Role of 5-HT_{1A} receptors in the cardiovascular response elicited from the dorsomedial hypothalamic nucleus in the rat

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The dorsomedial hypothalamic nucleus (DMH) mediates the cardiovascular response to stressors such as air jet stress or cold stress. Activation of the DMH causes an increase in mean arterial pressure (MAP), heart rate (HR) and renal sympathetic nerve activity (RSNA). We have shown that the sympathoexcitatory vasomotor and cardiac components of the DMH-evoked response are dependent upon neurons in the rostral ventrolateral medulla and raphe pallidus in the medulla.[1,2)] Both of these regions contain serotonin receptors of the 5-hydroxytryptamine 1A (5-HT_{1A}) subtype. Recently, Ootsuka and Blessing[3)] have shown that intravenous administration of the selective 5-HT_{1A} agonist, 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) centrally inhibited cold-induced sympathetically mediated cutaneous vasoconstricton in the rabbit. The aim of the present study was to determine whether intravenous administration of the selective 5-HT_{1A} agonist, 8-OH-DPAT also affects the cardiovascular response to the DMH-evoked response. In urethane-anaesthetized rats (1.3 g/kg, iv), microinjection of bicuculline (10 pmol in 20nl) into the DMH caused increases in MAP (17±2 mmHg), HR (85±15 bpm) and RSNA (48±5% of baseline). Intravenous injection of 8-OH-DPAT (0.1 mg/kg) resulted in small decreases in resting MAP (~10 mmHg) and HR (~30 bpm) and had no effect on resting RSNA, but greatly reduced the increases in MAP, HR and RSNA evoked by DMH activation (to 20±12%, 18±3% and 9±5% of their respective increases before 8-OH-DPAT injection). Subsequent administration of the selective 5-HT_{1A} receptor antagonist, WAY-100635 completely reversed the cardiovascular effects of 8-OH-DPAT, restoring the DMH-evoked increases in MAP, HR and RSNA to those observed before 8-OH-DPAT administration. The results indicate that 5-HT_{1A} receptor have a critical role in mediating the cardiovascular response evoked from the DMH.

(1) Fontes, M.A. et al (2001) American Journal of Physiology, 280, H2891-H2901.
(2) Horiuchi, J. et al (2004) American Journal of Physiology, in press.
(3) Ootsuka, Y. and Blessing, W.W. (2003) Journal of Physiology, 552, 303-314.