# EXPLORING LINKS BETWEEN THE BRAIN AND SKIN

The connection between psychological well-being and skin health is a rapidly growing area of scientific interest. Researchers are exploring how stress affects skin conditions and wound healing, as well as the underlying biological mechanisms.

Recent studies have deepened the understanding of the brain-skin axis, including how the nervous-, immune- and endocrine systems might mediate how psychological wellbeing affects skin.

Since its founding in London in 1985, EVE LOM has worked to harness botanical science to support skin health. EVE LOM is now expanding its mission to explore the forefront of the connection between emotional well-being and skin health. In 2024, it led the development of China's first guideline for skincare cosmetics based on emotional well-being, filling a gap in the country's evaluation system for such products and offering consumers a science-based reference.

As a research-driven skincare brand, EVE LOM is committed to advancing understanding in this emerging area. Here you will find summaries of some of the latest studies from academic research teams around the world on how stress affects skin health; the role of pain-sensing neuropeptides in modulating immune function and supporting tissue repair; and how pressure-sensitive proteins contribute to wound healing.

# 大脑情绪与肌肤健康的内在关联

精神状态与肌肤健康之间的关系正得到科学界越来越多的关注。研究人员正在努力探索精神压力如何影响肌肤状况和伤口愈合，并揭示其背后的生物学机制。

最近的研究增进了我们对脑 - 皮轴的理解，包括神经系统、免疫系统和内分泌系统如何参与及协调精神状态对肌肤的影响。

自 1985 年于伦敦创立至今，护肤品牌 EVE LOM 伊芙珑致力于从植物学中寻找健康肌肤之道。如今，EVE LOM 伊芙珑不断推陈出新，引领情绪健康与肌肤健康关系的前沿探索。2024 年，EVE LOM 伊芙珑牵头制定了中国首个《情绪护肤化妆品开发和技术评价指南》，填补了中国同类产品评价体系的空白，为消费者提供了一份基于科学的参考标准。

作为一个科研赋能的护肤品牌，EVE LOM 伊芙珑坚持加深对这一新兴领域的知识积淀。在接下来的内容中，您将读到全球学术团队的最新研究成果，这些研究探讨了压力如何影响肌肤健康，感知疼痛的神经肽在调节免疫功能和支持组织修复中的作用，以及压力敏感蛋白如何调控伤口愈合。

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# HOW STRESS MAKES ALLERGIC DERMATITIS WORSE

Researchers find a protein trigger that links stress to nerve inflammation in mice with dermatitis, and even those with healthy skin.

Skin can react in unexpected ways to stress. Dermatologists have long observed that stress can trigger or worsen allergic skin conditions, often leading to increased itchiness and inflammation.

To explore the biological mechanisms behind these effects, researchers from Germany and the United Kingdom identified a possible pathway through which stress may influence the onset or severity of atopic dermatitis. Their findings point to 'substance P' as a key player in the skin's response to psychological stress[1]. This is a small, protein-like molecule used by nerve cells to transmit pain signals and trigger inflammation.

The study used mice engineered to be allergic to an egg white protein, which cause them to develop allergic-dermatitis-like symptoms upon exposure. To induce stress, the researchers exposed them, and a control group of healthy mice to a repellent high-frequency noise.

## Noise stressor

When the allergy-prone mice were sensitized with an injection of egg white protein, they developed skin redness and scaling around the injection site. The researchers also observed increased growth of nerve fibres containing substance P in the affected skin.

When the mice were later exposed to the noise stressor, the growth of substance P-containing nerve fibres in the skin increased even further. The stress also significantly worsened other dermatitis features, including skin thickening, heightened activation of white blood cells linked to allergic responses, and a breakdown in the structure and organization of nerve fibres. Overall, stress exacerbated their symptoms by around 33%.

To further investigate the role of substance P, the researchers engineered a separate group of allergic-prone mice with a defective receptor for substance P. While these mice still developed some symptoms of allergic dermatitis when exposed to the allergen, their symptoms did not worsen in response to noise stress.

## Key mediator

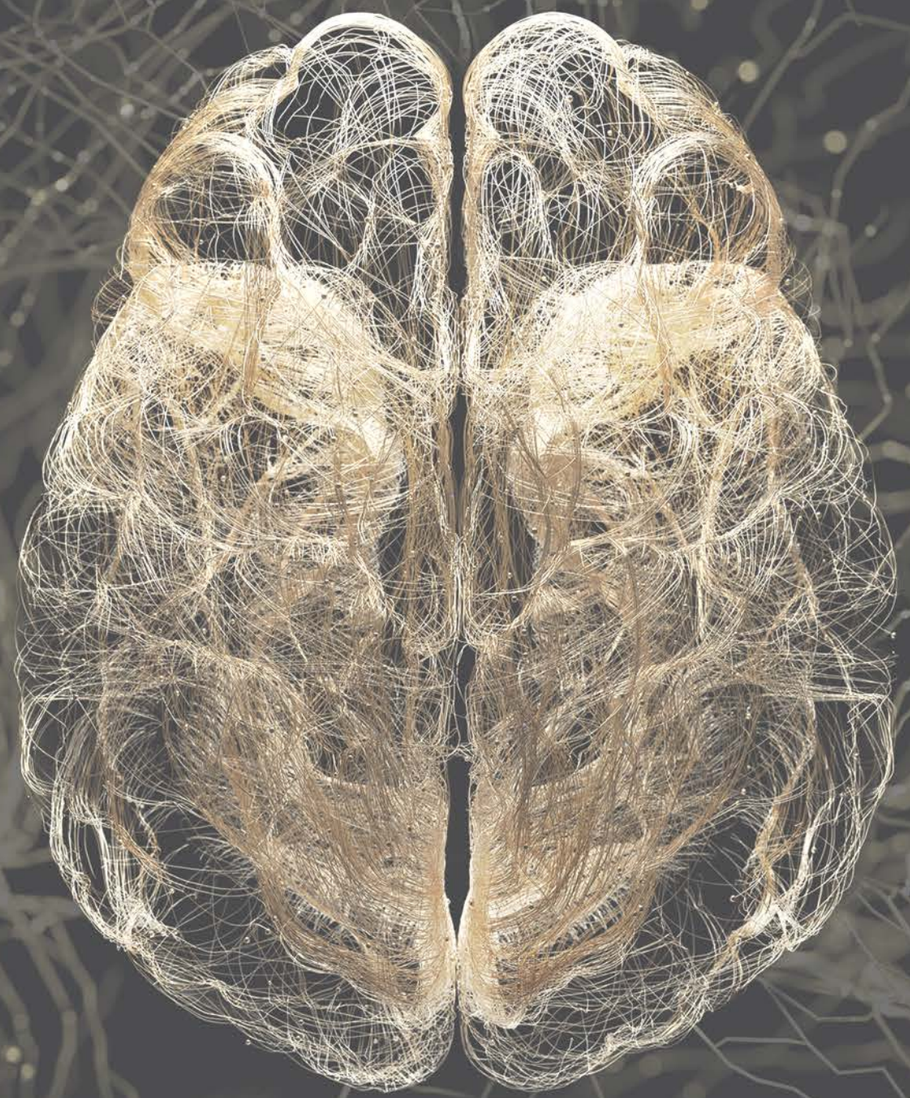
The researchers also exposed normal mice to the same noise stress and saw that these non-allergic mice also developed increased levels of substance P-containing nerve fibres in the skin, even without having dermatitis, compared to control mice that were not exposed to stress.

These findings demonstrate that substance P is probably a key mediator of the skin's inflammatory response to psychological stress.

The authors also suggested that stress alone can induce some of the same neurological changes in healthy skin similar to those caused by allergen-induced dermatitis, highlighting stress may not only worsen existing skin conditions, but may also trigger them in the first place. They propose that substance P may serve as a potential therapeutic target for allergic skin conditions, while also providing a compelling pathogenic explanation that could help alleviate psychological stress in affected patients.

Reference

1. Pavlovic, S. *et al. J. Invest. Dermatol.* **128**, 434-446 (2008).



Noise, as a form of psychological stress, can trigger skin inflammation by activating nerve-cell signals through substance P — a key molecule in pain transmission.

噪音作为一种心理压力，可以通过 P 物质这一在疼痛传导中起关键作用的分子激活神经细胞信号通路，从而引发皮肤炎症。

Andriy Onufriyenko/Moment/Getty



# 压力触发因子如何加重过敏性皮炎

研究人员发现了一种将压力与患有皮炎小鼠的神经炎症联系起来的蛋白质触发因子，在皮肤健康的小鼠中也存在这种关联。

皮肤对压力的反应可能出乎意料。皮肤科医生一直以来观察到，压力可能诱发或加重过敏性皮肤疾病，常常导致瘙痒或炎症反应加剧。

为探索这些影响背后的生物学机制，来自德国和英国的研究人员识别出一种可能的通路，压力可能通过该通路影响特应性皮炎的发生或病情严重程度。他们的研究结果指出，神经肽“P 物质”是皮肤对心理压力反应中的关键介质[1]。这是一种类似蛋白质的小分子，神经细胞利用它来传递疼痛信号并引发炎症反应。

研究团队采用了一种蛋清蛋白过敏小鼠模型，小鼠接触该蛋白后会出现类似过敏性皮炎的症状。为了诱导压力，研究人员将这些小鼠及一组健康小鼠暴露于令人不适的高频噪声压力刺激中。

## 噪音压力源

当过敏易感小鼠接受注射蛋清蛋白以诱发过敏反应时，注射部位出现了皮肤红肿和脱屑。研究人员还观察到受影响皮肤中含有 P 物质的神经纤维数量增加。

当这些小鼠随后暴露于噪声压力刺激时，皮肤中含有 P 物质的神经纤维生长进一步增加。压力还显著加重了其他皮炎特征，包括皮肤增厚、过敏反应相关白细胞活化增强，以及神经纤维结构和排列受损。总体而言，压力使症状加重了约 33%。

为了进一步研究 P 物质的作用，研究人员对另一组易过敏的小鼠进行了基因工程改造，使其 P 物质受体产生缺陷。尽管这些小鼠在接触过敏原时仍会出现一些过敏性皮炎症状，但在噪声压力下症状未再加重。

## 关键介质

研究人员还让正常小鼠暴露于相同的噪声压力，结果发现，与未受压对照组相比，这些非过敏性小鼠即使未患皮炎，其皮肤中含 P 物质神经纤维的水平也显著升高。

这些发现表明，P 物质可能是皮肤对心理压力产生炎症反应的关键介质。

研究人员还提出，压力本身可能直接诱发健康皮肤中与过敏原诱导的皮炎类似的神经学变化，提示压力不仅会加重现有皮肤疾病，也可能成为疾病的触发因素。研究团队认为，P 物质有望成为过敏性皮肤疾病的潜在治疗靶点，同时提供了有力的病理学解释，或有助于缓解患者心理压力。

# SENSORY NEURONS HELP TISSUE REPAIR VIA IMMUNE SIGNALLING

Pain-sensing neurons help orchestrate tissue repair through interactions with the immune system, potentially opening new avenues for treating hard-to-heal wounds.

The immune system plays a key role in wound healing by detecting injury, clearing damaged cells, and coordinating tissue repair through inflammation and regeneration. New research is focused on how the nervous system interacts with the immune system to support the healing process.

To investigate how neuro-immune interactions — particularly between sensory neurons in skin and the immune system — could be harnessed to promote tissue healing, researchers from Monash University, in Australia, and Osaka University, in Japan, studied nociceptors. These are specialized pain-sensing neurons that have nerve endings in skin, muscles and joints.

In a 2024 study in *Nature*, the researchers reported that nociceptors mediate healing by releasing a neuropeptide into injured skin and muscle tissues. Known as the calcitonin gene-related peptide (CGRP), it signals to immune cells to help regenerate tissues[1].

## Neuro-immune interactions

The researchers used a mouse model to examine how the absence of nociceptors affects healing. Mice engineered to lack a subset of nociceptors exhibited delayed skin wound closure after acute injury and impaired muscle regeneration, suggesting an important role for these sensory neurons in regeneration.

The team then used a different mouse model with nociceptors labelled with a fluorescent protein, enabling them to track these sensory neurons during skin and muscle healing. They observed that nociceptor nerve endings growing into injured tissues and release CGRP, implicating it as a key signalling molecule mediating nervous–immune system communication during tissue repair.

Researchers later applied an engineered form of CGRP, which accelerated wound healing, and enhanced muscle regeneration both in mice lacking nociceptors, and in diabetic mice with peripheral nerve damage beyond the brain and spinal cord.

## Modulating immune response

The researchers explored how CGRP influences the immune system to promote tissue regeneration. In mouse and *in vitro* cell studies, they found that CGRP signals via receptor-activity-modifying protein 1 (RAMP1) to key immune cells — specifically neutrophils, monocytes and macrophages.

These white blood cells play crucial roles during wound healing by regulating inflammation, clearing damaged tissue and promoting repair. CGRP signalling shifted them towards an anti-inflammatory and pro-repair state.

Gene expression analysis revealed that the effects of CGRP on neutrophils and macrophages are mediated by thrombospondin-1 (TSP-1), a multifunctional protein known to support healing.

This study uncovers a significant neuro–immune regenerative axis activated after acute tissue injury, highlighting the complex interactions between nociceptors, immune cells and tissue repair.

The authors suggest that the findings may have implications for regenerative medicine, particularly for patients with hard-to-heal wounds resulting from dysregulated neuro–immune interactions. Harnessing this neuro-immune regenerative axis opens new avenues for potential new therapies, either as standalone treatments or in combination with existing approaches, they suggest.


Reference

1. Lu, YZ. et al. *Nature* **628**, 604–611 (2024).


koto_feja/E+/Getty

An artist's impression of interconnected neuron cells with electrical pulses. Pain sensing neurons play a key role in wound healing and regeneration.

相互连接的神经元细胞通过电脉冲进行通信的艺术化插图。感知疼痛的神经元在伤口愈合和再生中发挥着关键作用。



# 感觉神经元通过免疫信号促进组织修复

痛觉神经元通过与免疫系统相互作用协调组织修复，有望为难愈性伤口的治疗提供新思路。

免疫系统在伤口愈合中发挥关键作用，能够识别损伤、清除受损细胞，并通过炎症反应和组织再生协调修复过程。最新研究关注神经系统如何与免疫系统相互作用，从而促进愈合。

为探究神经 - 免疫相互作用（尤其是皮肤的感觉神经元与免疫系统的相互作用）如何用于促进组织愈合，澳大利亚莫纳什大学和日本大阪大学的研究人员研究了痛觉神经元。这些是专门感知疼痛的神经元，末梢分布于皮肤、肌肉和关节中。

在 2024 年发表于《自然》的一项研究中，研究人员表示，痛觉神经元通过向受伤的皮肤和肌肉组织释放一种神经肽介导愈合。这种神经肽称为降钙素基因相关肽（CGRP），可向免疫细胞发出信号，促进组织再生[1]。

## 神经 – 免疫相互作用

研究人员利用小鼠模型研究了痛觉神经元缺失对愈合的影响。缺乏特定类型痛觉神经元的小鼠在急性损伤后，表现出皮肤伤口闭合延迟和肌肉再生受损，提示这些神经元在组织再生中具有重要作用。

随后，研究团队采用另一种小鼠模型，用荧光蛋白标记痛觉神经元，以追踪其在皮肤和肌肉愈合过程中的动态变化。他们观察到，这些神经元的末梢会向受伤组织延伸并释放 CGRP，提示 CGRP 是组织修复过程中神经系统与免疫系统之间沟通的关键信号分子。

研究人员随后使用改造后的 CGRP，在缺乏痛觉神经元或周围神经受损的糖尿病小鼠中均加快了伤口愈合，并促进了肌肉再生。

## 调节免疫反应

研究人员探讨了 CGRP 如何影响免疫系统以促进组织再生。通过小鼠模型和体外细胞研究，他们发现 CGRP 通过受体活性调节蛋白 1（RAMP1）作用于关键免疫细胞，包括中性粒细胞、单核细胞和巨噬细胞。

这些白细胞在伤口愈合过程中通过调节炎症、清除受损组织、促进修复，在伤口愈合中发挥重要作用，而 CGRP 信号可促使它们向抗炎、促修复状态转变。

基因表达分析显示，CGRP 对中性粒细胞和巨噬细胞的作用是通过血小板反应蛋白 1（TSP -1）介导的，这是一种已知可促进愈合的多功能蛋白。

这项研究揭示了急性组织损伤后被激活的重要神经 - 免疫再生轴，凸显出痛觉神经元、免疫细胞与组织修复之间的复杂相互作用。

研究人员指出，这些发现可能对再生医学具有重要意义，特别适用于因神经 - 免疫相互作用失调导致伤口难以愈合的患者。他们认为，利用这一神经 - 免疫再生轴有望开辟新的治疗途径，无论是单独应用还是与现有方法联合使用。

# A CELLULAR ‘MECHANICAL SENSOR’ THAT REGULATES SKIN REPAIR

Biologists have found that a protein that senses mechanical forces can play a key role in wound healing, and may have wider implications.

Can your cells ‘feel’ what is happening around them? In 2010, a team at the Scripps Research Institute in California uncovered how the body converts physical pressure into biological signals.

The research led by neuroscientist, Ardem Patapoutian, revealed two sensor proteins — PIEZO1 and PIEZO2 — located in the membranes of certain cells. These act as tiny pressure detectors, allowing cells to sense and respond to mechanical forces such as touch or movement. This breakthrough earned Patapoutian the 2021 Nobel Prize in Physiology or Medicine.

Building on this discovery, researchers at the University of California, Irvine, in collaboration with the Scripps Research Institute, began investigating the mechanisms of these sensor proteins in greater detail — particularly their role in the process of wound healing.

In 2021, they reported that PIEZO1 can slow the healing process by regulating the movement of keratinocytes, the primary cell type in the outermost layer of the skin, based on experiments conducted on an animal model lacking this protein[1].

## Mechanics of skin healing

To explore whether PIEZO1 plays a role in wound healing, the researchers carried out experiments using mice whose PIEZO1 proteins were removed in their keratinocytes.

They found that mice lacking PIEZO1 healed faster than mice with normal levels. A similar pattern was observed in lab-grown keratinocytes treated with a chemical that activates PIEZO1. The researchers used time-lapse imaging on migrating keratinocytes from mice engineered expressing a fluorescently tagged PIEZO1, allowing them to track its location in cells over time.

## Regulating cell migration

Using a lab-based model of a skin wound — created by scratching a gap into a single layer of keratinocytes grown in a dish — they observed that the distribution of PIEZO1 changes over time. It tends to accumulate in certain areas near the wound edge, where it makes the cells move backwards.

Additional experiments in individual migrating keratinocytes showed that PIEZO1 tends to gather at the rear of the cell, a region critical for its forward movement.

The authors identify PIEZO1 as a key regulator of keratinocyte migration during skin repair, with implications beyond wound healing, opening new directions for investigating its role in development, homeostasis, disease, and repair. They also propose PIEZO1 as a promising target for new therapies to enhance wound healing — potentially through topical treatments.

Researchers are also exploring PIEZO1’s broader impact on skin health and ageing. In 2024, a team from South Korea investigated how PIEZO1 could help boost collagen production in the skin. They found that a certain synthetic polymer could activate PIEZO1, prompting skin cells to grow and produce more collagen[2].


References

1. Holt, J. R. *et al. Elife* **10**, e65415 (2021).
2. Byun, K. A. *et al. Int. J. Mol. Sci.* **25**, 7232 (2024).


An artistic impression of the PIEZO 1 structure. This tripod-shaped sensor protein sits in the membranes of keratinocyte cells, where it plays a key role in regulating their movement during skin repair.

PIEZO 1 结构的艺术示意图。这种三脚架形状的机械传感蛋白质位于角质形成细胞的膜上，在皮肤修复过程中对细胞运动起着重要的调控作用。

RCSB PDB (PDB ID: 5Z10)



# 一种调控皮肤修复的细胞“力学传感器”

生物学家发现，一种能够感知机械力的蛋白质在皮肤伤口愈合中发挥关键作用，并可能在人体内有更广泛的影响。

细胞是否能够“感知”周围环境的变化？2010 年，加州斯克里普斯研究所的一个团队揭示了身体如何将物理压力转化为生物信号。

由神经科学家 Ardem Patapoutian 领导的研究揭示了两种机械传感蛋白——PIEZO1 和 PIEZO2，它们位于特定细胞的膜上，充当微小压力传感器，使细胞能够感知并响应触摸或运动等机械力。这一突破性发现使 Patapoutian 获得了 2021 年诺贝尔生理学或医学奖。

在此发现的基础上，加利福尼亚大学欧文分校的研究人员与斯克里普斯研究所合作，深入探究这些机械传感蛋白的作用机制，特别关注它们在伤口愈合过程中的功能。

2021 年，他们报告称，基于在缺失 PIEZO1 的动物模型上进行的实验，发现该蛋白可通过调节角质形成细胞（皮肤表层的主要细胞类型）的运动来延缓伤口愈合过程[1]。

## 皮肤愈合的机制

为了探讨 PIEZO1 在伤口愈合中的作用，研究人员对基因工程小鼠进行了实验，这些小鼠的角质形成细胞中 PIEZO1 蛋白被去除。

他们发现，缺乏 PIEZO1 的小鼠伤口愈合速度快于正常水平的小鼠。在实验室培养的角质形成细胞中，使用一种能激活 PIEZO1 的化学物质进行处理后，也观察到了类似的模式。研究人员对经过基因工程改造、表达荧光标记 PIEZO1 的小鼠迁移角质形成细胞进行了延时成像，从而能够追踪其在细胞内的位置随时间的变化。

## 调控细胞迁移

研究人员利用一种体外构建的皮肤伤口模型——通过在培养皿中单层角质形成细胞上划出裂口——观察到 PIEZO1 的分布随时间变化。它倾向于在伤口边缘附近的特定区域积累，并在该区域诱导细胞向后移动。

在单个迁移角质形成细胞中的实验表明，PIEZO1 倾向于聚集在细胞后部，该区域对细胞的前向运动至关重要。

研究人员认为，PIEZO1 是皮肤修复过程中角质形成细胞迁移的关键调控因子，其作用不仅限于伤口愈合，还为进一步研究其在发育、稳态、疾病及组织修复中的作用开辟了新方向。他们还提出，PIEZO1 可作为促进伤口愈合的新型治疗策略的潜在靶点，或可通过外用治疗实现。

研究人员也在探索 PIEZO1 对皮肤健康和老化过程的更广泛影响。2024 年，韩国研究团队研究了 PIEZO1 在促进皮肤胶原蛋白合成中的潜在作用。他们发现，某种合成聚合物可激活 PIEZO1，从而促进皮肤细胞增殖和更多胶原蛋白生成[2]。