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# Stress as a migraine trigger: clinical evidence and pathophysiological insights – A narrative review

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**ABSTRACT**

**Background:** Stress can influence migraine burden and act as a trigger for attacks. However, the relationship between stress and migraine attacks, including its pathophysiological mechanisms, remains unclear.

**Methods:** In this narrative review, we summarized the latest evidence on stress as a potential trigger of migraine attacks and investigated the underlying pathophysiological mechanisms. The literature search was conducted in PubMed, focusing on the time window from 2015 to September 2025.

**Results:** Several studies reported stress as one of the most common migraine triggers. The hypothalamus plays a pivotal role in the stress response and influences its impact on migraine attacks. On one hand, it influences pain perception by modulating pain regions through direct anatomic connections and the release of neuropeptides, such as orexin A and B. On the other hand, through the hypothalamo-pituitary-adrenocortical (HPA) axis, the hypothalamus releases glucocorticoids that can influence cortical excitability and sensitize peripheral structures. Biological sex differences, such as female sex, seem to play an additional and significant role in all these mechanisms.

**Conclusions:** Stress can increase the likelihood of a migraine attack acting as a "catalyst" by influencing cortical excitability and predisposing to nociception. However, other permissive factors must be present to make stress an effective trigger. These include the patient's state of brain excitability and other biological factors, such as the female sex. Additional and dedicated studies are needed to fully elucidate the relationship between stress and migraine attacks.

**Key words:** stress, trigger, hypothalamus, migraine, cortisol.

## Introduction

Migraine is a highly prevalent disorder and one of the leading causes of disability in women under the age of 50. (1) It is characterized by recurrent attacks with different individual frequencies, spanning from a very episodic form to chronic and daily headaches.

Triggers are factors or stimuli that can initiate a migraine attack, influencing the frequency and recurrence of attacks. Several triggers have been investigated over the years, and stress is one of the common triggers reported by patients. (2-4) Additionally, stress seems to negatively influence the burden of the disease in other aspects, including predisposing to chronicity and increasing the perception and intensity of pain. (5,6)

However, there is little evidence of an increased biological stress response in the days preceding migraine attacks, with most studies failing to show differences in cortisol levels between patients and controls. (7) Only a few studies have shown altered corticotrope responsiveness (7) and greater fluctuations of cortisol levels in patients with migraine in comparison to healthy controls. (8,9)

Preclinical evidence suggests that activation of the glucocorticoid receptor by corticosterone, a stress hormone, can enhance susceptibility to cortical spreading depression (CSD) in a transgenic mouse model of familial hemiplegic migraine type 1. (10) This suggests that stress, through the hypothalamo-pituitary-adrenocortical (HPA) axis, may influence the migraine threshold in susceptible individuals. However, contrasting results emerged from other preclinical studies. (11,12) Interestingly, Balkaya *et al.* found that neither acute nor chronic stress can affect CSD susceptibility by itself, while only chronic stress, if followed by relief, may lower CSD threshold. (12)

Despite the proposed pathophysiological links, the exact causal relationship between stress and migraine is still unclear. (6) Additionally, it is important to note that patients' perceptions of a specific trigger may be influenced by their prior beliefs about the trigger's importance. (13) Considering that stress is the trigger that patients are most aware of, (14,15) this further complicates the investigation into the relationship between stress and migraine attacks.

To clarify the relationship between stress and migraine attacks, we summarized the latest evidence on stress as a potential trigger of migraine attacks and investigated the underlying pathophysiological mechanisms.

## Methods

A non-systematic literature search restricted to the last 10 years (2015-2025) was conducted in PubMed. The following string was used for the literature search: "migraine" AND "trigger" AND "stress". Additionally, the reference lists of included articles and relevant reviews were screened for additional eligible studies. We included preclinical and clinical studies that investigated stress or stress-related factors as triggers or modulators of migraine attacks. Eligible publications consisted of original studies and systematic or narrative reviews published in peer-reviewed journals in English between January 2015 and September 2025. Conference abstracts, editorials, and studies focusing on other headache disorders or not directly addressing stress as a trigger were excluded.

## Clinical evidence of stress as a migraine trigger

Stress is the migraine trigger that patients are most aware of and is one of the most common trigger factors reported by patients in several studies (**Table 1**). (14, 16-19) Indeed, a prospective study using a smartphone headache diary application for 3 months found that stress was the most frequently reported trigger on headache days, as well as the trigger with the highest likelihood of a following migraine attack. (20) Interestingly, although it is commonly reported as a trigger by both sexes, female patients reported stress as a trigger more often than male patients, (21) suggesting a sexual dimorphism in the ability of stress to trigger migraine attacks. Additionally, stress is also a common trigger for vestibular migraine (22) and for migraine attacks in the pediatric and teen population. (23,24)

Different types of stress were associated with migraine attacks, including perceived stress, (20) different types of social stressors – such as those that occurred during the COVID-19 pandemic (25,26) – and stress related to school in the pediatric population. (27) Perceived stress is the most investigated and has been shown to vary during the migraine cycle with both intra- and inter-variability. One study revealed three different patterns of perceived stress across the migraine cycle: perceived stress in the interictal phase that tends to fall progressively over the following phases ("let down" pattern, 16.7% of episodes); perceived stress that remains stable throughout the phases ("flat" pattern, 59.2% of episodes); perceived stress that increases during the pain phase ("stress as a trigger/symptom" pattern, 24% of episodes). (28) Additionally, patients with chronic migraine have been shown to have higher levels of perceived stress. (29) However, while a direct relationship between perceived stress and peak severity emerged on an aggregate level, this effect was influenced by a substantial degree of variation between individuals. (30)

Given its high prevalence as a migraine trigger, perceived stress was used to forecast migraine attacks. Houle *et al.* developed and validated a prediction model for following migraine attacks within 24 hours based on the levels of stress. They used several aspects of the Daily Stress Inventory – a measure of daily hassles completed at the end of each day – and the current headache state, achieving an area under the curve in prediction of 0.73 and 0.65 in training and validation samples, respectively. (31) However, contrasting results emerged from another study that showed that, while a higher level of stress was positively associated with next-day migraine risk, episodic migraine attacks were not predictable based on self-prediction or on self-reported exposure to common trigger factors. (32)

## Pathophysiological mechanisms

Different mechanisms were proposed to explain the ability of stress to increase vulnerability to migraine attacks. These included the direct effects of glucocorticoids on cortical excitability and sensitization of peripheral structures, as well as the direct role of the hypothalamus in influencing pain-modulating regions (**Figure 1**).

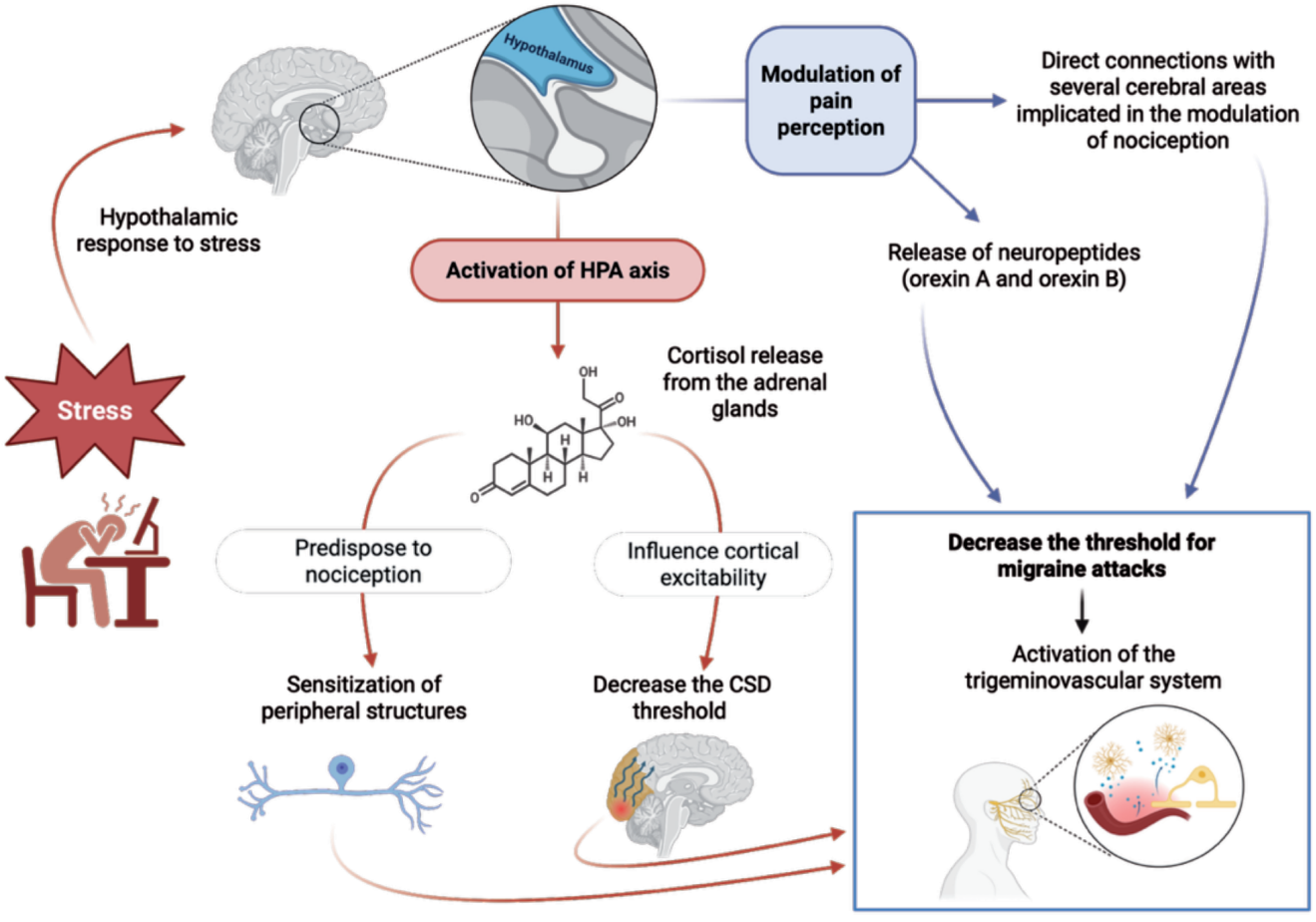


**Figure 1.** Pathophysiological mechanisms through which stress increases the likelihood of migraine attacks.

**Table 1.** Clinical studies that investigated stress as a migraine trigger between 2015 and 2025.

| Publication year, authors | Study design | Sample size (n) | Methods to evaluate stress | Main findings on stress as a trigger |
|---|---|---|---|---|
| 2016, Park *et al.* (20) | Prospective: smartphone headache diary application for 3 months | 62 (4,579 days analyzed; 1,099 headache days) | List of 18 trigger factors presented during the same day of headache | The likelihood for stress as a headache trigger was the highest among all the triggers (57.7%) |
| 2016, Kemper *et al.* (23) | Cross-sectional | 29 teens with migraine (12-18 years) | Questionnaire and stress scale (Cohen's 10-item PSS) | Stress was the most reported trigger (86%) and was positively correlated with depression |
| 2017, Moon *et al.* (29) | Case-control study | 227 | PSS | Higher PSS scores in patients with CMGAD-7 score. PHQ-9 score, ISI score, and CM were major predictors for PSS |
| 2017, Solotareff *et al.* (24) | Prospective study with a diary for 3 months | 101 pediatric patients (532 attacks collected) | List of 22 potential trigger factors | Stress was the second most frequently reported trigger (44.6%) after lack of sleep (51.4%) |
| 2019, Beh *et al.* (22) | Retrospective chart review | 105 with vestibular migraine | Self-reported triggers | Common triggers:<br>- stress (39.7%)<br>- bright lights (26.7%)<br>- weather changes (26.0%)<br>- sleep deprivation (26.0%) |
| 2020, Vives-Mestres *et al.* (28) | Prospective: 90 days of daily data entry through a digital health platform | 351 (2,115 episodes included) | Perceived stress rated once a day (0-10 scale) | 3 common patterns of perceived stress:<br>- "let down" pattern: progressive increase from the interictal phase (16.7% of episodes)<br>- "flat" pattern: relatively stable throughout the phases (59.2% of episodes)<br>- "stress as a trigger/symptom" pattern: peak in ictal phase (24% of episodes) |
| 2024, Son *et al.* (27) | Retrospective | 102 | Questionnaire with questions regarding 4 trigger factors | Academic stress was the second most common trigger for pediatric migraine (66.7%) and a significant trigger for pain severity in 44.1% of patient |
| 2021, Gonzalez-Martinez *et al.* (25) | Retrospective survey | 222 (subjects included in the final analysis) | Web-based survey composed of 108 questions | Subjective worsening of migraine in 47.3% during COVID-19 lockdown. The worsening was associated with changes in migraine triggers such as stress related to going outdoors and intake of specific foods or drinks |
| 2020, Holsteen *et al.* (32) | Prospective daily-diary cohort study (90 days) | 178 (1,870 migraine events) | Perceived stress level for a day (0-10 scale) | Higher level of stress, along with other triggers, was positively associated with next-day migraine risk. However, the multivariable model predicted migraine risk only slightly better than chance |
| 2020, Polk *et al.* (39) | Cross-sectional study | 147 | DASS-21 | Small associations between increases in allodynia and increases in stress. Stress mediated the allodynia-disability relationship |
| 2021, Karsan *et al.* (19) | Human pharmacological triggering study | 53 | List of 10 triggers | Stress was the most common reported spontaneous trigger (26/53). Good agreement between stress and premonitory triggered mood change (64%) |
| 2021, Vives-Mestres *et al.* (30) | Observational prospective longitudinal cohort study | 136 patients with CM (8216 migraine days) | Perceived stress rated once a day (0-10 scale) | Higher perceived stress was associated with higher peak severity. However, there were large differences in individuals' reporting of peak severity and in the relationship between perceived stress and peak severity |

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**Table 1.** Continued from previous page.

| Publication year, authors | Study design | Sample size (n) | Methods to evaluate stress | Main findings on stress as a trigger |
|---|---|---|---|---|
| 2021, Kato *et al.* (26) | Retrospective analysis of self-reported data via the Migraine Buddy smartphone application | 163,176 users in USA (1,116,605 migraine records) | List of triggers | The proportion of stress-related migraine attacks peaked on March 21 to 23 following the declaration of the COVID-19 national emergency one week before a spike in the number of COVID-19 cases in the United States |
| 2021, Van Casteren *et al.* (21) | Cross-sectional study | 6,786 (5,725 females and 1,061 males) | Online questionnaire with 11 items on trigger factors | Top three most reported triggers regarding to sex:<br>Female, 2° most common (77%)<br>-Male, 1° most common (69%)<br>-Female patients reported stress as a migraine trigger more often than men |
| 2023, Ashina *et al.* (36) | Prospective study | 46 | List of 11 triggers | Stress was the third most common trigger reported at baseline (58.7%)<br>After 3 months of galcanezumab treatment, a reduction of the occurrence of headache after stress as a trigger was observed only in the super-responders (≥70% reduction in monthly migraine days) |
| 2025, Thuraiaiyah *et al.* (18) | Cross-sectional study | 632 | Semi-structured interview | Stress was the second most common trigger reported by patients (67.7%) |
| 2025, Elmazny *et al.* (14) | Cross-sectional study | 515 | Questionnaire about the knowledge of common migraine triggers | Stress emerged as the trigger with the highest awareness level (93.4%) followed by sleep-related issues |

CM, chronic migraine; PSS, Perceived Stress Scale; DASS-21, Depression, Anxiety, and Stress Scale 21; GAD-7, Generalized Anxiety Disorder-7; ISI, Insomnia Severity Index; PHQ-9, Patient Health Questionnaire-9.

During stressful conditions, glucocorticoids are physiologically released through the HPA axis to maintain homeostasis. (33) Although the immediate HPA response to exogenous stressors is advantageous, its chronic activation through chronic or traumatic stress can result in HPA axis dysregulation and potential health issues. (33) Preclinical evidence showed that stress can lower the threshold for CSD induction through both α2-adrenergic and glucocorticoid receptors. (34) The role of glucocorticoid receptors was further confirmed by the evidence that pre-administration of a glucocorticoid receptor antagonist normalized the increased CSD frequency induced by corticosterone administration in a transgenic mouse model of familial hemiplegic migraine type 1. In contrast, despite the rise in plasma corticosterone levels, restraint stress alone did not influence the CSD threshold, suggesting that the increase in corticosterone levels occurring during acute stress may not be sufficient to reduce the CSD threshold by itself due to the presence of multiple positive and negative modulators. (10) In line with these findings, Balkaya *et al.* showed that neither acute nor chronic stress affected the electrical CSD threshold, while relief after chronic stress did. (12) Additional data on the effect of stress on cortical excitability has also been provided in humans using visual evoked potentials, with subjects who reported stress as a migraine trigger having deficient habituation after repetitive visual stimulation. (35) Interestingly, one clinical study reported a reduction in the ability of stress to act as a migraine trigger only in patients who achieved a ≥70% reduction in monthly migraine days (super-responders) after three months of galcanezumab treatment, suggesting that the decrease in migraine frequency may reverse the brain excitability and responsivity of neurons involved in generating certain triggers. (36)

Stress can also predispose peripheral structures to sensitization through both the HPA axis and melanocortin signaling. (37) Indeed, chronic stress reduces the mechanical withdrawal threshold (11) and induces facial mechanical hypersensitivity in adult female and male mice, resulting in a hyperalgesic priming that is reversed by the administration of the calcitonin gene-related peptide monoclonal antibody. (38) A relationship between stress and allodynia also emerged in a cross-sectional human study, further confirming the influence of stress on pain perception. (39)

In addition to the release of glucocorticoids, the hypothalamus plays a major role in modulating the impact of stress on pain perception through direct anatomic connections and the release of neuropeptides. The hypothalamus is anatomically and functionally connected with several cerebral areas, including the trigeminocervical complex (40,41) and other regions implicated in the modulation of nociception, such as the dorsal ventromedial medulla. (42) Additionally, the hypothalamus can influence nociceptive processing by releasing orexin A and orexin B to numerous areas involved in pain perception. (43)

Biological sex differences seem to play a significant role in all these mechanisms. Hu *et al.* showed that while the synthesis of corticosterone and activation of the glucocorticoid receptor are necessary to trigger migraine-like behaviors after repeated stress, they are only sufficient in females. (44) A more pro-

nounced stress-induced shift in the balance of inflammatory mediator expression was found in dural immune cells of females. (45) This is further supported by the clinical evidence that females report migraine triggers to be provocative of their attacks more frequently than males, suggesting that biological sex differences play a role in lowering migraine threshold. (21) Additionally, a sexually dimorphic mechanism has also been shown on the hypothalamic dynorphin/kappa opioid receptor (KOR). Through activation of hypothalamic dynorphin/KOR, stress may increase circulating prolactin, leading to the dysregulation of prolactin receptor isoforms and resulting in female-selective sensitization of trigeminal nociceptors. These findings suggest a possible mechanistic connection between hypothalamic activation caused by stress and the trigeminal nociceptor effectors responsible for trigeminal sensitization and migraine-like pain. (46)

## Discussion and Conclusions

Given all the above-mentioned evidence, it is tempting to hypothesize that stress, through the hypothalamus and HPA activation, may act as a "catalyst" for migraine attacks by influencing cortical excitability and predisposing to nociception; however, to make stress an effective trigger, other permissive conditions must be present, including the patient's state and other biological factors. (2)

The clinical relationship between stress and the increased likelihood of migraine attacks is straightforward. The hypothalamus plays a pivotal role in this relationship by directly influencing pain-modulating regions and by releasing glucocorticoids and other neuropeptides that can influence cortical excitability and sensitize the trigeminal system. However, stress cannot drive a migraine attack by itself, and it can act as a "catalyst" if other permissive factors are present. These include the patient's state of brain excitability and other biological factors, such as the female sex. For these reasons, although it is a common migraine trigger, its variations cannot be used to predict an impending attack. Additional studies are needed to fully elucidate the relationship between stress and migraine attacks.

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