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S-1 Developmental Origin of the Hypothalamo-hypophyseal System in the Amphibian Embryo and its Relationships to the Olfactory Primordium

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One of the strategies to study the principles underlying the communication systems among different types of cells, such as sensory, neural and neuroendocrine cells is to elucidate the ontogenetic relationships among the functionally related cells. Amphibian embryo is a good material for an approach from this aspect. A series of experiments was performed using toad and newt embryos to determine the localization of the primordia of the hypothalamo-hypophyseal, as well as the olfactory systems. Small portions of the neural ridge and the neural plate taken from the wild-type embryos of *Bufo haponicus* neurulae were transplanted to the corresponding sites of the albino embryos at the same developmental stage. The melanin granules contained in the wild-type cells in the graft served as a visible cell marker which can be detected easily under the light and electron microscope, allowing to trace the developmental fate of the graft. First, the developmental fate of the neural ridge was determined. The outermost layer(ectodermal) of the anterior part of the neural ridge(ANR) was found to be the anlage of the upper lip. The middle layer(also ectodermal) of the same region developed into the pars distalis, pars intermedia and pars tuberalis of the adenohypophysis. This region was confirmed to be the almost exclusive source of the secretory cells in the adenohypophysis by immunohistochemical staining of the pituitary hormones. Thus the epidermal hypophysis is neurectodermal in origin rather than stomodeal as described in the classical literature. The primordium of the posterior hypothalamus (infundibulum and medial eminence) was located in the central portion of the anterior neural plate just behind the ANR. A part of the ANR was also incorporated into the neural tissue in the preoptic region of the hypothalamus. These results indicate that the primordial cells of the adenohypophysis and the presumptive hypothalamic neurons, the latter regulating the former, are in a close topographical relationship from the primary stage of histogenesis. In fact, they are not only related topographically at the embryonic stage, but are functionally related during the developmental process. If the primordium of the posterior hypothalamus is removed from the open neurulae, the infundibulum was not formed and the epithelial pituitary gland developed away from the normal position without contact with the posterior hypothalamus. In these cases, the pituitary POMC cells(MSH and ACTH cells) were not detectable by immunohistochemistry, indication that the contact between the pituitary primordium and the hypothalamus is essentical for these cells to develop. More caudo-lateral portions of the NR were found to be the anlagen of the olfactory placodes, including the olfactory receptor cells. It was noteworthy that the same group of cells developed into the olfactory bulbs and the anteriormost part of the olfactory lobes.

These results indicated that the anlagen of both central and peripheral parts of each of the hypothalamo-hypophyseal system and the olfactory system constitute a closely affiliated cell population at the open neurula stage, suggesting that they are clonally related. This leads to the hypophesis that the establishment of the periphero-central organization in these two systems reflect possible clonal relationships of the constituent cells. Moreover, the fact that the primordia of the adenohypophysis and the olfactory placodes are closely affiliated support the view that, from an evolutionally viewpoint, the adenohypophysis was originally a chemosensory part of the olfactory system. Recently, it has been suggested by mainly descriptive works on mammalian and avian embryos that the primordial cells of the GnRH neurons in the anterior hypothalamus originate in the olfactory placodes and migrate to the hypothalamus before maturation. An experimental approach to this hypothesis was performed by our groups using newt embryos. In these studies, unilateral ablation of the olfactory placode was carried out on the tail-bud embryos of the *Cynops pyrrhogaster*, resulting in a loss of GnRH neurons uniquely on the operated side of the hypothlamus. On the unoperated side of the embryos, immunoreactive GnRH cells were located at first in the olfactory placodes, then along the tracts of the olfactory or terminal nerves, finally in the anterior hypothalamus. Bilateral removal of the olfactory placodes resulted in a total loss of the GnRH neurons from both sides of the hypothalamus. From these results it was concluded that the prospective GnRH neurons in the newt hypothalamus have their exclusive origin in the olfactory placodes and then migrate along the olfactory or terminal nerves before settling themselves in the final position in the anterior hypothalamus. This and the above-mentioned discussion developed from works on toad embryos indicate that the primordial cells of the hypothalamo-hypophyseal system as well as the central and the peripheral parts of the olfactory system are supplied from the common sources in the anterior and the antero-lateral parts of neural ridge.