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Editorial

Hypothalamo-hypophysial connection revisited

Almost exactly 50 years ago, G. W. Harris published four papers in the *Journal of Physiology* on the hypothalamo-hypophysial connection (1–4). Shortly before this, he and J.D. Green had studied the portal vessels around the pituitary (5). Although the hypothalamo-hypophysial portal vessels had been described still earlier by Popa & Fielding (6), for about 15 years it was not even certain whether the blood in these vessels flowed from the hypothalamus towards the pituitary, or the other way round (7). Now that Green & Harris (5) put that controversy at rest, several groups of workers remained occupied for a few decades in establishing the route, nature and identity of hypothalamic influences impinging on the pituitary. As is well established now, these influences form two distinct but incompletely divided systems. The first of these systems concerns the posterior pituitary. Posterior pituitary hormones are synthesized in the magnocellular neurons of the supraoptic and paraventricular nuclei of the hypothalamus, travel along the axons of these neurons in the hypothalamo-hypophysial tracts, and release their secretions in the posterior pituitary, from where they enter the general circulation. The second system concerns the anterior pituitary, which is influenced by the releasing and release-inhibiting hormones secreted by parvocellular neurons of the hypothalamus. The releasing and release-inhibiting hormones are secreted into the hypothalamo-hypophysial portal vessels, which in turn convey them to the anterior pituitary (7).

Besides the contributions of Harris, Ranson and Guillemin's groups, a few Indian contributions to the the early phases of the development of this story are also worth mentioning (8, 9). Some of the early studies make interesting reading. The mode of stimulation chosen by Harris (1–4) was ingenious. The electrode was connected to a coil (the 'secondary coil') which was buried in the rabbit's head under the skin. The primary coil was held close to the animal's head. This mode of stimulation, called the 'remote control method', had two advantages: first, it reduced the chances of infection travelling along the electrode; and second, it prevented the possibility of the electrode breaking during stimulation. How the possibility of neurovascular transmission from the hypothalamus to the anterior pituitary was deduced also makes interesting reading. It was found that stimulation of tuber cinereum induced ovulation in as short a period as 3 minutes, but

direct stimulation of the pituitary was ineffective. This suggested to Harris neurovascular transmission (2) employing the vessels which he and Green had studied (5). Anand and Dua (8) demonstrated the hypothalamic region which releases corticotropin releasing hormone by monitoring the eosinopenic response to adrenal corticosteroids, and Thomas and Anand (9) demonstrated the region which releases thyrotropin releasing hormone by monitoring ^{131}I turnover. Today when we cannot think of monitoring hormonal responses except through radioimmunoassay, learning about the knowledge that was generated by rather primitive techniques has a very salubrious effect. To update the story, in just 50 years, not only have five releasing hormones and three release-inhibiting hypothalamic hormones been identified and their molecular structure worked out, the genes coding them (10) and the receptors which mediate their action are also in the process of being characterized in detail (11). Impressive as these advances are, a conceptual revolution of far reaching importance which has resulted from recent work is the breakdown of barriers between the nervous system, endocrine system and now even the immune system (12–14). All these systems which have indispensable regulatory and protective functions are closely interlinked and employ many molecules in common. Synthesis holds a charm no less than analysis, specially to the Indian mind.

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