

Seeing Red, Feeling Pain: Decoding the Neurological Connection Between Rosacea and Migraines



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INTRODUCTION

More Than Meets the Eye: Skin and Brain Connection

Migraine headaches are a neurological disorder characterized by throbbing, disabling intensity, while rosacea is a chronic inflammatory skin condition [1,2]. Despite these conditions impacting very different organ systems, recent studies reveal a notable overlap: rosacea patients have notably higher rates of migraine (12.1%) compared to the general population (7.3%), especially among women over 50 [1,3]. Understanding this link is clinically vital, as shared neurovascular pathways can lead to potential pleiotropic treatment, and encourage physicians to evaluate for both conditions upon presentation.

Headaches That Halt Life: Understanding Migraine

Migraines are characterized as pulsating headaches typically lasting between 4–72 hours. Migraines can severely interfere with daily activities, and are frequently accompanied with sensory disturbances (e.g. visual, auditory, olfaction), nausea, or vomiting [4].

Epidemiology and Pathophysiology

Typically manifests during adolescence or early adulthood and peaking in middle age. While most individuals experience episodic migraines with sporadic attacks, 1–2% suffer from chronic migraines—experiencing headaches 15 or more days each month [4]. Though not yet fully understood, current literature suggests that migraines involve the activation of trigeminal afferents, which leads to the release of proinflammatory neuropeptides such as calcitonin gene-related peptide (CGRP), pituitary adenylate cyclase-activating polypeptide (PACAP), and substance P (SP) [5]. Elevated CGRP, in particular, is correlated with the throbbing pain and inflammation characteristic of migraine attacks, highlighting its importance as a therapeutic target.

Clinical Features and Triggers

Migraine attacks can spontaneously arise but frequently follow identifiable triggers. Common triggers include stress, inadequate sleep, hormonal changes, diet (cheese, alcohol), bright lights, and strong odors [6]. Interestingly, triggers such as emotional stress and alcohol overlap with those in rosacea, suggesting possible shared biological pathways involving nerves and vascular responses.

Red Alert: Decoding Rosacea

Rosacea is a common inflammatory skin condition marked by recurrent episodes of facial redness, flushing, visible blood vessels, and sensitive skin.

Epidemiology and Pathophysiology

Rosacea affects approximately 5–10% of the global population, often emerging between ages 30 and 50, predominantly affecting women and those with fair skin [2]. Its pathophysiology involves a combination of neurovascular dysregulation and immune system overactivity. Facial skin in rosacea patients are notably sensitive, with exaggerated vasodilatory responses to mild stimuli [2,7]. Key molecules implicated include neuropeptides like CGRP SP, both causing blood vessel dilation and inflammation (neurogenic inflammation) [7]. Additionally, upregulated transient receptor potential (TRP) ion channels (particularly TRPV1) on sensory nerves enhance responsiveness to heat, spice, and alcohol [8].

Clinical Features and Triggers

Primarily presents as facial flushing, visible blood vessels, skin thickening, and occasionally acne-like bumps often develop over time [8]. Common rosacea triggers include heat exposure, spicy foods, alcohol, sun exposure, emotional stress, hot beverages, and vigorous exercise [8]. Such triggers rapidly provoke flushing by activating sensory nerves and blood vessels, underscoring the importance of trigger avoidance in managing symptoms.

NEUROINFLAMMATORY CONNECTIONS

CN V Trigeminal Nerve

The trigeminal nerve plays a central role in the pathophysiology of both rosacea and migraines, acting as the primary sensory pathway for the face and head. Upon activation, it releases key neuropeptides such as CGRP, PACAP, and Substance P (SP), which contribute to inflammation, vasodilation, and pain sensitization [9]. In migraines, trigeminal activation leads to meningeal inflammation and cranial vasodilation, while in rosacea, it triggers facial flushing, burning sensations, and neurogenic inflammation in the skin [9].

PACAP (Pituitary Adenylate Cyclase-Activating Polypeptide)

One of the most studied peptides, PACAP (Pituitary Adenylate Cyclase-Activating Polypeptide), has been shown to induce both migraine-like headaches and rosacea-like flushing and edema when infused in susceptible individuals. PACAP exerts its effects through PAC1 and VPAC receptors, promoting vasodilation and mast cell activation. In rosacea, this can manifest as prolonged facial redness and swelling, whereas in migraine, it contributes to premonitory symptoms and headache initiation [10].

CGRP (Calcitonin gene-related peptide)

Calcitonin gene-related peptide (CGRP) is a sensory neuropeptide that induces vasodilation and drives neurogenic inflammation, linking the pathophysiology of migraine and rosacea. In migraine, CGRP released from trigeminal neurons dilates cranial blood vessels and heightens nociceptive signaling, fueling headache pain [11]. In rosacea, elevated CGRP in the skin provokes marked vasodilation (flushing) and triggers inflammatory cascades via immune cell activation.

Substance P (SP)

Substance P (SP) is a trigeminal neuropeptide that contributes significantly to migraine and rosacea by triggering neurogenic inflammation and pain. During a migraine, SP is released from trigeminal nerve endings, where it dilates meningeal blood vessels and increases their permeability, causing swelling and the release of inflammatory molecules. SP also facilitates mast cell degranulation, leading to histamine release and immune activation, further amplifying the inflammatory cascade. In rosacea, similar mechanisms occur in the skin, contributing to the painful burning sensations and persistent inflammation seen in affected patients [12].

Shared Mechanisms

Both conditions share common neurovascular and neuroinflammatory mechanisms, including the release of neuropeptides from sensory nerves, immune cell recruitment, vasodilation, and edema (Figure 1). Environmental triggers such as heat, alcohol, and stress often activate TRP channels (especially TRPV1) on trigeminal nerve endings, further sensitizing the system. Repeated activation of these pathways may lead to central and peripheral sensitization, offering a potential explanation for chronicity and overlapping symptoms seen in both rosacea and migraines [13].

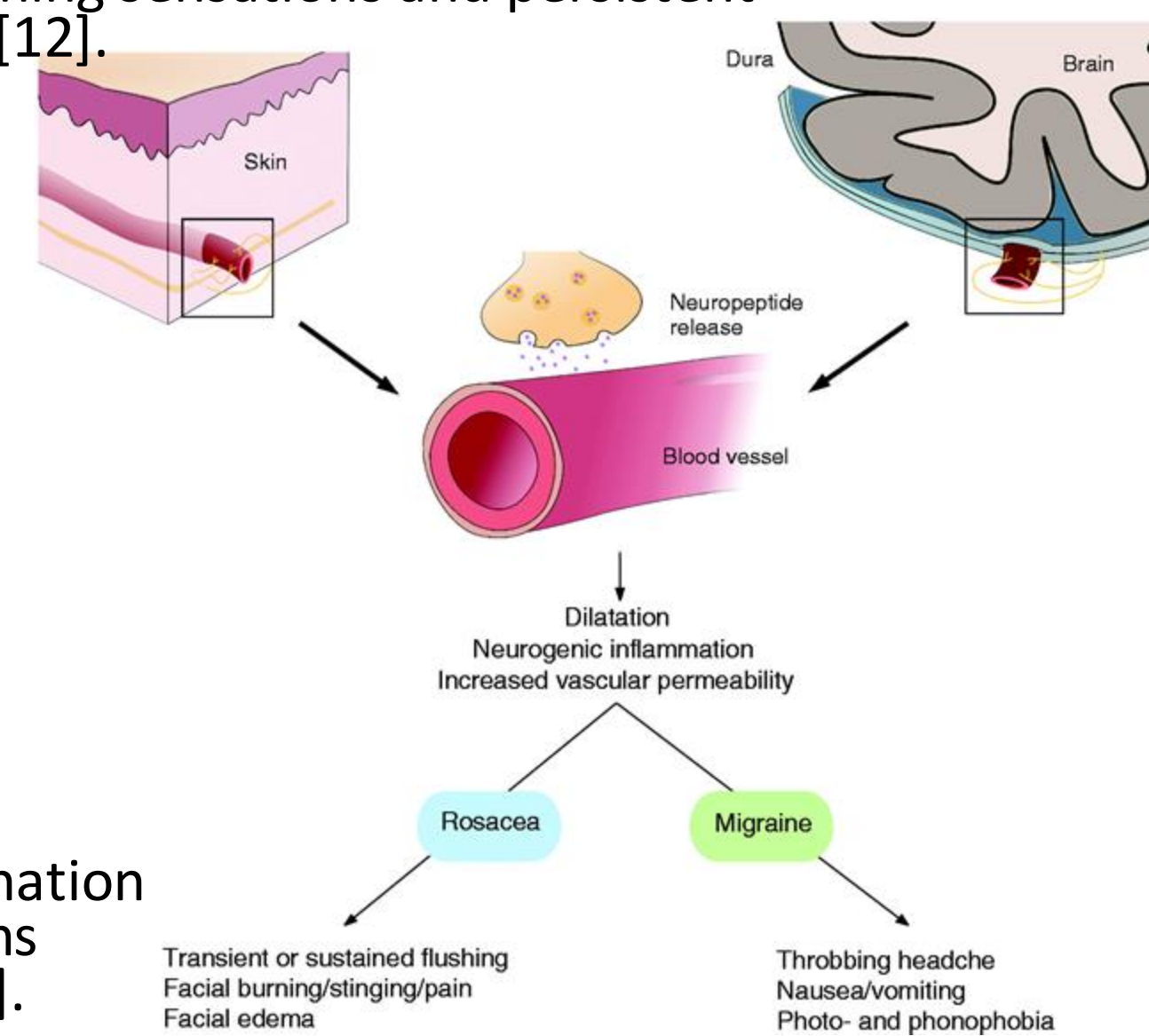


Figure 1: Shared neurovascular pathway in rosacea and migraine.

GAPS IN CURRENT LITERATURE & FUTURE DIRECTIONS

Gap in Current Literature

While the overlap between rosacea and migraine is increasingly recognized, the exact mechanisms linking the two remain underexplored. Few studies have directly investigated how trigeminal neuropeptides like CGRP and PACAP function in facial skin compared to meningeal tissue. Additionally, PACAP's dual role in promoting and potentially resolving inflammation remains poorly understood in the context of skin disease. Most clinical evidence is derived from isolated case reports or migraine studies, and rosacea-specific trials involving neuropeptide-targeted therapies are lacking. There is also limited understanding of how central versus peripheral trigeminal sensitization contributes to the chronicity of symptoms in both conditions.

Future Research

Future research should explore PACAP and CGRP expression in rosacea-affected skin and assess systemic neuropeptide levels during flares. Clinical trials investigating CGRP- or PACAP-targeted therapies in rosacea populations are warranted. Comparative studies using human tissue and animal models could clarify differences in trigeminal signaling between cutaneous and intracranial regions. Additionally, identifying biomarkers of trigeminal sensitization may help distinguish neurogenic rosacea subtypes and personalize treatment. Integration of dermatology and neurology research may lead to novel cross-disciplinary therapies for patients suffering from both rosacea and migraine.

CONCLUSIONS

- Shared trigeminal neurovascular pathways help explain the overlap between rosacea and migraine, particularly symptoms like flushing, pain, and sensory hypersensitivity.
- Neuropeptides such as CGRP and PACAP play critical roles in both conditions, mediating vasodilation, inflammation, and neural sensitization, which opens doors for shared treatment strategies.
- A deeper understanding of neuroimmune interactions in the skin and brain may guide future therapies, emphasizing the need for interdisciplinary research between dermatology and neurology.

TREATMENT IMPLICATIONS & CLINICAL CONNECTIONS

Treatment	Use in Migraine	Use in Rosacea	Mechanism linking both conditions
CGRP-Pathway Inhibitors (fremanezumab, erenumab)	Prevents migraines by inhibiting CGRP, which reduces cranial inflammation and vasodilation [14].	Initial studies suggest that it has the potential to be a novel rosacea treatment, as it reduces flushing and redness [15].	Blocks CGRP, a neuropeptide involved in neurogenic inflammation in both conditions.
Triptan (sumatriptan)	Stops migraine attacks by contracting cranial vessels and inhibiting neuropeptide release (CGRP, SP) [16].	Experimental studies have shown that rosacea flushing can be reduced, implying that it has the ability to possibly treat rosacea flares [17].	Reduces the release of CGRP and SP, targeting the common neurogenic inflammation pathway.
Beta Blockers (Propranolol, carvedilol)	Used to prevent migraines by regulating vascular tone and reducing neuronal hyperexcitability [18].	Proven efficacy in lowering rosacea related facial redness and flushing caused by stress induced vasodilation [19].	Decreases neurovascular dysregulation

REFERENCES

