AREA POSTREMA

Authored by

mohammad looti

November 11, 2025

AREA POSTREMA

Primary Disciplinary Field(s): Neurobiology, Anatomy, Physiology, Pharmacology

1. Core Definition

The **Area Postrema** (AP) is a specialized paired structure of the central nervous system located within the caudal region of the medulla oblongata, situated on the basal wall of the lateral ventricle, specifically near the obex of the fourth ventricle. Functionally, the Area Postrema is classified as a circumventricular organ (CVO), a group of specialized structures characterized by their strategic positioning adjacent to the third and fourth ventricles. Unlike most areas of the brain, the AP lacks a fully intact blood-brain barrier, making it uniquely sensitive to chemical changes and circulating substances in the blood plasma.

This structural anomaly--the highly permeable nature of its capillary network--is central to its primary physiological role. It allows the AP to act as the primary **chemoreceptor trigger zone** (CTZ). The CTZ serves as a critical biological defense mechanism, constantly monitoring the systemic circulation for toxins, drugs, or other noxious substances. When these harmful agents are detected, the Area Postrema initiates the complex neural cascade necessary to elicit the protective physiological response known as emesis, or vomiting.

Because it is highly vascularized and directly exposed to the systemic circulation, the AP provides the brain with a vital sentinel post. It bypasses the protection typically afforded by the blood-brain barrier, ensuring immediate detection of circulating toxins that could otherwise damage sensitive neural tissue or indicate poisoning. This rapid detection capability underscores the critical importance of the Area Postrema in maintaining systemic homeostasis and protecting the organism from acute toxic threats.

2. Anatomical Location and Structure

Anatomically, the Area Postrema is situated symmetrically on either side of the midline adjacent to the caudal extent of the fourth ventricle, surrounding the opening known as the obex. It appears as a small, paired nodule of highly specialized neural tissue. Its location places it in close proximity to other vital brainstem nuclei, including the Nucleus Tractus Solitarii (NTS), which is the definitive brainstem center for coordinating the motor components of the vomiting reflex.

Histologically, the AP is distinct from surrounding medullary tissue. It possesses an unusually dense network of fenestrated capillaries. While typical brain capillaries are characterized by tight junctions between endothelial cells that form the restrictive blood-brain barrier, the capillaries within the Area Postrema contain small pores or fenestrations. These fenestrations allow for the easy passage of large molecules and substances, including toxins and certain neuropharmacological

agents, from the blood directly into the interstitial fluid surrounding the AP's chemosensory neurons.

The cellular composition of the AP includes specialized neurons and glial cells, particularly tanycytes, which are thought to play a role in regulating the movement of substances between the cerebrospinal fluid and the blood. The dense distribution of various neurotransmitter receptors--such as Dopamine D2, Serotonin 5-HT3, Opioid, and Acetylcholine receptors--on the surface of AP neurons allows this region to respond to a wide variety of circulating chemical signals that might indicate sickness or poisoning.

3. Role in the Blood-Brain Barrier and Circumventricular Organs

The concept of the Area Postrema being a "weak point" in the blood-brain barrier is fundamental to its function. The **blood-brain barrier** (BBB) normally functions as a highly selective semipermeable membrane that separates circulating blood from the brain extracellular fluid, strictly regulating the passage of ions, molecules, and cells to maintain the delicate neural environment. However, this protective mechanism is counterproductive when the brain needs to monitor the blood's chemical composition directly.

The Area Postrema belongs to the class of structures known as **Circumventricular Organs** (CVOs), which share the common characteristic of lacking a conventional BBB. CVOs are strategically located around the ventricles and act as sensory or secretory centers. Sensory CVOs, like the AP, are designed to sample the blood to detect changes in osmolality (Subfornical Organ), hormone levels (Organum Vasculosum of the Lamina Terminalis), or, in the case of the AP, the presence of circulating toxins.

The structural compromise of the BBB in the AP enables it to effectively "taste" the blood. This allows molecules that are typically excluded from the brain--such as certain chemotherapy drugs, endogenous toxins produced during illness (e.g., uremia), or ingested poisons--to bind directly to the specialized chemoreceptors located within the AP tissue. This direct binding initiates the neural signaling required to activate the central vomiting network, ensuring that the body attempts to expel the noxious substance rapidly.

4. Function as the Chemoreceptor Trigger Zone (CTZ)

The most critical function of the Area Postrema is its role as the **Chemoreceptor Trigger Zone** (CTZ). The CTZ is not the vomiting center itself, but rather the sensory interface that detects toxins and relays this information to the actual central pattern generator for vomiting, located primarily within the adjacent Nucleus Tractus Solitarii (NTS) and reticular formation.

The activation of the CTZ occurs when circulating emetogenic substances bind to the high

concentration of specific receptors present in the AP. Key receptors implicated in CTZ activation include the D2 dopamine receptors, targeted by drugs like apomorphine; the 5-HT3 serotonin receptors, which are particularly relevant in chemotherapy-induced nausea and vomiting (CINV); and various opioid receptors. The binding of toxins to these receptors generates action potentials within the AP neurons.

These neural signals are then rapidly transmitted via projections to the NTS, vagal afferents, and other brainstem nuclei that collectively form the central vomiting center. The NTS then coordinates the highly complex motor sequence required for emesis, involving involuntary actions across the digestive tract, diaphragm, abdominal muscles, and larynx. Thus, the Area Postrema acts as the essential gatekeeper, translating systemic chemical warnings into a protective neurological command.

5. Clinical Significance and Pharmacology

The understanding of the Area Postrema's function as the CTZ holds immense **clinical significance**, particularly in the fields of toxicology and oncology. Many clinical conditions, including gastroenteritis, uremia, radiation sickness, and particularly the side effects of cancer chemotherapy, rely on the activation of the AP to trigger nausea and vomiting.

Pharmacological research has heavily focused on developing antiemetic drugs that target the specific receptors concentrated within the Area Postrema. For instance, the development of **5-HT3 receptor antagonists**, such as ondansetron and granisetron, revolutionized the management of CINV. These drugs work by blocking the binding of serotonin, released from damaged gastrointestinal cells, to the 5-HT3 receptors in the AP, thereby preventing the initiation of the emetic reflex centrally.

Similarly, dopamine antagonists, such as metoclopramide, exert their antiemetic effects by blocking D2 receptors in the Area Postrema. By selectively interfering with the signaling pathways within the AP, clinicians can effectively manage debilitating symptoms of nausea and vomiting without necessarily addressing the underlying systemic cause, providing critical symptomatic relief for patients undergoing difficult medical treatments. The AP's role therefore defines a major therapeutic target in modern medicine.

Further Reading

Area Postrema (Wikipedia)
Blood-brain barrier (Wikipedia)
Circumventricular Organs (Wikipedia)
Nucleus Tractus Solitarii (Wikipedia)

Medulla Oblongata (Wikipedia)