THE VISCERAL NEURAXIS IN THIRST AND RENAL FUNCTION

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INTRODUCTION

Truisms are, of course, self evident. In spite of their obviousness we need to reconsider some in order to appreciate understanding that we take for granted and to remind ourselves of the value of particular approaches we use in our research on brain function. It seems evident to me that understanding behavior and higher order brain function reduces to knowing the rules governing the flow of information in neural networks. Biochemical, molecular, cellular and pharmacological events affect brain function by rising to modulate this flow of information in neural circuits. Given these axioms it is, therefore, important to learn the organization of the brain's neural networks.

In the last decade there has been tremendous progress in identifying elements of the neurocircuity which modulate visceral function. The advance is due to the improvement in neuroanatomical methodology which is now sensitive enough to follow the projections of the finest diameter axonal fibers over long distances both anterogradely and retrogradely. One of the major observations emerging from the new data is that there are long, and much more direct connections than previously known relaying sensory information up to the hypothalamus, limbic structures and the cortex from visceral organs. This is reciprocated by newly discovered long and direct connections from cortex, limbic structures and hypothalamus to the brainstem visceral relay nuclei and motor output nuclei of the autonomic nervous system. The network modulates the autonomic nervous system.
Some elements of this network also have strong connections with both the posterior and anterior pituitary gland which brings modulation of endocrine function within its domain. A neurocircuitry encompassing both the autonomic nervous system and the pituitary gland enables the broad function of homeostasis.

Behavior is of great importance in the goals of homeostatic and visceral function. Not surprisingly, the neurocircuitry modulating endocrine and ANS function also relates to regions of the hypothalamus traditionally implicated in the control of ingestive behavior. These areas include the preoptic region and the lateral hypothalamus.

Another important finding emerging from recent neuroanatomical studies is the realization that the circumventricular organs of the brain are likely sites for the central receptors to physiological parameters so long hypothesized to play a role in the behavioral and physiological controls of homeostasis. This is reinforced by the fact that they have neural projections to elements of the network of neural circuitry referred to above which modulates the pituitary gland and the autonomic nervous system. In the remainder of this review I will discuss the neurocircuitry of the two circumventricular organs (CVO) which have a prominent connectivity with other brain structures and a third CVO which is part of the anteroventral third ventricular (AV3V) area of the preoptic region. All are implicated in thirst and renal function. It is this circuitry and those elements which modulate endocrine, autonomic and perhaps behavioral function which I refer to as the visceral neuraxis.

CIRCUMVENTRICULAR ORGANS

Circumventricular organs (CVOs) are small midline structures lying at strategic positions on the surface of the cerebral ventricles. See figure 1. They interface subarachnoid, ventricular and vascular spaces. The capillary density is extremely high and there is a fenestrated endothelial lining to the capillaries indicating a lack of the blood brain barrier in CVOs. This feature suggests that they could be sites of central receptors particularly for circulating factors that are excluded from the brain by the blood brain barrier. To fulfill this role there would have to be neuronal elements and neural projections to other structures of the brain in order to transfer the information. Indeed, two CVOs meet this requirement quite well. The subfornical organ (SFO) and the area postrema (AP) have many neuronal elements and both have profound efferent projections to very specific sites within the brain. They project heavily to particular components of the visceral neuraxis.