UDC: 616.858-008.6 + 612.397

CLINICAL CORRELATES OF CENTRAL SENSITIZATION AND AUTONOMIC-PSYCHOEMOTIONAL DYSFUNCTION IN TRIGEMINAL NEURALGIA

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Annotation. *Trigeminal neuralgia is a severe neuropathic facial pain disorder characterized by recurrent unilateral paroxysmal attacks of electric shock-like or stabbing pain, frequently triggered by otherwise innocuous sensory stimuli. Although neurovascular compression and focal demyelination of the trigeminal root represent major mechanisms in classical disease, contemporary evidence indicates that the clinical phenotype cannot be explained exclusively by peripheral pathology. Repeated nociceptive input may induce adaptive and maladaptive changes within the trigeminal brainstem complex, thalamocortical networks, limbic structures, and descending pain-modulatory systems, thereby contributing to central sensitization and altered pain processing [1–8].Recent quantitative sensory testing studies demonstrate subtle bilateral abnormalities in thermal and pain processing in patients with trigeminal neuralgia, supporting the concept that central sensory modulation may occur even when conventional neurological examination is normal [9,10]. Neuroimaging studies similarly identify structural and functional abnormalities involving the thalamus, cingulate cortex, insula, frontal regions, cerebellum, and other pain-related networks [11–14]. In parallel, autonomic studies have demonstrated abnormal cardiovascular responses to experimental pain, with increased sympathetic and reduced parasympathetic reactivity in patients with trigeminal neuralgia [15].The psychological burden of the disease is substantial. Systematic reviews and population-based studies indicate increased risks of anxiety, depressive disorders, sleep disturbances, functional limitation, and reduced quality of life [16–19]. These factors are not merely consequences of pain; they may participate in a bidirectional pain–emotion–sleep interaction capable of amplifying central pain processing and worsening disability. The present review synthesizes contemporary evidence regarding the relationships between peripheral trigeminal pathology, central sensitization, autonomic dysregulation, anxiety, depression, sleep disturbance, and functional impairment. An integrated clinical model is proposed to support multidimensional assessment and individualized management of patients with trigeminal neuralgia.*

Keywords: *trigeminal neuralgia; central sensitization; autonomic dysfunction; psychoemotional dysfunction; anxiety; depression; sleep disturbance; quantitative sensory testing; neuroplasticity; neuropathic pain; quality of life.*

КЛИНИЧЕСКИЕ КОРРЕЛЯТЫ ЦЕНТРАЛЬНОЙ СЕНСИТИЗАЦИИ И ВЕГЕТАТИВНО-ПСИХОЭМОЦИОНАЛЬНОЙ ДИСФУНКЦИИ ПРИ НЕВРАЛГИИ ТРОЙНИЧНОГО НЕРВА

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Аннотация. *Невралгия тройничного нерва является тяжелым нейропатическим болевым синдромом, характеризующимся повторяющимися односторонними пароксизмами чрезвычайно интенсивной боли в зоне иннервации тройничного нерва. Несмотря на доказанную роль нейроваскулярного конфликта и очаговой демиелинизации корешка тройничного нерва при классической форме заболевания, современные представления о патогенезе значительно шире и включают изменения центральной обработки болевых сигналов, нейропластичность, нарушение нисходящей модуляции боли, вегетативную реактивность и психоэмоциональные факторы [1–8].Результаты количественного сенсорного тестирования свидетельствуют о наличии у части пациентов двусторонних изменений температурной и болевой чувствительности, которые могут отражать изменения центральной сенсорной обработки даже при отсутствии выраженного неврологического дефицита при стандартном обследовании[9,10].Нейровизуализационные исследования выявляют функциональные и структурные изменения таламуса, островковой коры, поясной извилины, префронтальных областей, мозжечка и других структур, участвующих в формировании и модуляции боли [11–14].Экспериментальные исследования также демонстрируют изменение сердечно-вегетативной реактивности при болевой стимуляции, характеризующееся усилением симпатической и снижением парасимпатической активности [15].Значимым компонентом заболевания является психоэмоциональная нагрузка. У пациентов с невралгией тройничного нерва повышается риск тревожных, депрессивных и нарушений сна, а также*

значительно ухудшается качество жизни [16–19]. Психологические факторы следует рассматривать не только как следствие хронической боли, но и как потенциальные модуляторы центральной обработки сенсорных сигналов. В настоящем обзоре обобщены современные данные о взаимодействии периферической тригеминальной патологии, центральной сенситизации, вегетативной дисрегуляции, тревоги, депрессии и нарушений сна. Предложена интегративная клиническая модель, ориентированная на комплексную диагностику и индивидуализацию лечения.

Ключевые слова: *невралгия тройничного нерва; центральная сенситизация; вегетативная дисфункция; тревога; депрессия; нарушения сна; количественное сенсорное тестирование; нейропластичность; нейропатическая боль; качество жизни.*

UCH SHOHLI NERV NEVRALGIYASIDA MARKAZIY SENSIBILIZATSIYA VA VEGETATIV-PSIXOEMOTSIONAL DISFUNKSIYASINING KLINIK KORRELYATLARI

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Annotatsiya. *Uch shoxli nerv nevralgiyasi yuz sohasida juda kuchli, qisqa davom etuvchi, paroksizmal og‘riq xurujlari bilan kechadigan og‘ir neyropatik og‘riq sindromidir. Kasallikning klassik shaklida uch shoxli nerv ildizining neyrovaskulyar kompressiyasi va fokal demiyelinizatsiyasi muhim patogenetik omillar hisoblanadi. Biroq zamonaviy tadqiqotlar kasallik klinikasini faqat periferik nerv zararlanishi bilan izohlash yetarli emasligini ko‘rsatmoqda. Takroriy patologik afferent impulslar trigeminal miya ustuni kompleksi, talamokortikal tarmoqlar, limbik tuzilmalar va og‘riqni nazorat qiluvchi markaziy tizimlarda neyroplastik o‘zgarishlarni yuzaga keltirishi mumkin [1–8].Miqdoriy sensor testlash uch shoxli nerv nevralgiyasi bo‘lgan bemorlarda ikki tomonlama termal va og‘riq sezgirligi o‘zgarishlari mavjudligini ko‘rsatib, an’anaviy nevrologik tekshiruv normal bo‘lgan hollarda ham markaziy sensor qayta ishlashning buzilishi mumkinligini ko‘rsatadi [9,10]. Neyroimaging tadqiqotlarida talamus, insula, singulyar korteks, frontal sohalar, miyacha va boshqa og‘riq bilan bog‘liq miya tarmoqlarida strukturaviy va funksional o‘zgarishlar aniqlangan [11–14]. Vegetativ tizimni o‘rgangan tadqiqotlarda og‘riqli stimulyatsiya vaqtida simpatik faollikning kuchayishi va parasimpatik javobning pasayishi kuzatilgan [15].Kasallikning psixoemotsional yuklamasi ham muhim. Uch shoxli nerv nevralgiyasi xavotir, depressiya, uyqu buzilishi, kundalik faoliyatning cheklanishi va hayot sifatining pasayishi bilan bog‘liq [16–19]. Ushbu omillar faqat og‘riqning oqibati emas, balki og‘riqni markaziy qayta ishlash jarayonlarini kuchaytiruvchi ikki tomonlama tizimning tarkibiy qismlari bo‘lishi mumkin. Ushbu sharhda periferik trigeminal patologiya, markaziy sensibilizatsiya, vegetativ disfunksiya, xavotir, depressiya va uyqu buzilishlarining o‘zaro munosabati tahlil qilinadi hamda bemorlarni kompleks baholash uchun integrativ klinik model taklif etiladi.*

Kalit so‘zlar: *uch shoxli nerv nevralgiyasi; markaziy sensibilizatsiya; vegetativ disfunksiya; xavotir; depressiya; uyqu buzilishi; miqdoriy sensor testlash; neyroplastiklik; neyropatik og‘riq; hayot sifati.*

Abstract. Trigeminal neuralgia is a disabling neuropathic pain disorder characterized by recurrent unilateral paroxysmal attacks of severe facial pain, commonly described as electric shock-like, stabbing, or shooting pain. Classical trigeminal neuralgia is strongly associated with neurovascular compression and focal demyelination of the trigeminal root; however, these peripheral mechanisms do not fully explain the diversity of clinical phenotypes or the persistence of pain-related disability [1–8]. Accumulating evidence suggests that repetitive trigeminal nociceptive input may produce functional reorganization of the trigeminal brainstem complex and higher-order pain networks. Quantitative sensory testing has demonstrated bilateral alterations in thermal and pain processing, while neuroimaging studies have identified structural and functional abnormalities in the thalamus, insula, cingulate cortex, frontal regions, cerebellum, and other components of the pain network [9–14]. These observations provide a neurobiological framework for considering central sensitization as a clinically relevant mechanism in at least a subgroup of patients. Autonomic regulation represents another potentially important component. Experimental pain testing has demonstrated exaggerated sympathetic and reduced parasympathetic cardiac reactivity in patients with trigeminal neuralgia compared with healthy controls [15]. Psychoemotional dysfunction is also clinically relevant. Patients with trigeminal neuralgia demonstrate increased risks of anxiety, depressive disorders, sleep disturbance, and impaired quality of life [16–19]. Recent systematic evidence further suggests that psychological symptoms may improve following effective surgical treatment, supporting the existence of a dynamic interaction between pain and emotional well-being. The available evidence supports a multidimensional model in which peripheral trigeminal

pathology, central sensitization, autonomic reactivity, sleep disturbance, anxiety, depression, and behavioral avoidance interact. Therefore, clinical assessment should not be limited to pain intensity and attack frequency. Sensory phenotype, psychological state, sleep quality, functional impairment, and appropriate neuroimaging should also be considered. Future longitudinal studies integrating quantitative sensory testing, autonomic measurements, neuroimaging, and standardized psychological assessment may facilitate identification of biologically meaningful phenotypes and contribute to personalized treatment strategies.

Objectives. The present review aimed to evaluate contemporary evidence regarding central sensitization and autonomic-psychoemotional dysfunction in patients with trigeminal neuralgia and to determine their potential clinical correlates.

Materials and Methods. Narrative and analytical review focused on trigeminal neuralgia, central sensitization, autonomic dysfunction, psychological comorbidity, sleep disturbance, neuroimaging, and contemporary treatment.

Epidemiology and clinical significance. Trigeminal neuralgia is an uncommon but highly disabling neurological disorder. Epidemiological estimates vary considerably because historical studies used different diagnostic criteria and coding systems. A recent global systematic review and meta-regression including more than 170 million individuals estimated a pooled incidence of approximately 25.33 cases per 100,000 person-years and an annual prevalence of approximately 45.38 cases per 100,000 inhabitants [1]. Earlier systematic review data similarly demonstrated a predominance among women and greater involvement of the maxillary and mandibular divisions [2]. The clinical significance of trigeminal neuralgia is disproportionate to its epidemiological frequency. Pain attacks may be extremely brief, but their intensity and unpredictability can profoundly affect eating, speaking, facial hygiene, sleep, professional activity, and social interaction. The characteristic attacks are often triggered by innocuous stimuli such as touching the face, speaking, chewing, washing, or brushing the teeth. This unusual relationship between an apparently harmless sensory stimulus and extreme pain suggests that trigeminal neuralgia represents not simply increased nociceptive input but abnormal transformation of sensory information into pain.

Peripheral pathology and neurovascular compression. The classical pathophysiological model proposes that neurovascular compression of the trigeminal root entry zone causes focal demyelination. Histopathological evidence supports demyelination of sensory fibers, particularly in the proximal central nervous system portion of the trigeminal root [3,4]. Demyelination may facilitate ectopic impulse generation and ephaptic transmission between adjacent axons. Such pathological electrical communication can explain why a weak mechanical stimulus may produce synchronous high-frequency activity interpreted centrally as severe pain. However, neurovascular contact is not synonymous with symptomatic trigeminal neuralgia. Vascular contact may occur in individuals without clinical disease, and therefore radiological identification of contact should be interpreted in the context of clinical phenotype [5,6].The European Academy of Neurology guideline recommends magnetic resonance imaging as part of the diagnostic evaluation because secondary causes should be excluded and the presence and anatomical characteristics of neurovascular relationships may influence treatment selection [6].Thus, peripheral pathology represents an important initiating mechanism, but it does not necessarily account for all downstream manifestations.

Central sensitization as an additional mechanism. Central sensitization refers to increased responsiveness of central nociceptive neurons to afferent input. In clinical terms, this may manifest as hyperalgesia, allodynia, temporal summation, expanded receptive fields, and increased responsiveness to repetitive stimulation. In trigeminal neuralgia, the evidence for central sensitization is emerging rather than definitive. The most convincing evidence comes from quantitative sensory testing and neuroimaging. An observational study of patients with idiopathic trigeminal neuralgia demonstrated subtle bilateral changes in warm and cold detection thresholds despite the absence of major sensory abnormalities on routine clinical examination [9]. These bilateral abnormalities are difficult to explain exclusively by a unilateral peripheral lesion.

More recent quantitative sensory testing involving 65 patients with classical or idiopathic trigeminal neuralgia identified bilateral thermal hypoesthesia and pain hyperesthesia. Mechanical hyperalgesia and thermal hyperalgesia were prominent sensory phenotypes, while a sensory-loss phenotype was associated with poorer response to sodium-channel blockers [10]. These findings are clinically important because they suggest that trigeminal neuralgia may include biologically distinct sensory phenotypes. The presence of bilateral sensory abnormalities may reflect central modulation of trigeminal sensory processing rather than direct bilateral peripheral nerve injury.

Quantitative sensory testing and sensory phenotyping. Quantitative sensory testing provides a standardized method for examining somatosensory function. Parameters may include warm and cold detection thresholds, thermal pain thresholds, mechanical detection thresholds, mechanical pain

sensitivity, pressure pain thresholds, vibration detection, and wind-up responses.

In trigeminal neuralgia, quantitative sensory testing may identify abnormalities that are not detectable through routine bedside neurological examination [9,10]. The recent study of 65 patients demonstrated that sensory phenotyping was heterogeneous. Mechanical hyperalgesia was identified in approximately 49% and thermal hyperalgesia in approximately 35% of patients [10]. Of particular clinical interest, the sensory-loss phenotype was associated with a poorer response to sodium-channel blockers. Although this observation requires replication, it suggests that sensory phenotyping could eventually contribute to treatment stratification. The current evidence does not justify using quantitative sensory testing as a standalone diagnostic test for trigeminal neuralgia. Rather, it should be considered an adjunctive tool for mechanistic characterization.

Neuroimaging evidence of central remodeling.Neuroimaging has substantially expanded the understanding of trigeminal neuralgia.A systematic review and meta-analysis of structural and functional magnetic resonance imaging studies identified gray-matter reductions in multiple areas, including the thalamus, cingulate cortex, striatum, temporal cortex, insula, precentral and postcentral gyri, frontal cortex, and cerebellum [11].The same analysis identified increased gray matter in the periaqueductal gray and altered resting-state functional organization involving frontal regions, cingulate cortex, and thalamic structures [11].A subsequent systematic review found structural changes in both gray and white matter and emphasized the heterogeneity of functional alterations across studies [12].A more recent 2025 meta-analysis included 13 structural studies comprising 538 patients and 11 resting-state functional connectivity studies comprising 368 patients. Consistent alteration of the left thalamus was identified across analyses [13]. This finding is particularly relevant because the thalamus represents a major relay and integration structure in nociceptive processing.A 2026 activation likelihood estimation meta-analysis further demonstrated that different resting-state functional metrics identify partially distinct abnormalities, including reduced activity in the medial prefrontal cortex and increased activity in posterior cerebellar and temporal-pole regions [14].These results suggest that trigeminal neuralgia should not be conceptualized as dysfunction of a single “pain center”. Instead, the disease appears to involve a distributed network responsible for sensory discrimination, salience detection, emotional evaluation, cognitive control, and descending pain modulation.

Autonomic dysfunction. Pain is closely linked to the autonomic nervous system. Acute nociceptive stimulation normally produces cardiovascular and autonomic responses, including changes in heart rate, sympathetic activity, and parasympathetic regulation. A particularly relevant study evaluated autonomic reactivity in 12 patients with classical trigeminal neuralgia and 12 healthy controls [15]. At baseline, autonomic measures did not significantly differ between the groups. During a cold pressor test, however, patients with trigeminal neuralgia demonstrated greater increases in cardiac sympathetic activity and greater reductions in parasympathetic activity compared with controls [15].Interestingly, the magnitude of sympathetic reactivity was negatively associated with the number of daily pain paroxysms during the preceding week.This finding supports the concept that autonomic dysfunction in trigeminal neuralgia may be better understood as abnormal reactivity to pain rather than persistent autonomic failure.The direction of causality remains unresolved. Repeated severe pain may modify autonomic regulation, while altered autonomic responsiveness may in turn influence pain processing. Longitudinal studies are required to determine whether autonomic measures can predict disease severity or treatment response.

Anxiety and depression. Psychological dysfunction is one of the most clinically relevant dimensions of trigeminal neuralgia. The unpredictability of attacks can lead to anticipatory anxiety. Patients may begin to avoid eating, speaking, touching the face, social interaction, and other activities that they associate with pain provocation.

A systematic review examining the psychosocial impact of trigeminal neuralgia identified mild-to-moderate depressive symptoms, moderate-to-severe anxiety, and substantial functional limitation [16]. A nationwide population-based cohort study involving 3,273 individuals with trigeminal neuralgia and 13,092 matched controls demonstrated increased risks of subsequently diagnosed depressive, anxiety, and sleep disorders. Adjusted hazard ratios were 2.85 for depressive disorder, 2.98 for anxiety disorder, and 2.17 for sleep disorder [17]. These findings indicate that psychological morbidity is not an incidental phenomenon. However, it would be incorrect to interpret anxiety and depression as evidence that trigeminal neuralgia is a primarily psychological disorder. Instead, the relationship is bidirectional.

Quality of life and functional disability. The impact of trigeminal neuralgia extends beyond pain intensity. Patients may have difficulty eating, speaking, brushing their teeth, washing the face, sleeping, working, and participating in social activities.

Studies comparing trigeminal neuralgia with painful post-traumatic trigeminal neuropathy demonstrate significant impairment in oral and general health-related quality of life in both disorders [28].Anxiety and self-efficacy were associated with

oral and general health status, suggesting that psychological variables may influence functional outcomes even when pain intensity is not the only determinant.Therefore, treatment success should ideally be evaluated using multiple dimensions rather than pain intensity alone.

Interaction between central sensitization and psychoemotional dysfunction

Central sensitization and psychoemotional dysfunction should not be considered independent processes.The central nervous system integrates sensory information with emotional, cognitive, autonomic, and behavioral information. The insula, anterior cingulate cortex, prefrontal cortex, amygdala, thalamus, and brainstem structures participate in this integrated network. Repeated pain can increase attention to sensory signals and strengthen pain-related expectations. Anxiety may increase vigilance toward potential triggers. Sleep deprivation can further increase pain sensitivity. Autonomic arousal may reinforce the perception of threat. Thus, a patient with recurrent trigeminal attacks may gradually develop a state in which the nervous system becomes increasingly prepared to detect and respond to potential pain. This does not imply that the patient consciously exaggerates symptoms. Rather, it represents a neurobehavioral adaptation involving central sensory, autonomic, and emotional networks.

Pharmacological management. Carbamazepine and oxcarbazepine remain the principal first-line pharmacological treatments for classical trigeminal neuralgia [20–23].

The European Academy of Neurology guideline recommends carbamazepine or oxcarbazepine for initial pharmacological treatment, while lamotrigine, baclofen, gabapentin, pregabalin, and other agents may be considered in selected patients or when first-line therapy is insufficient or poorly tolerated [6].An umbrella review of pharmacological treatments confirmed that carbamazepine and oxcarbazepine remain the principal first-choice medications, while evidence for many alternative agents is less robust [20].A 2026 systematic review and meta-analysis comparing carbamazepine and gabapentin included 19 randomized trials and 1,650 participants. The authors reported comparable overall effectiveness estimates but emphasized limitations in the methodological quality of available trials [21]. Therefore, medication selection should take into account efficacy, tolerability, age, comorbidities, drug interactions, and the clinical phenotype.

Surgical treatment

Patients with inadequate pain control, intolerable medication adverse effects, or clinically appropriate neurovascular compression may require surgical assessment.

Available procedures include:

- microvascular decompression;
- percutaneous ablative procedures;
- stereotactic radiosurgery.

Microvascular decompression has the advantage of treating the presumed anatomical cause without intentionally destroying the trigeminal nerve.A systematic review and meta-analysis of nine studies involving 2,102 patients reported immediate complete pain freedom in 82.9% of patients and complete pain freedom at final follow-up in 64.7% [24].Another long-term series reported complete pain relief without medication in 71% of patients at 10 years after microvascular decompression [25].A separate cohort of 425 patients demonstrated pain-free rates of 89.3% at 1 year, 80.5% at 3 years, 75.6% at 5 years, and 71.2% at 8 years [26].A meta-analysis of 8,172 patients found a pooled recurrence rate of approximately 9.6% after microvascular decompression, with higher recurrence associated with atypical symptoms, non-arterial compression, longer disease duration, and other factors [27].These data demonstrate that microvascular decompression can provide durable pain relief, but recurrence remains possible.

Multidimensional clinical assessment

Domain	Parameters	Clinical purpose
Pain	Attack duration, frequency, intensity, triggers	Phenotype and treatment monitoring
Sensory function	Hypoesthesia, hyperalgesia, allodynia	Peripheral/central characterization
Quantitative sensory testing	Thermal, mechanical, pressure thresholds, wind-up	Mechanistic phenotyping
Neuroimaging	Brain MRI and trigeminal root assessment	Exclude secondary causes and characterize neurovascular conflict
Autonomic function	Heart rate and heart-rate variability response	Evaluate autonomic reactivity
Psychological status	Anxiety and depressive symptoms	Identify psychoemotional burden

Sleep	Sleep quality, duration, nocturnal disturbance	Identify pain-modulating factor
Function	Eating, speaking, work, social activity	Determine disability
Quality of life	Disease-specific and general measures	Evaluate global treatment effect

Such an approach is consistent with the modern concept of neuropathic pain assessment, in which clinical examination remains central and quantitative sensory testing is considered an adjunct rather than a standalone diagnostic method [30].

Results Summary. The literature demonstrates several converging observations.First, classical trigeminal neuralgia frequently involves neurovascular compression and focal demyelination of the trigeminal root [3–6].Second, sensory testing demonstrates subtle bilateral abnormalities in a proportion of patients, suggesting altered central sensory processing [9,10].Third, neuroimaging studies identify abnormalities in distributed pain-related networks rather than a single anatomical center [11–14].Fourth, autonomic responses to experimental pain may be exaggerated, with increased sympathetic and decreased parasympathetic activity [15].Fifth, anxiety, depression, sleep disorders and functional impairment are clinically important and occur at higher rates than would be expected from pain intensity alone [16–19].Sixth, effective treatment, particularly successful surgical treatment in appropriately selected patients, may improve both pain and psychological well-being [19,24–27].These observations support a model in which peripheral pathology initiates the disease in many patients, while central sensory processing, autonomic regulation, sleep, and psychological factors influence the severity and persistence of the clinical phenotype.

Conclusion. Postulated mechanisms of trigeminal neuralgia extend beyond a purely peripheral neurovascular model. Although neurovascular compression and focal demyelination remain fundamental mechanisms in classical disease, increasing evidence demonstrates alterations in central sensory processing, autonomic reactivity, psychological state, sleep, and brain network organization.

Central sensitization should therefore be considered a potential contributor to selected clinical phenotypes, particularly in patients demonstrating bilateral sensory abnormalities, hyperalgesia, allodynia, concomitant continuous pain, or substantial functional and psychological burden.

Autonomic studies suggest that patients with trigeminal neuralgia may exhibit an exaggerated sympathetic response and reduced parasympathetic response during painful stimulation. Psychological studies consistently demonstrate increased anxiety, depressive symptoms, sleep disturbance, and impaired quality of life.

The available evidence supports a multidimensional clinical approach in which pain phenotype, sensory phenotype, autonomic reactivity, psychological status, sleep, neuroimaging findings, and functional disability are considered together. Pharmacological treatment remains the initial therapeutic strategy for most patients, with carbamazepine and oxcarbazepine representing established first-line options. In selected refractory patients, botulinum toxin type A and neurosurgical procedures may provide additional benefit. Microvascular decompression offers durable pain relief for appropriately selected patients with classical trigeminal neuralgia and clinically relevant neurovascular conflict. Future prospective studies should combine quantitative sensory testing, autonomic assessment, neuroimaging, sleep monitoring, and standardized psychological evaluation. Identification of reproducible multimodal phenotypes may ultimately allow treatment to be tailored according to the dominant mechanisms in each patient rather than relying exclusively on pain intensity or anatomical findings. Thus, the most clinically relevant contemporary concept is that trigeminal neuralgia represents an interaction between peripheral trigeminal pathology and central sensory, autonomic, emotional, and behavioral regulation. Recognition of this interaction may improve diagnostic accuracy, treatment selection, rehabilitation, and long-term quality of life.

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