Glial Activities at the Circumventricular Organs in Blood-Brain Connection

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Abstract

All of the body's tissues and organs depend on blood arteries to carry oxygen and nutrients to them. The blood-brain barrier, a special property of the blood arteries that vascularize the Central Nervous System (CNS), enables these vessels to tightly control the transit of ions, chemicals, and cells between the blood and the brain. Correct neuronal function is enabled by the careful regulation of CNS homeostasis, which also safeguards neural tissue from toxins and infections. Alterations to these barrier qualities play a significant role in the pathophysiology and development of many neurological illnesses. The Endothelial Cells (ECs), which make up the blood vessel walls, have a variety of physical, transport, and metabolic characteristics that help to coordinate the physiological barrier.

Keywords: Physiological barrier

Introduction

The Blood-Brain Barrier (BBB) is absent in the Circumventricular Organs (CVOs), which surround the cerebral ventricles and perceive chemicals originating from blood. This study highlights current developments about the significance of CVO activities, particularly how glial cells transmit signals of inflammation from the periphery to the brain. The CVOs exhibit size-limited vascular permeability, enabling molecules with molecular weights under 10,000 to pass through. This proves that blood-derived chemicals cannot freely enter the CVO parenchyma despite the absence of an endothelial cell barrier.

At the distal CVO subdivision, astrocytes and tanycytes form a thick barrier that prevents blood-derived chemicals from freely diffusing into nearby brain areas. By transcytosis, tanycytes in the CVOs facilitate communication between the brain parenchyma and cerebrospinal fluid. The CVOs' microglia and macrophages are crucial for using toll-like receptor 2 to relay peripheral information to other brain areas (TLR2). TLR2-dependent inflammatory responses are eliminated when TLR2 signaling is inhibited or when microglia and macrophage numbers are reduced in the brain. In contrast to TLR2, astrocytes and tanycytes in the brain's CVOs are essential for starting TLR4-mediated inflammatory reactions brought on by Lipopolysaccharide (LPS). Depletion of macrophages and microglia intensifies the fever and chronic illness responses brought on by LPS.

Even under physiologically normal circumstances, the CVOs' microglia and macrophages are always active because they have an activated morphology and express the M1/M2 marker proteins. In addition, low-dose LPS administration causes microglial proliferation in a number of areas, including the hypothalamus, medulla oblongata, and telencephalon, with a noticeable increase in the CVOs; after high-dose LPS administration, proliferation is seen in the majority of brain regions, with the exception of the cerebral cortex and hippocampus. During LPS-induced inflammation, a temporary rise in the microglial population is advantageous for reducing the body's immune response. When exposed to a warm environment that is less than 37°C, the transient receptor potential receptor vanilloid 1, which is expressed in the astrocytes and tanycytes of the CVOs, regulates body temperature. As an alternative, Nax was expressed in the CVOs' astrocytes and tanycytes.

The discovery that intravenous dye injection may reach all organs except the brain but not the Blood-Brain Barrier (BBB) was made more than a century ago. The BBB is made up of a highly specialized brain endothelial cellular layer that keeps the brain's homeostasis by forming adherent junctions and separating it from circulating blood. The BBB does not block blood-to-brain communication because it allows the interchange of chemicals including peptides, proteins, vitamins, hormones, amino acids, nucleotides, fatty acids, and other substances via transporters and transcytosis.

The Circumventricular Organs (CVOs), which surround the brain ventricles and are devoid of the Blood-Brain Barrier (BBB), are able to sense blood-derived molecules and release neuropeptides produced in the brain into circulation. As a result, the CVOs are known as the "windows of the brain". The lamina terminalis' Organum Vasculosum (OVLT), the Subfornical Organ (SFO), the Median Eminence (ME), the Area Postrema (AP), the Neurohypophysis (NH), the pineal gland, and the choroid plexus make up the CVOs. Based on their basic function, the CVOs are split into two groups: secretory and sensory.

The OVLT, SFO, and AP are examples of sensory CVOs, and they use a variety of receptors to track ions, osmolality, pH, lipophobic amino acids, and neuropeptides in blood circulation. In order to regulate inflammation as well as bodily fluid and temperature balance, they also integrate and transport information from the blood to nearby brain areas. The ME, NH, and pineal glands, which make up the secretory CVOs, produce melatonin among other neuropeptides. In some areas of the ventricles, the innermost layer of the meninges creates vascularized invaginations known as choroid plexus, which generate CSF. The secretory CVOs' specific roles are described in depth in our prior review.

The Median Preoptic Region (MnPO), which regulates osmoregulation, thermoregulation, and sleep homeostasis, receives thermal and osmotic signals from the OVLT and SFO. The supraoptic and paraventricular nuclei, which are the autonomic center, oxytocin, and vasopressin-producing areas, are also locations that the OVLT and SFO project to.