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Expression of ZO1, vimentin, pan-cadherin and AGTR1 in tanycyte-like cells of the sulcus medianus organum

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ABSTRACT

Tanycytes are a specialized ependymal lining of brain ventricles with exceptional features of having long basal processes and junctional complexes between cell bodies. These tanycytes are present at the regions of circumventricular organs (CVOs) which possess common morphological and functional features enabling them to be described as the brain windows where the barrier systems have special properties. Previous studies detailed seven of these CVOs but little information is available regarding another putative site at the rostral part of the median sulcus of the 4th ventricle, or the sulcus medianus organum (SMO). Here we performed a pilot immunohistochemical study to support earlier observations suggesting the SMO as a novel CVO. We labeled rat brain with ZO1, vimentin, pan-cadherin and angiotensin II type 1 receptors markers which showed a morphologically distinct population of cells at the region of the SMO similar to tanycytes present in the median eminence, a known CVO. These cells had basal processes reaching the deeply seated blood vessels while the caudal part of the median sulcus did not show similar long cellular extensions. We concluded that tanycyte-like cells are present in the SMO in a pattern resembling that of other CVOs where the strategic location of the SMO is probably for signal integration between brainstem nuclei and the rostrally located neuronal centers.

1. Introduction

Circumventricular organs (CVOs), refer to small structures bordering the ventricular spaces in the midline of the brain which share common morphological and endocrine-like characteristics that distinguish them from the rest of the nervous system. These specialized areas are points of communication between the blood, the brain parenchyma, and the CSF [1]. Among their unique features are cellular contacts with two fluid phases (blood and cerebrospinal fluid) and neural connections with strategic brain nuclei establishing circuitry for communications throughout the neuraxis [2]. Most of them develop in close apposition to rich, fenestrated capillary networks. They share a common ontogeny, being differentiated from and remaining within the ependymal layer of the neural tube [3]. Topographically, they are found in the midline either in the recesses or they cover the commissures within the ventricular system. CVOs are characterized by their extensive vasculature and lack of the usual blood brain barrier (BBB) [4]. There are seven known CVOs, namely, the median eminence (ME) [5], neurohypophysis, vascular organ of the lamina terminalis, subfornical organ, pineal gland, subcommissural organ and area postrema (AP) [6].

The BBB is present throughout the central nervous system except for the CVOs located around the third and fourth cerebral ventricles, in addition to the choroid plexuses. Thus, CVOs are in persistent contact with signaling molecules circulating in the bloodstream. Neurons at the CVOs have a variety of receptors for hormones and other signaling molecules, and they have extensive connections to hypothalamic and brainstem nuclei. Therefore, lying at the blood–brain interface, the sensory CVOs are in a unique position of being able to detect and integrate humoral and neural

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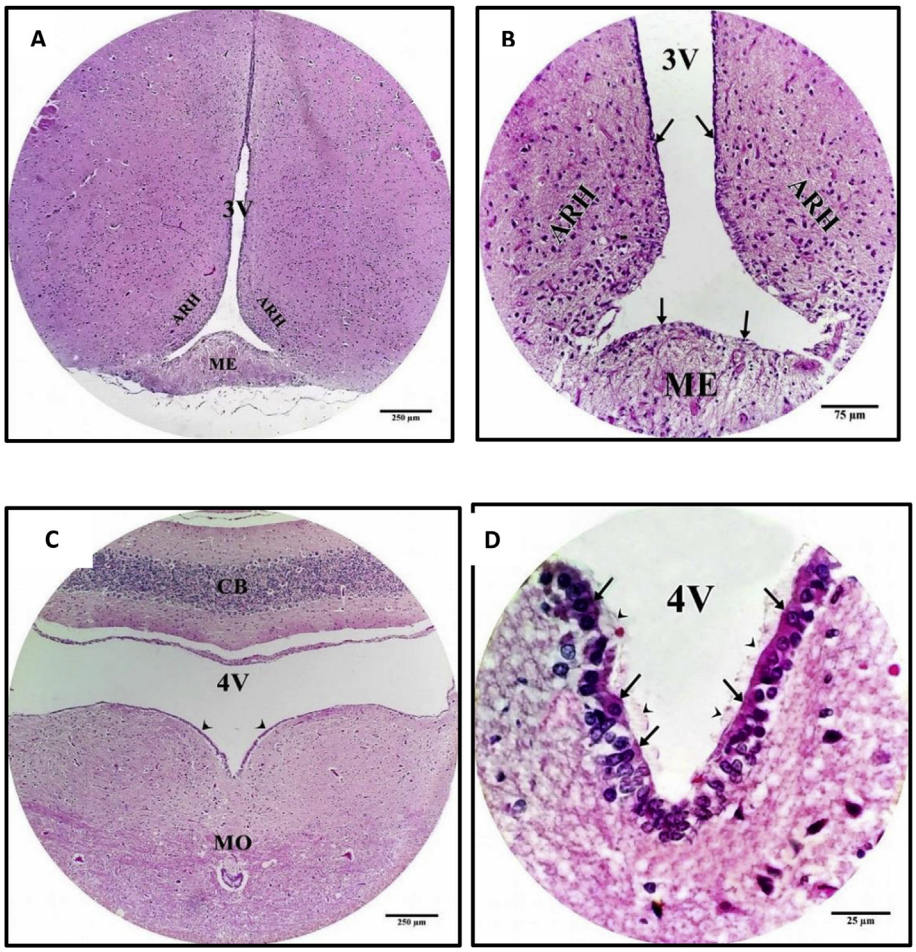

Fig. 1. A & B Coronal sections of rat brain at the region of ME. Ependymal lining of 3rd ventricle consists of a single layer of cuboidal or columnar cells (arrows). H. & E. stain. (A) 100X. (B) 400X. 3 V: 3rd ventricle. ME: median eminence. ARH: arcuate hypothalamic nucleus.
C & D. Coronal sections of rat brainstem at the region of SMO. Ependymal lining of 4th ventricle consists of a single layer of cuboidal or columnar cells (arrow heads in C) except at the deepest part of the median sulcus of the SMO (arrows in D) where they are arranged in 2–3 layers. These cells ciliated (arrow heads in D). H. & E. stain. (C) 100X. (D) 1250X. 4 V: 4th ventricle. CB: cerebellum. MO: medulla oblongata.

information and relay the resulting signals to autonomic control centers of the hypothalamus and medulla [7]. They have a proven role in the control of cardiovascular function and body fluid regulation, and have significant involvement in central immune response, feeding behavior and reproduction [8]. In that aspect, tanycytes, a unique cell population present in the lining of the third and fourth ventricles, may bridge the gap between the central nervous system via cerebrospinal fluid (CSF) to the portal blood. This may also link the CSF to neuroendocrine events [9,10]. These tanycytes are highly specialized ependymoglial cells that form a blood–CSF barrier at the level of the CVOs; such a barrier has well documented properties through the presence of tight junctions at the ventricular pole of tanycytes [11].

Tanycytes, which are considered as specialized ependymal cells (ECs) connected by tight junctions, form a complex network that seal the CNS from the CVOs, creating a distinct blood–CSF barrier. This barrier is detected in the floor and walls of the third ventricle [9,10,12] as well as in the floor of the fourth ventricle [4].

At present, few studies explored whether the rostral part of the median sulcus of the fourth ventricle or the sulcus medianus organum (SMO) is another CVO. The ependymal epithelium of this region is pseudostratified; the cells possess narrow necks and long basal processes that either reach deep into the neuropil or end adjacent to blood vessels. The apical surface of these ependyma has microvilli but only a few cilial clumps are present where supraependymal cells are commonly seen. A characteristic feature of this region is the presence of tight junctions just beneath the apical surface of the cells [4]. In another study, tanycyte shafts in the midline floor of the fourth ventricle were suggested to transduce fourth ventricular CSF-borne influences to neurons of the midline medullary raphe bundle through communication channels [13]. Investigations done with electron microscope showed pinocytotic vesicles between the microvilli on the cell surface with complex interdigitations on the lateral walls of ECs including electron-dense desmosomes and tight junctions. Numerous free cytoplasmic ribosomes are present in each cell which possesses a thin basal process that has desmosome-like contacts with other cell processes [4,14].

This study aims for investigating the possible localization of tanycyte-like cells in the floor of the fourth ventricle through the identification of the morphological and structural features of specialized ECs at the region of the SMO.

2. Materials and methods

2.1. Sample collection and tissue preparation

Ten adult male Sprague Dawley rats (*Rattus norvegicus albinus*), aged 3 months with body weight of 250–350 g from the Cambridge

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