in the DRN, resulting in differences in basal firing rate. When responses are considered as *spikes suppressed*, MRN 5-HT neurones also appear less sensitive to 5-HT_{1A} receptor inhibition than those in the DRN, a factor which cannot be accounted for by their lower basal firing rate.

Innis, RB *et al.* (1988) *Brain Res.* **459**:27-36.

Judge, SJ *et al.* (2004) *Neurochem. Int.* **45**:1057-1065.