

CROSSING THE SUBTLE BARRIER: AN AYURVEDIC INTERPRETATIVE FRAMEWORK FOR BRAIN TRANSPORT AND THE BLOOD - BRAIN BARRIER

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Abstract:

The blood–brain barrier (BBB) is a highly selective component of the neurovascular unit that regulates the movement of substances between the systemic circulation and the central nervous system. Contemporary strategies for brain delivery include passive diffusion, carrier-mediated transport, receptor-mediated transcytosis, nanoparticle-based approaches, and intranasal delivery. Ayurveda describes nourishment, distribution, and movement within the body through concepts such as *Doshas*, *Srotas*, *Agni*, and *Nyayas* including *Kedara-Kulya* and *Khale-Kapota*.

This narrative, integrative review examines these classical concepts alongside contemporary understanding of BBB structure and transport mechanisms, with the aim of developing a cautious interdisciplinary interpretative framework. Classical Ayurvedic sources and selected scientific literature were examined to identify conceptual correspondences, evidence gaps, and potential areas for future research.

The review distinguishes classical descriptions from modern interpretations and hypothesis-generating analogies. *Srotas* may be considered a functional concept related to movement and distribution, while comparisons with specific vascular structures, cellular components, molecular dimensions, or membrane transport mechanisms remain interpretative rather than established equivalences. Similarly, the lipid-rich nature of *Ghrita* and the absorption of lipid-associated phytoconstituents may influence formulation-dependent solubilization, systemic absorption, and pharmacokinetics; however, these properties alone do not demonstrate BBB penetration or central nervous system exposure. *Nasya* may be interpreted in relation to contemporary intranasal drug-delivery pathways, whereas proposed mechanisms of *Sirodhara* involving central neurophysiological effects require further investigation. Thus, this framework identifies testable points of correspondence without claiming direct equivalence between Ayurvedic concepts and modern BBB mechanisms.

Key words: Transport, *Srotas*, Blood Brain Barrier, *Ghrita*, *Nyaya*

Introduction

The brain requires a tightly regulated nutrient supply to sustain cognition and homeostasis. Essential nutrients are delivered to the brain by selective transport mechanisms, such as glucose transporters and amino acid transporters.^[1,2] Although most drugs enter by passive diffusion based on lipophilicity and molecular properties, some utilize endogenous transporters, where competition may reduce transfer efficiency. Nutrient exchange at the capillary wall is mediated through the blood–brain barrier (BBB), and blood – CSF barriers which maintains cerebral homeostasis and function.^[3] Ayurveda describes brain nourishment through metabolic transformation by *Jatharagni*, *Bhutagni*, and *Dhatwagni*, followed by distribution via *Srotas* and principles such as *Kedara Kulya* and *Khale Kapotha Nyayas*.

Methods

Primary Ayurvedic sources were drawn from the *Brihatrayis*—Charaka Samhitha, Susrutha Samhitha, and Ashtanga Hridaya—with emphasis on *Srotas*, *Agni*, *Doshas*, and principles of nourishment and distribution.

Standard interpretations of commentators were cited in the manuscript where they were relevant. Contemporary scientific literature was identified from PubMed, Google Scholar, and Scopus using combinations of terms including “blood-brain barrier,” “brain transport,” “carrier-mediated transport,” “receptor-mediated transcytosis,” “lipid-based drug delivery,” “intranasal delivery,” “*Srotas*,” “*Agni*,” and “*Dosha*.” Peer-reviewed literature in English published between January 2000 and January 2026 was considered, together with the cited classical sources.

The evidence was synthesized thematically. The themes were: (1) contemporary BBB structure and transport; (2) Ayurvedic concepts of *Srotas*, *Agni*, *Vayu*, *Doṣhas*, and *Nyayas*; (3) possible interpretative relationships between these concepts and modern physiology; and (4) formulation- and procedure-related hypotheses concerning *Ghrita*, *Nasya*, and *Sirodhara*. Claims were therefore framed according to the available level of evidence, with established modern mechanisms distinguished from conceptual analogies and hypotheses.

Results & discussion:

Ayurveda describes the movement, transformation, distribution and utilization of substances through several interconnected physiological concepts. Among these, *Srotas*, *Agni*, *Doṣhas*, *Dhatus* and the principles of *Dhathu poshana* provide a framework for understanding the movement of nutrients and other substances within the body. In the present review, these concepts are considered in relation to contemporary understanding of physiological transport and the blood–brain barrier (BBB). The proposed relationships are interpreted as conceptual parallels rather than direct equivalences.

1. *Srotas* as a Classical Framework for Movement and Distribution

Acharya Charaka describes the body as consisting of innumerable minute components referred to as *Paramanus*.^[4] The body has also been described as an aggregation of innumerable *Srotamsi*, which are pathways involved in the movement, transformation, and distribution of substances and physiological functions. Similarly, references to *Anu srotas* have been interpreted in relation to minute structural or functional components.^[5] Although these concepts cannot be directly correlated with cells or brain cells, they may be considered conceptually parallel to the contemporary understanding of microscopic functional units, emphasizing the minute organization underlying bodily structure and function.

Acharya Charaka, while describing *Vata Karmas*, mentions briefly *Sthula* and *Anu Srotas*, representing gross and subtle levels of organization.^[6] *Sthula Srotas* may be considered to be carrying *Poshya* or *Sthayi Dhathu*, while *Anu Srotas* facilitates the distribution of *Poshaka* or *Asthayi Dhathu* for tissue nourishment. Through successive levels of *Srotas*, these nutritive components may ultimately reach tissues including the brain. The *Sajatiya nature of the nutrients*, interpreted along with *Samanya Vishesha Siddhantha*, suggests that substances with similar properties or structural nature may be preferentially assimilated and utilized by a tissue. This provides a conceptual basis for discussing the selective availability of nutritive components to neural tissue, without equating these Ayurvedic concepts with the molecular mechanisms of BBB transport.

Anu Srotas is described as innumerable, whereas *Sthula Srotas* are countable and include *Bahirmukha* and *Antarmukha Srotas*.^[7] The *Antarmukha Srotas* are described as 13 by Acharya Charaka and 11 pairs by Acharya Sushruta.

These 13 *Srotas* can be broadly reclassified based on their physiological functions^[8]:

1. *Srotas* carrying Nutrients: *Pranavaha*, *Udakavaha*, *Annavaha*
2. Transformative *Srotas* (*Sapta Dhatusvaha*): *Rasavaha* to *Shukravaha*, aiding in nutrient transport and tissue transformation
3. *Srotas* carrying out Excretory function: *Mutravaha*, *Purishavaha*, *Swedavaha*

2. Contemporary Understanding of BBB Transport

BBB permeability is generally favoured for small, sufficiently lipophilic molecules, although molecular size, polarity, ionization, hydrogen-bonding capacity, and transporter interactions collectively influence CNS penetration^[9]

The BBB is a multicellular interface within the neurovascular unit (NVU), rather than a single membrane or cell. Its core barrier is formed by specialized brain microvascular endothelial cells joined by tight junctions, while pericytes, astrocytic end-feet, the basement membrane, and associated intercellular signalling mechanisms contribute to the formation, maintenance, and regulation of BBB function.^[10]

BBB transport therefore operates through several coordinated pathways^[11,12] :

- Paracellular movement is strongly restricted by endothelial tight junctions, particularly for hydrophilic solutes.
- Passive transcellular diffusion permits movement of some small, sufficiently lipophilic substances, but permeability depends on multiple physicochemical properties rather than a single molecular-weight threshold.
- Carrier-mediated transport enables the regulated entry of endogenous substrates such as glucose and selected amino acids.
- Receptor-mediated transcytosis can transport selected macromolecules through ligand–receptor interactions, whereas adsorptive-mediated transcytosis depends on electrostatic interactions.
- Efflux transporters, including P-glycoprotein and other ATP-binding cassette transporters, can limit brain exposure to endogenous compounds and xenobiotics, including some drugs.

Consequently, BBB passage should be described as a regulated and substance-specific process. The presence of lipid solubility, low molecular weight, or a particular charge may influence permeability, but none of these properties alone establishes BBB penetration or therapeutic brain delivery.

3. Functions of BBB:

- Maintains the biochemical environment required for neuronal function and cerebral homeostasis.
- Restricts entry of potentially harmful substances and many xenobiotics.
- Regulates the entry of essential nutrients through selective transport systems.
- Contributes to the controlled removal of substances through efflux systems.
- Participates in neurovascular and immune signalling as part of the broader neurovascular unit.^[11]

4. Interpretative Correlation of Cellular Domains with Ayurvedic Concepts

Cellular domains may be correlated with selected Ayurvedic anatomical and physiological concepts as follows:^[13]

Table No.1: Interpretative correlation of Cellular Structure in Ayurveda

Cellular domain	Ayurvedic interpretative association	Functional interpretation
Nucleus	<i>Vata</i>	Regulation and coordination
Cytoplasm (cell organelles)	<i>Pitta</i>	Transformation and metabolic activity
Cell membrane	<i>Kapha</i>	Structure, stability and protection

The dominance of the *Pancha mahabhutas* aligns accordingly, with *Parthiva* and *Apya dravya* dominating structural components that exhibit Murti bhava, such as the cell wall.^[13]

The cellular organization described in Ayurvedic anatomy, comprising central, middle, and peripheral zones, may be interpreted in relation to the structural and functional organization of the blood–brain barrier (BBB). The central zone, represented by the nucleus, may be considered *Vata*-predominant in view of its regulatory functions. This finds a functional parallel in the regulatory role of BBB endothelial cells, which control transport and signalling through regulated expression of membrane transporters, tight-junction proteins, and receptors.^[14] The middle zone, comprising the cytoplasm and its organelles, may be interpreted as *Pitta*-predominant owing to its role in transformation and metabolism. This may be considered alongside the metabolic, enzymatic, and transport activities occurring within BBB endothelial cells that contribute to its selective permeability. The outer zone, represented by the cell membrane, may be viewed in relation to *Kapha* owing to its structural, cohesive, and protective attributes, providing a functional parallel with the barrier-forming properties of endothelial tight junctions and the basal lamina.

The predominance of *Parthiva* and *Apya Mahabhutas* further provides an Ayurvedic basis for interpreting these structural characteristics. The *Guru*, *Kathina*, *Sandra*, and *Sthira* attributes of *Parthiva Dravya* described by Vagbhata may be considered in relation to the stability, compactness, and restrictive nature of the BBB. Conversely, the *Drava*, *Snigdha*, and *Picchila* attributes of *Apya Dravya* may be interpreted in relation to fluidity, cohesion, and nourishment within the cellular and perivascular environment.^[13,14] In this

context, the structural attributes of the BBB and its role in maintaining a selectively regulated interface may be understood through the complementary functional principles of stability, cohesion, regulation, and transformation described in Ayurveda.

5. *Bhutagni* and the Concept of Transformation

For nutrients to effectively reach the brain, they must be transformed into forms that permit cerebral entry. This transformative process underscores the relevance of *Bhutagni*, described by Acharya Charaka as the metabolic force that converts ingested food of external origin (*Vijatiya*) into substances compatible with bodily tissues (*Sajatiya*), through the orchestrated action of *Bhutagnis* such as *Parthivagni* and *Apyagni*.^[15] A broad conceptual comparison can therefore be made with the modern recognition that digestion, metabolism, absorption, and biotransformation alter the physicochemical form and disposition of nutrients and xenobiotics.

6. *Doshas* in the Context of Brain Nourishment

Classical descriptions attribute important roles in movement, circulation, respiration, and nourishment to different forms of *Vayu* and to *Tarpaka Kapha*.^[16] *Prana Vayu* may be interpreted functionally in relation to respiration and processes supporting intake, while *Vyana Vayu* may be discussed in relation to systemic distribution and circulation. *Tarpaka Kapha* is described in relation to the head and nourishment of the nervous system.

Prana Vayu plays a pivotal role in systemic nutrition by facilitating the transport of respiratory gases essential for cellular metabolism. It also helps in deglutition, which essentially aids in nutrient transport.^[17] In contrast, *Vyana Vayu* governs the circulatory dynamics throughout the body, including the brain, by ensuring effective *rasa* distribution (*rasa samvahana*) to peripheral and central tissues. *Tarpaka Kapha* is described in relation to the head and nourishment of nervous tissues; its functional attributes may therefore be discussed alongside the nutritive and homeostatic roles attributed to CSF.^[17]

7. *Kedāra-Kūlya* and *Khale-Kapota Nyayas*

Kedara-Kūlya Nyaya describes distribution of nourishment through channels toward tissues, whereas *Khale-Kapota Nyaya* uses the analogy of selective allocation according to tissue requirement. These models can be interpreted as classical descriptions of distribution and differential availability. Their conceptual relationship to modern perfusion and regulated substrate delivery is therefore potentially useful.

1. *Kedara-Kūlya Nyaya*: Describes tissues as fields irrigated by nutrient channels from a central reservoir. Flow depends on pressure gradients, similar to the principles of fluid dynamics.
2. *Khale-Kapota Nyaya*: Explains autoregulation of nutrient distribution according to tissue demand, similar to pigeons selectively picking grains.

In earlier deliberations, attention was focused on the plausible mechanisms that enable the transport of nutrients to the brain, including the regulatory processes involved in cerebral uptake. Despite these factors, the consistency and physicochemical nature of the *dravya* play crucial roles in determining effective delivery to neural tissues. In this context, ghee is particularly important.

8. *Ghrita* and Brain delivery

For lipid-associated phytoconstituents, modern gastrointestinal physiology provides a plausible basis for considering the role of *Ghrita* as a lipid-rich formulation vehicle. Lipid-based formulations may influence the solubilization, gastrointestinal absorption, systemic disposition, and bioavailability of lipophilic constituents. Emulsification may enhance the bioavailability of certain phytochemicals; however, such effects are compound- and formulation-specific and cannot be generalized to all *Ghrita* preparations.^[18] Although these findings highlight the lipid composition of *Ghrita*, they do not, by themselves, establish that *Ghrita* crosses the BBB or that its herbal constituents are directly delivered to the brain.^[19]

Based on established principles of lipid digestion and absorption and emerging evidence regarding lymphatic and meningeal transport, a hypothetical pathway for the disposition of lipid-associated phytoconstituents administered in *Ghrita* is proposed below in Figure 1: ^[20]

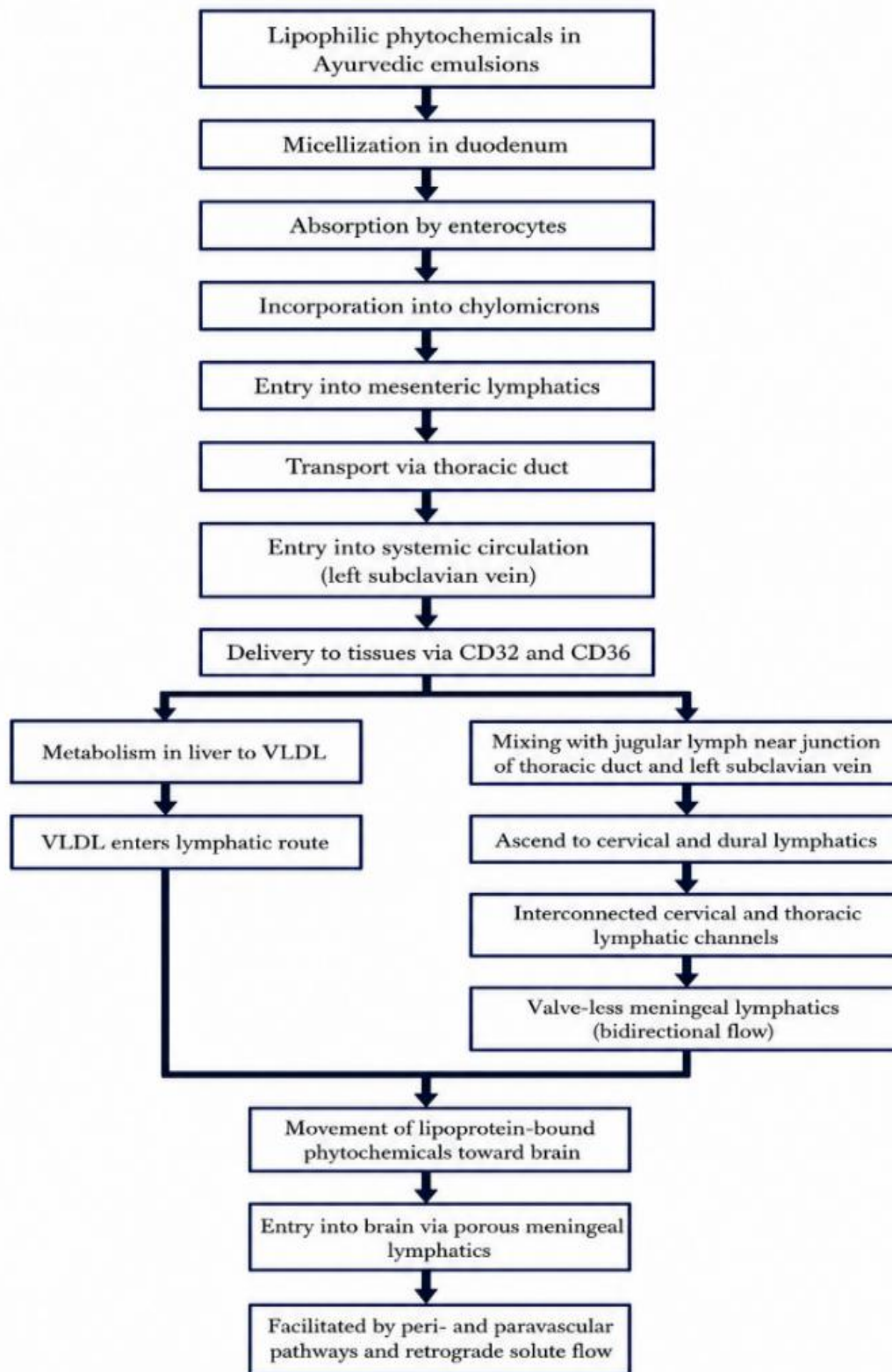


Figure 1: Proposed Hypothetical Pathway of *Ghrita*-Associated Phytoconstituent Delivery:

As elucidated by Kang et al., emulsification can enhance the bioavailability of lipophilic phytochemicals, providing a plausible basis for considering the lipid-rich nature of in the delivery of its associated phytoconstituents.^[18]

It contains various fatty acids, including polyunsaturated fatty acids, and its lipidic nature may facilitate the solubilization, gastrointestinal absorption, and membrane partitioning of compatible lipophilic constituents. Since cellular membranes are predominantly composed of phospholipid bilayers, such lipid-soluble constituents may interact favourably with membrane lipids, potentially facilitating their intracellular distribution and tissue availability, including within the central nervous system.^[21]

However, the extent to which individual constituents reach the brain depends on their physicochemical properties, metabolism, and the selective transport mechanisms of the blood–brain barrier. Thus, the lipidic character of may be considered a plausible formulation-related factor contributing to the delivery of lipophilic constituents, rather than evidence that itself readily traverses the BBB.^[19]

Apart from internal administration, Ayurveda also employs external therapeutic procedures that facilitate the transfer of therapeutic substances through specialized routes. These therapies provide alternative pathways for absorption and action, particularly in the nervous system and brain. Among them, *Nasya* and *Sirodhara* are important modalities used to influence central nervous system functions through localized delivery and physiological modulation. The following sections describe the mechanisms and therapeutic actions of *Nasya* and *Sirodhara* in detail.

9. *Nasya* and the Broader Field of Intranasal Brain Delivery

Nasya Karma is regarded as a *Jatrurdhwa doshahara* procedure and is usually preceded by local *Snehana* and *Swedana*, which promote facial hyperaemia through vasodilation and efferent vasomotor stimulation. The resulting increase in regional blood flow may enhance cerebral perfusion and facilitate fluid exchange within the brain tissue.^[22]

In certain therapeutic sequences, *Sodhana Nasya* precedes *Brumhana Nasya*, with *Srotho-sodhana* traditionally considered to facilitate the unobstructed delivery and enhancing the action of subsequently administered substances. In this context, *Nasya* preparations using oil or as a base may be considered beneficial for delivering compatible lipophilic constituents, as discussed above.

However, the extent to which individual *Nasya* formulations achieve CNS delivery remains dependent on their composition, dose, mucosal residence, absorption, and pharmacokinetic properties; therefore, this relationship remains a hypothesis requiring further investigation.

10. *Sirodhara*: Proposed Neurophysiological Effects

Sirodhara is considered to stimulate *Marmas* such as *Shankha*, *Adhipathi*, and *Utkshepa*. The warm fluid used during the procedure may induce vasodilatation and enhance regional circulation, potentially improving cerebral perfusion and higher cognitive functions.^[23]

During *Sirodhara*, the continuous stream of fluid produces gentle pressure and mechanical stimulation over the forehead. These sensory stimuli have been proposed to influence central neural structures, including the thalamus and basal forebrain, and may modulate serotonergic and catecholaminergic activity, thereby promoting relaxation and sleep.^[24]

When oil is used as the *Sirodhara* medium, its lipid nature may additionally facilitate the interaction and delivery of compatible lipophilic constituents through the skin, as discussed above. However, the extent of transdermal penetration and subsequent CNS effects of specific *Sirodhara* formulations requires further investigation.

Conclusion:

The present review highlights the potential for an integrative interpretation of Ayurvedic concepts of *Srotas*, *Agni*, *Doshas*, *Vāyu*, *Dhatus*, and *Dhatu poshana* alongside contemporary understanding of physiological transport and blood–brain barrier function. Concepts such as *Srotas*, *Bhutagni*, *Kedara - Kulya Nyaya*, and *Khale-Kapota Nyaya* provide classical frameworks for understanding movement, transformation, distribution, and selective availability of substances, while contemporary BBB physiology demonstrates that cerebral delivery is a highly regulated and substance-specific process.

Within this framework, may be considered a lipid-rich formulation vehicle that can influence the solubilization, absorption, and disposition of compatible lipophilic phytoconstituents. Similarly, *Nasya* provides a localized intranasal route that may be relevant to contemporary concepts of nasal-to-CNS delivery, while *Sirodhara* may exert effects through sensory, thermal, and mechanical stimulation, with the properties of the therapeutic medium potentially contributing to its action. These relationships provide plausible physiological hypotheses rather than evidence of direct equivalence between Ayurvedic procedures and modern molecular mechanisms.

Thus, abovesaid Ayurvedic concepts may offer useful conceptual frameworks for generating testable hypotheses concerning substance movement and delivery to neural tissues. However, direct correlation of these concepts with specific BBB transport mechanisms, cellular structures, or CNS delivery may not be

possible, given the fundamental differences between the conceptual frameworks and the levels of evidence available. Future studies integrating pharmacokinetics, tissue distribution, trans-nasal and transdermal absorption, BBB permeability, and formulation-specific characteristics may help clarify the physiological basis of these traditional therapeutic approaches and establish which proposed mechanisms are experimentally reproducible.

Limitation and future directions

This review is narrative and integrative in nature. The interdisciplinary comparisons are constrained by differences in terminology, epistemology, historical context, and levels of biological organization. Classical concepts cannot be assumed to represent modern cellular or molecular mechanisms merely because a functional resemblance can be proposed. The proposed correspondences should therefore be regarded as conceptual parallels and hypothesis-generating frameworks rather than established mechanistic equivalences. Future research should test specific, falsifiable hypotheses rather than attempt broad one-to-one equivalences. Priority areas include pharmacokinetic studies of defined Ayurvedic formulations, measurement of brain and plasma concentrations of identified constituents, in vitro BBB models, assessment of endothelial transporter and efflux activity, evaluation of BBB integrity, and controlled investigation of intranasal and external procedures. Such studies could determine which proposed correspondences have measurable biological correlates and which remain primarily conceptual.

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