Thyrotropin-Releasing Hormone–induced Hindquarter Vasodilation Is Mediated by β_2-Adrenoceptors

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Thyrotropin-releasing hormone (TRH) has been shown to increase mean arterial pressure (MAP), heart rate (HR), and cardiac index (CI) and induce hindquarter (HQ) skeletal muscle vasodilation and renal (R) and mesenteric (M) vasoconstriction when administered into the cerebroventricular space (i.c.v.) of conscious rats.[1] The mechanism of the vasodilator effect of TRH was examined in the present study.

Male Sprague-Dawley rats were anesthetized with ketamine-acepromazine and underwent surgery for either blood flow (BF) monitoring by the directional pulsed Doppler method or CI measurement with the thermodiluton technique. A guide cannula was also placed on the skull for i.c.v. injections, and PE-50 catheters were placed into the femoral vessels for recording of MAP and HR, as previously described.[1] The cardiovascular variables were continuously recorded in conscious rats.

TRH (8 nmol/kg i.c.v.) increased HQBF and decreased HQ vascular resistance (VR). These changes were accompanied by increments in MAP, HR, CI, RVR, and MVR. The HQ vasodilation by TRH was not altered by atropine, the β_1-selective adrenoceptor blocker, practolol, or the α-adrenoceptor antagonist, phentolamine, though practolol effectively blocked cardiac, and phentolamine the vasoconstrictor and pressor, effects of TRH (TABLES 1 and 2). The selective β_2-adrenoceptor blocker (ICI-118,551) completely blocked the increase in HQBF and decrease in HQVR without having any effect on the other cardiovascular responses to TRH (TABLE 1). Thus, catecholamines acting on the β_2-receptors rather than activation of cholinergic nerves or withdrawal of vasoconstrictor tone seem to account for the HQ vasodilation produced by TRH. A key role, however, for adrenal medulla in mediation of this effect is contradicted by our recent findings that adrenal demedullation (ADM-x) per se did not significantly reduce the TRH-induced vasodilation, although it was effectively blocked by further treatment of the ADM-x rats with the sympatholytic agent, bretylium.[1] Interestingly, vasodilation evoked by electrical stimulation of the preoptic regions has been argued to be mediated by epinephrine stored in the sympathetic nerves.[2] Our present data support this assumption and suggest that TRH in the brain induces HQ skeletal muscle vasodilation that is mediated by sympathetic adrenergic nerves.

TABLE 1. Effect of the Adrenoceptor Blockers Phentolamine (α-Blocker), Practolol (β_1-Blocker), and ICI-118,551 (β_2-Blocker) on Cardiovascular Responses to TRH in Conscious Rats[a]

	N	HQBF (percent)	HQVR (percent)	Change in MAP (mmHg)	CI (ml/min/kg)
TRH	20	+43 ± 6	−23 ± 3	+18 ± 2	+67 ± 15
TRH after Phenotolamine	6	+20 ± 5	−17 ± 2	+3 ± 4[b]	+113 ± 26
TRH after Practolol	7	+33 ± 7	−19 ± 7	+14 ± 4	−87 ± 57[b]
TRH after ICI-118,551	7	0 ± 5[b]	+19 ± 6[b]	+27 ± 4[b]	+43 ± 14

[a] Phentolamine (2 mg/kg), practolol (10 mg/kg), or ICI-118,551 (1–2 mg/kg) was injected intravenously 10–20 min before TRH (8 nmol/kg i.c.v.). Values (mean ± SEM) indicate maximum changes 2 min after TRH.

[b] $p < 0.01$ versus changes before blockers (Student-Newman-Keul test).

TABLE 2. Effect of Atropine on the Cardiovascular Responses to TRH in Conscious Rats[a]

	HQBF (percentage)	HQVR (percentage)	Change in MAP (mmHg)	HR (bpm[b])
Saline	+1 ± 1	−3 ± 3	0 ± 1	20 ± 4
TRH	+70 ± 17	−35 ± 7	+15 ± 4	+84 ± 18
TRH after Atropine	+40 ± 8	−24 ± 8	+13 ± 4	+40 ± 12[c]

[a] Atropine (2 mg/kg) was injected intravenously 20 min before TRH (8 nmol/kg i.c.v.). Values (mean ± SEM) indicate maximum changes 2 min after TRH. There were 6 rats in each group.

[b] bpm = beats/min.

[c] $p < 0.05$ versus TRH (Student-Newman-Keul test).

REFERENCES

1. SIRÉN, A.-L., C. R. LAKE & G. FEUERSTEIN. 1988. Hemodynamic and neural mechanisms of action of thyrotropin releasing hormone in the rat. Circ. Res. **62:** 139–154.
2. BERECEK, K. H. & M. J. BRODY. 1982. Evidence for a neurotransmitter role for epinephrine derived from the adrenal medulla. Am. J. Physiol. **242:** H593–H601.