

Multimodal Study of Brain Structural Alterations, Functional Gradient Perturbations, and Transcriptomic Specialization in Trigeminal Neuralgia Using 5.0 Tesla MRI

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Research Article

Keywords: 5.0 T MRI, trigeminal neuralgia, gray matter volume, functional gradient, gene expression

Posted Date: September 24th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10949981/v1>

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Additional Declarations: No competing interests reported.

Abstract

Objective: This study aimed to harness the superior imaging capability of 5.0 T MRI to comprehensively characterize structural brain alterations, functional connectome gradient perturbations, and their underlying transcriptomic correlates in patients with trigeminal neuralgia (TN). By constructing an interpretative framework linking macroscopic gradient changes to microscale gene specialization.

Methods: Thirty-five TN patients and sixty-four healthy controls (HC) were enrolled. All participants underwent 3D high-resolution T1 and resting-state functional MRI (rs-fMRI) on a 5.0 T scanner. Functional connectome gradients were derived from the functional connectivity (FC) matrix via diffusion map embedding. Gray matter volume (GMV) was computed using voxel-based morphometry (VBM), and structure-function coupling was assessed via spatial correlations. Partial least squares (PLS) regression was employed to identify gene sets associated with gradient perturbations, followed by enrichment analysis to reveal the underlying biological processes.

Results: TN patients exhibited attenuated extreme values and increased intermediate values on the primary gradient, with altered gradient scores across multiple networks, indicative of a global gradient compression. GMV reductions were observed in the medial prefrontal cortex (mPFC) and superior frontal gyrus (SFG), while gradient scores were decreased in the mPFC and ventral anterior cingulate cortex (vACC). Spatial correlation analyses revealed structure-function decoupling in the sensorimotor (SMN), limbic (LIB), and frontoparietal (FPN) networks. Transcriptomic analyses showed that cortical gradient perturbations were strongly associated with genes involved in voltage-gated ion channels, membrane potential regulation, and neurotransmitter release. Significant enrichment of sodium channel, Na^+/K^+ -ATPase, and GABA receptor genes further corroborated the ion channelopathy basis of TN.

Conclusion: 5.0T MRI-based connectome gradient analysis reveals global compression and network-specific reorganization in TN. mPFC/vACC dedifferentiation reflects hierarchical collapse of descending pain inhibition, underpinning chronification. Gene enrichment corroborates ion channelopathy and suggests novel targets. This multi-scale framework integrates structure, function, and transcriptomics to advance mechanistic insights.

Introduction

Trigeminal neuralgia (TN) is a chronic neuropathic facial pain disorder characterized by paroxysmal, severe, electric-shock-like pain within the distribution of the trigeminal nerve, profoundly impairing patients' quality of life^{1, 2}. According to the third edition of the International Classification of Headache Disorders (ICHD-3)³, TN is classified into classical, idiopathic, and secondary subtypes. Classical TN accounts for approximately 75% of cases and is primarily attributed to neurovascular compression of the trigeminal root by the superior cerebellar artery or the petrosal vein, leading to focal demyelination and ectopic neuronal firing⁴. Although microvascular decompression (MVD) is the mainstay surgical treatment with significant efficacy, a subset of patients experience persistent or recurrent pain

postoperatively⁵⁻⁷. Moreover, some TN patients suffer from continuous pain, sensory disturbances, and mood alterations such as anxiety and depression^{6,8}, suggesting that structural and functional plasticity of the central nervous system plays a critical role in the chronification of TN.

Recent multimodal magnetic resonance imaging (MRI) studies have revealed widespread structural and functional abnormalities in TN, involving the thalamus, anterior cingulate cortex, insula, and default-mode network⁹⁻¹³. These alterations not only reflect pain processing but also relate to emotional regulation and cognitive dysfunction¹⁰.

However, most existing resting-state functional MRI (rs-fMRI) studies on TN have focused on connectivity strengths between specific regions or networks, often constrained to a few predefined networks, without investigating intrinsic alterations from a macroscopic functional hierarchy perspective¹². The brain hierarchical theory posits that functional connectivity is not randomly distributed; rather, the connectome is governed by a principal gradient axis extending from primary sensorimotor areas to transmodal default mode regions¹⁴⁻¹⁶. This primary functional gradient captures the macro-scale organization of the brain and offers a novel framework to understand disease-related functional reorganization. Gradient analysis decomposes the connectome into continuous dimensions, revealing topological properties of the connectome. Importantly, the cortical macro-scale axis also reflects underlying gene expression and microstructural attributes, indicating that functional architecture is supported by intact genetic and microstructural features^{17,18}.

Notably, most prior studies used conventional 3.0 T MRI, which, despite revealing central changes in TN, are limited in spatial resolution and signal-to-noise ratio, hampering the assessment of fine structural details. The 5.0 T MRI provides superior signal-to-noise ratio and spatial resolution¹⁹, improving image quality and enabling refined structural investigations.

Furthermore, the occurrence of familial TN cases suggests a genetic contribution, and several genes, such as *SCN8A*, *SCN9A*, and *SCN10A*, have been implicated²⁰⁻²². Although genes profoundly influence brain function, no study has yet examined how their spatially patterned gene expression modulate functional gradient perturbations in TN. Therefore, we aimed to leverage the advantages of 5.0 T MRI to explore the relationships among functional hierarchy perturbations, structural alterations, and gene expression in TN, thereby providing complementary insights into central mechanisms and lay empirical groundwork for novel therapeutic targets. We mapped functional gradients using resting-state fMRI to detect perturbations of the macro-scale hierarchy, assessed GMV from 3D-T1 images and correlated it spatially with gradient changes to reveal structure-function decoupling, and finally used the Allen Human Brain Atlas (AHBA)²³ transcriptomic data with enrichment analysis to identify potential genes underlying gradient perturbations.

Materials and Methods

This study used rs-fMRI to compute functional gradients, high-resolution T1-weighted imaging to assess GMV, and spatial correlation analyses to evaluate structure-function coupling. PLS regression was performed to link gene expression to gradient perturbations, followed by enrichment analysis to identify biological processes.

Participants

We enrolled 35 TN patients and 64 healthy controls from the First Affiliated Hospital of USTC. Inclusion criteria for patients: (1) diagnosis of TN according to ICHD-3; (2) complete acquisition of all required MRI sequences. Exclusion criteria: (1) secondary TN; (2) concurrent chronic pain conditions (e.g., migraine); (3) other neuropsychiatric disorders. Healthy controls had no history of neuropsychiatric disorders or chronic pain. All participants provided written informed consent, and the study protocol received ethical clearance from the Ethics Committee of the First Affiliated Hospital of USTC. The study was conducted in strict accordance with the principles of the Declaration of Helsinki.

Data Acquisition and Preprocessing

All scans were completed on a United Imaging uMR Jupiter 5.0 T scanner. For GMV, a gradient-recalled echo (GRE) sequence was used with the following parameters: TR = 9.1 ms, TE = 2.7 ms, flip angle = 9°, FOV = 224×224 mm², matrix = 320×320, slice thickness = 0.7 mm. rs-fMRI data were acquired using an EPI-BOLD sequence with parameters: TR = 1600 ms, TE = 25 ms, flip angle = 70°, FOV = 224×224 mm², matrix = 112×112, slice thickness = 2 mm, 350 time points, 75 slices per volume. Preprocessing of rs-fMRI followed standard steps including slice-timing correction, head-motion realignment, spatial normalization, nuisance-covariate regression, detrending, and band-pass filtering (see Supplementary Materials for details).

Gray Matter Volume Measurement

GMV was measured using VBM via the FSL-VBM toolbox²⁴. Briefly, gray matter was segmented from the 3D-T1 images and normalized to the MNI152 standard space. A cohort-specific gray matter template was created, and all individual images were registered to this template, with modulation to preserve GMV. The modulated images were smoothed using a Gaussian kernel with $\sigma = 3$ mm.

Gene Data Preprocessing

Microarray transcriptomic data were obtained from the Allen Human Brain Atlas (AHBA) provided by the Allen Institute for Brain Science^{23, 25}. The dataset comprises six post-mortem adult donors without neuropsychiatric disorders; we included data from two male donors. All tissue samples were matched to MNI coordinates following standardized procedures as described by Arnatkevičiūtė et al²³.

Functional Gradient Analysis

Functional connectomes were constructed from preprocessed rs-fMRI data by extracting time series for each gray-matter voxel and computing Pearson's correlation coefficients between all voxel pairs, yielding a voxel-wise FC matrix. Diffusion map embedding was then applied to project the high-dimensional connectivity matrix into a low-dimensional gradient space²⁶. Specifically, we retained the top 10% of strongest connections per node, set the rest to zero, retained the manifold structure, computed cosine similarity among retained nodes to construct the diffusion kernel, and extracted eigenvectors as gradient values²⁷. The diffusion parameter α was set to 0.5^{26, 28}. We computed the primary and secondary gradients (which explained the largest variance) and focused on the primary gradient, as it captures the macro-scale axis from primary sensorimotor to transmodal regions¹⁶.

Two-sample t-tests were performed to compare gradient scores between TN and HC, with age and sex as covariates. Results were corrected for multiple comparisons using false discovery rate (FDR) at $q < 0.05$. To delineate network-specific perturbations, we parcellated the cortex into seven networks using a standard cortical atlas and defined subcortical regions using the Harvard-Oxford subcortical atlas, yielding eight systems in total. Paired t-tests (covarying age and sex) were applied to test network-wise differences, with FDR correction.

Relating Gray Matter Volume to Functional Gradient Perturbations

To detect structure-function decoupling in TN, we performed spatial correlation analyses between mean GMV and mean functional gradient scores at both whole-brain and system-wise levels. All spatial correlations were assessed with permutation-based inference (10,000 permutations, $p < 0.05$) and further corrected using FDR. We also computed individual-level structure-function correlations and compared the correlations between groups using two-sample t-tests with FDR correction.

Relating Gene Expression to Functional Gradient Perturbations

To investigate the association between gene expression and gradient perturbations, we correlated the Z-map of group differences in the primary gradient with regional gene expression, separately for cortical and subcortical regions due to their distinct transcriptomic profiles. Microarray probes were matched to cortical and subcortical parcellation maps^{29, 30}. Given that the number of genes far exceeded the number of regions, we applied PLS regression³¹ to extract weighted gene components that best explained gradient perturbations. The Z-map of gradient differences served as the dependent variable. The first two PLS components (PLS-1, PLS-2) were determined by permutation testing (10,000 permutations, $p < 0.05$)³². Bootstrap resampling estimated the standard errors and 95% confidence intervals of gene weights; genes with high bootstrap weights (top 10%) were retained as robust

contributing transcripts. These genes were then entered into WebGestalt (<https://www.webgestalt.org/>)³³ for gene ontology enrichment analysis, with FDR correction at $q < 0.05$.

Statistical analysis

Two-sample t-tests, with age and sex as covariates, were employed to compare GMV and functional gradients between TN patients and HC. For multiple comparisons, FWE correction was applied to GMV results, while FDR correction was applied to functional gradient results. Spatial correlation analyses were performed to evaluate the relationship between GMV and functional gradients, with significance assessed by permutation tests(10,000 permutations). Group differences in these spatial correlations were examined using two-sample t-tests. Additionally, spatial correlation analyses were conducted to explore the association between functional gradient changes and PLS components in TN, also using permutation tests (10,000 permutations) for significance. For gene enrichment, the enrichment ratio (ER) was defined as the observed number of overlapping PLS-derived genes divided by the expected number under random chance. The FDR was used to correct for multiple comparisons, with $q < 0.05$ considered statistically significant.

Results

Demographic and clinical characteristics of both groups are summarized in Table 1. The TN patients were significantly older than the HC group, while no significant difference was observed in sex distribution.

Table 1 Demographic and clinical characteristics of TN patients and healthy controls			
Age mean (SD), years	TN n = 35	HC n = 64	P value
	54.89 ± 7.85	49.25 ± 11.2	0.0045
Sex (male/female)	15/20	25/39	0.7130
Disease duration[months, median (IQR)]	12.0(64.0)	-	-
Laterality(left/right)	15/20	-	-

P-values were derived from Welch’s independent-samples t-test (age) and χ^2 test (sex).

Primary Gradient Perturbations in TN

The primary gradient reflected a macro-scale axis from primary sensorimotor (visual) to transmodal default mode networks (Fig. 1A), consistent with previous normative connectome studies. The spatial similarity of primary gradient maps between TN and HC was high (Supplementary Fig. 4). The global histogram (Fig. 1B) showed that TN patients had attenuated extreme values, reduced peaks, and

increased intermediate values, suggesting a contraction of the functional hierarchy with reduced differentiation. Network-stratified analyses (Fig. 1C and Supplementary Table 1) revealed that TN patients exhibited increased gradient scores in the visual (VIS), sensorimotor (SMN), and dorsal attention (DAN) networks, and decreased scores in subcortical (SUB), limbic (LIB), and default mode (DMN) networks. The secondary gradient analysis results are presented in Supplementary Fig. 2.

Alterations in GMV and functional gradient

TN patients showed significant GMV atrophy in the mPFC and SFG (Fig. 2A). Correspondingly, gradient scores were significantly reduced in the mPFC and vACC (Fig. 2B). We then performed structure-function spatial correlations.

Structure-Function Decoupling in TN

At the whole-brain level, no significant spatial correlation was detected between GMV and gradient in either group (Fig. 3A). However, at the network-stratified level, significant correlations were observed in SMN, LIB, and FPN. In SMN and LIB, both groups showed negative correlations; TN exhibited weaker correlation in SMN and stronger correlation in LIB relative to HC. In FPN, both groups showed positive correlations, with TN showing weaker correlation (Fig. 3B). Individual-level analysis further revealed significant differences between TN and HC in LIB and FPN, indicating structure-function decoupling (Fig. 3C). Correlations between the secondary gradient and GMV are reported in Supplementary Fig. 3.

Transcriptomic Correlates of Functional Gradient Perturbations

In the cortex, two PLS components explained 36% (PLS-1, $p < 0.001$) and 17% (PLS-2, $p < 0.05$) of the covariance between gradient alterations and transcriptomic profiles (Supplementary Fig. 4). PLS-1 exhibited high expression in SMN and DMN, and low expression in FPN and LIB; PLS-2 showed high expression in VIS and low in VAN (Fig. 4A). Gene set enrichment analyses revealed that PLS-1 genes were involved in ion transport, axon signaling, membrane potential regulation, and synaptic signaling; PLS-2 genes were over-represented in pathways governing neuronal development and sensory system development (Fig. 4B). Notably, significant enrichments were observed for sodium channel genes (*SCN9A*, *SCN1B*), Na^+/K^+ -ATPase genes (*ATP4A*, *ATP1B*), potassium channel genes (*KCNC1*, *KCNH6*, *KCNQ5*), and GABA receptor genes (*GABRA3*, *GABRB1*), with the latter showing down-regulation.

In subcortical regions, PLS-1 explained 52% of the covariance ($p < 0.001$); whereas PLS-2 did not reach statistical significance ($p = 0.787$) (Supplementary Fig. 4). PLS-1 expression was high in the thalamus and striatum, and low in the caudate nucleus. Gene set enrichment analyses showed that subcortical genes were mainly involved in vesicle-mediated transport and cytoplasmic translation (Fig. 5).

Discussion

Using 5.0 T MRI and integrating multimodal imaging with transcriptomic data, this study, for the first time, systematically revealed a compression and topological remodeling of the functional connectome gradient in TN at the whole-brain level, and elucidated the links between these macroscopic changes, gray matter structural damage, and specific gene expression profiles¹⁴. The brain's macro-scale axis represents an ordered arrangement from primary sensorimotor to transmodal default-mode network, with primary networks at one pole and higher-order integrative networks at the other¹⁵. Both TN and HC exhibited this continuous hierarchical axis. However, compared with HC, TN patients showed primary-gradient compression toward the center, with attenuated extremes and increased intermediate values. This contraction is not a simple global shift but a relative loss of extreme values, leading to reduced hierarchical differentiation and aberrantly increased crosstalk between primary and higher-order networks^{34, 35}. Such changes may amplify incoming nociceptive inputs and compromise integrative regulatory capacity, potentially explaining the phenomenon of “trigger zones” in TN³⁶. Notably, similar gradient contraction has been reported in other chronic pain conditions³⁷, suggesting that hierarchical disorganization may constitute a shared neurobiological hallmark of chronic pain pathophysiology³⁸.

At the individual level, GMV atrophy in SFG and mPFC, along with decreased gradient scores in mPFC and vACC, aligns with prior findings. The mPFC and vACC are core nodes of the descending pain inhibitory system^{39, 40}. Their structural loss and functional de-differentiation – i.e., a shift from a higher-order cognitive/abstract pole toward a sensorimotor-like identity – lends support to the notion of a compromised top-down inhibitory control, which may underpin pain chronification and the associated affective comorbidities^{14, 41}.

Structure-function coupling is fundamental to brain function⁴². The global spatial correlation between GMV and gradient remained similar between TN and HC, suggesting that the overall brain architecture is preserved and the hierarchical scaffold is not destroyed, but rather network-specific neuroplastic rearrangements occur. Network-stratified analyses confirmed structure-function decoupling in SMN, LIB, and FPN, indicating selective vulnerability of networks subserving pain processing and emotional regulation. Individual-level comparisons further highlighted significant decoupling in LIB and FPN, suggesting that long-term pain-related emotional changes have reshaped the macro-connectivity and internal spatial alignment of these networks⁴¹. Such dual decoupling implies that top-down emotional regulation is weakened while bottom-up aversive signals are amplified, which may account for why TN patients have difficulty modulating pain through cognitive coping strategies and are prone to affective comorbidities⁴³.

To unpack the molecular underpinnings of functional perturbations, we performed gene set enrichment analyses. In the cortex, PLS-1 genes were primarily involved in ion transport, membrane potential homeostasis, and neurotransmitter release – processes critical for excitability and action potential generation⁴⁴. Significant enrichment of sodium channel genes (e.g., *SCN9A*, *SCN1B*) is consistent with the established clinical efficacy of sodium channel blockers^{1, 45}. Moreover, our transcriptomic maps indicated elevated transcript levels for - Na⁺/K⁺-ATPase (*ATP4A*, *ATP1B*) and potassium channel genes

(*KCNC1*, *KCNH6*, *KCNQ5*), likely reflecting compensatory homeostatic responses aiming to sustain ionic equilibrium and neuronal repolarization, though insufficient to fully counteract pathological neuronal hyperexcitability. Conversely, GABA receptor genes (*GABRA3*, *GABRB1*) were down-regulated, which would plausibly attenuate inhibitory neurotransmission^{1, 22, 46}. These findings highlight potential novel therapeutic targets^{46, 47}. PLS-2 genes were involved in vesicle trafficking and nervous system development, suggesting ongoing neurodevelopmental processes that may relate to TN pathogenesis.

In subcortical regions, predominantly the thalamus, our AHBA-derived spatial maps revealed high expression of genes related to synaptic development and signaling, alongside low expression of cytoplasmic translation genes. The thalamus serves as a critical relay for sensory information^{48, 49}. The elevated synaptic signaling may promote aberrant amplification of nociceptive afferent signals, maintaining the thalamus in a hyper-excitable state. Conversely, suppressed translation may compromise protein biosynthesis and homeostatic adaptive regulation, rendering the thalamus a functionally labile nodal structure^{50, 51}. In light of these correlative findings, future pre-clinical and translational work may explore thalamic-targeted neuromodulation or strategies boosting neuronal protein biosynthesis as putative intervention avenues for refractory TN.

Several limitations should be acknowledged. First, we observed significant emotional-network decoupling, but we did not include standardized pain-related emotional scales to quantitatively correlate with imaging findings. Future studies should incorporate such scales to systematically examine interactions among pain, emotion, and brain function. Second, the transcriptomic data were derived from a small number of healthy donors, not from TN patients themselves. This inter-individual mismatch may limit the direct interpretation of spatial correlations and the dynamic transcriptional changes in disease states. Post-mortem transcriptomic data or in vivo transcriptomic imaging in TN patients would be valuable to confirm our findings. Third, this was a cross-sectional study; causality between structural/gradient changes and TN progression cannot be inferred. Longitudinal studies tracking changes before and after treatment would help clarify the plasticity and clinical relevance of these alterations.

In summary, using multimodal MRI, this study provides the first global view of functional connectome gradient perturbations in TN, characterized by global compression and local reorganization. We further established spatial associations between GMV atrophy to gradient changes, revealing structure-function decoupling in specific networks, indicating that chronic TN is not merely a peripheral neuropathy but also a condition of whole-brain macro-scale hierarchical remodeling. Although the thalamus has been the most extensively investigated seed region in previous studies, heterogeneous findings regarding its volume and function suggest that its phenotype is maybe influenced by disease duration^{10, 52}, subnuclei heterogeneity, and medication, making it an unstable biomarker. In contrast, our data nominate the mPFC and vACC as core neuroimaging signatures of TN, with both structural atrophy and functional gradient reduction, pointing to a functional dedifferentiation of the descending pain inhibitory system – a hierarchical collapse of higher-order cortical networks. We propose that TN fundamentally involves a

breakdown of the cortical pain-inhibitory hierarchy, with the thalamus playing a passive relay role, yet possibly affecting the process through synaptic and metabolic dyshomeostasis. This framework readily explains the chronification and affective-cognitive comorbidities of TN. Transcriptomic enrichment analysis further confirmed known risk-associated genes (e.g., *SCN9A*) and highlighted voltage-gated ion channels, synaptic signaling, and neurodevelopmental processes as potential intrinsic drivers of functional remodeling. These findings offer new insights into TN pathophysiology and provide a molecular basis for developing novel pharmacological targets.

Declarations

Acknowledgements

We sincerely acknowledge to all participants for their time, effort, and invaluable contribution to this research. We also acknowledge the Department of Radiology, The First Affiliated Hospital of USTC, for providing access to the 5.0T MRI scanner.

Author contributions

WYH, and CGA made substantial contributions to the conception, design, data acquisition, analysis, and interpretation, and drafted the manuscript. LMQ,CH, and XK contributed to data acquisition, analysis, and interpretation, and assisted in drafting the manuscript.YL contributed to the conception and design, and critically revised the manuscript for important intellectual content. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

Funding

This work was supported by the construction of a 5.0T ultra-high-field MRI musculoskeletal imaging protocol and a multi-center field strength-matched dataset, and enhancement of conventional field-strength musculoskeletal image quality(2023YFC240703).

Data availability

The informed consent obtained from the participants did not include permission for public sharing of individual raw data; therefore, these data cannot be made publicly available. De-identified data are available from the corresponding author upon reasonable request.. The gene expression data used for transcriptional analysis can be found in the ABHA database (<https://human.brain-map.org/static/download>).

Ethics approval and consent to participate

Approval was obtained from Medical Ethics Committee of the First Affiliated Hospital of USTC.All participants provided written informed consent.

Consent for publication

All authors authorize the publication.

Competing interests

The authors declare no competing interests.

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Figures

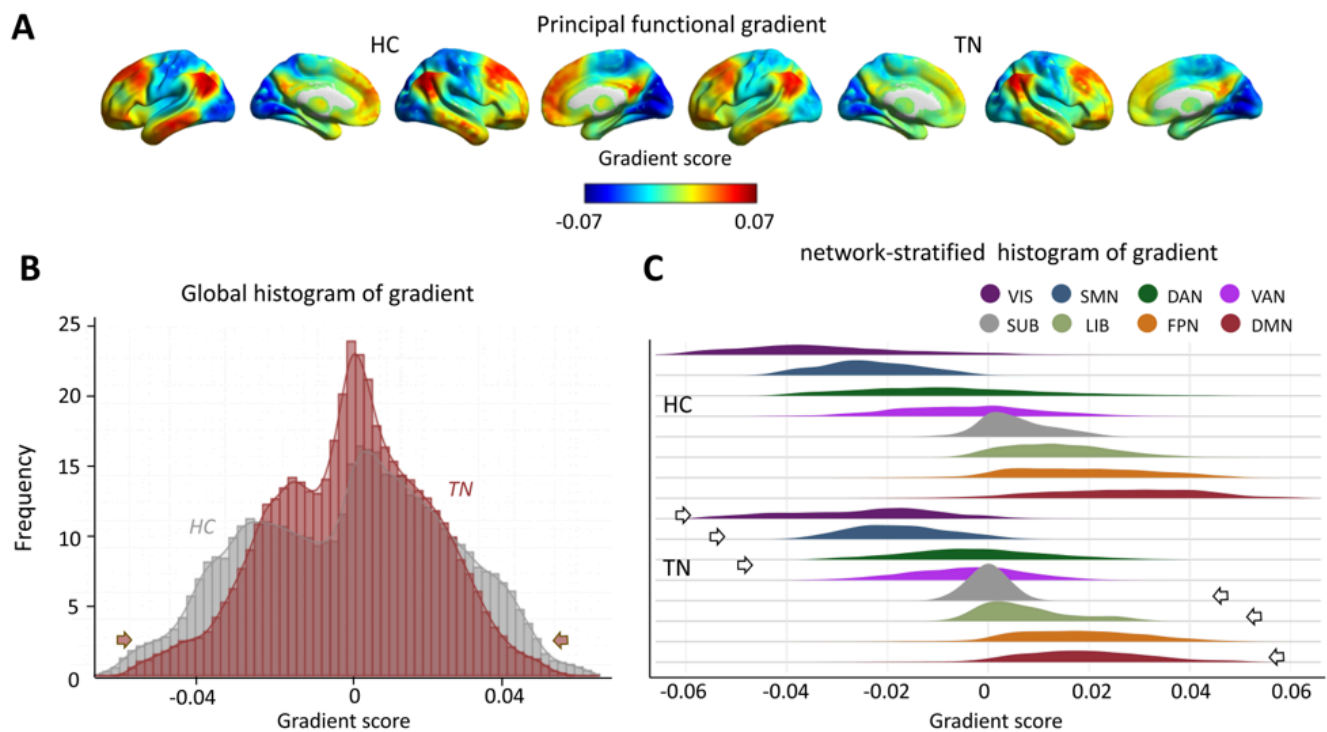


Figure 1

Connectome gradient maps in TN and HC. (A) Primary gradient showing a continuous transition from primary sensorimotor to default mode regions. (B) Global histogram of gradient values: TN patients show reduced extremes and increased intermediate values compared to HC. (C) Network-stratified gradient histogram with paired two-sample t-tests (covarying age and sex); arrows indicate direction of significant differences. FDR-corrected $p < 0.05$. VIS, visual network; SMN, sensorimotor network; DAN, dorsal attention network; VAN, ventral attention network; SUB, subcortical regions; LIB, limbic network; FPN, frontoparietal network; DMN, default mode network.

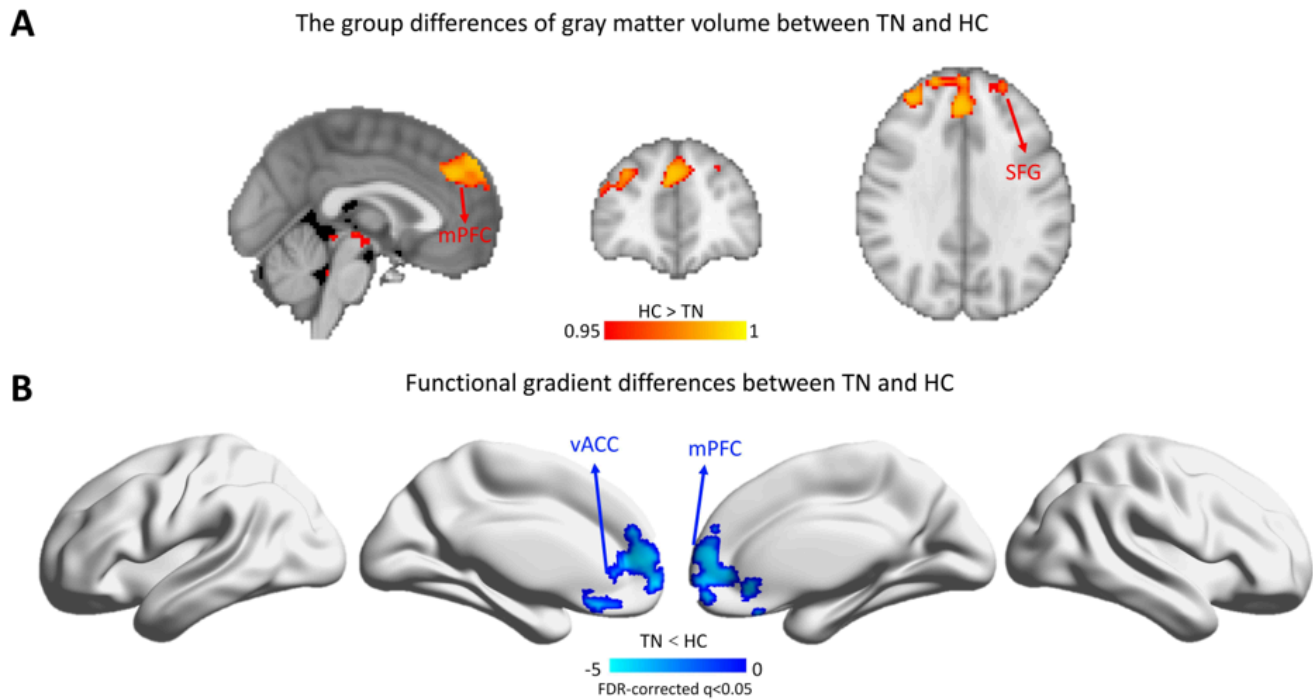


Figure 2

Differences in gray matter volume and functional gradient between trigeminal neuralgia patients and healthy controls. (A) Compared with HC, TN patients showed reduced gray matter volume in the superior frontal gyrus and medial prefrontal cortex. Statistical significance was set at $P < 0.05$ with family-wise error (FWE) correction. (B) Compared with HC, TN patients exhibited significantly decreased functional gradient values in the medial prefrontal cortex and ventral anterior cingulate cortex. False discovery rate (FDR) correction was applied, with $q < 0.05$ considered significant. mPFC, medial prefrontal cortex; SFG, superior frontal gyrus; vACC, ventral anterior cingulate cortex.

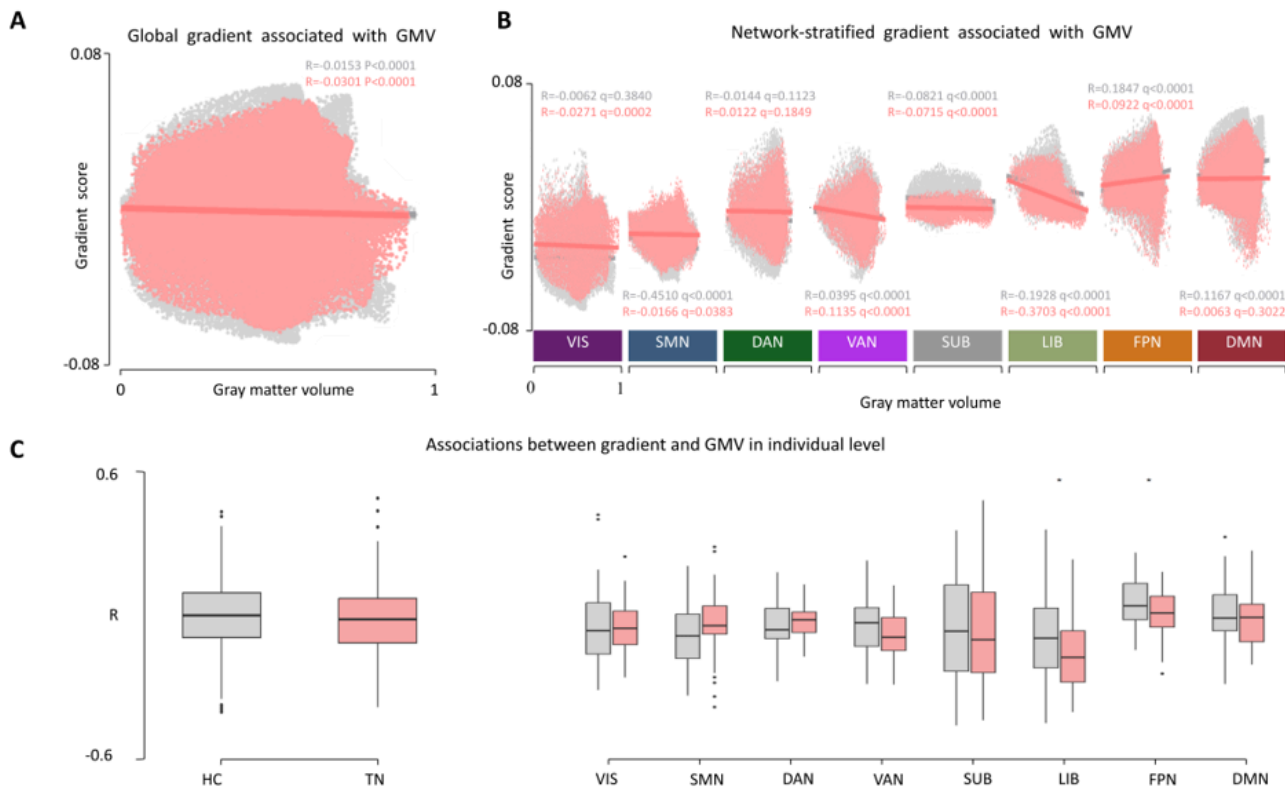


Figure 3

Correlation between gray matter volume and functional gradient, and the associated structure-function decoupling in TN patients. (A) Whole-brain correlation between GMV and gradient values in TN and HC. (B) Network-stratified correlations, with FDR-corrected q values. (C) Individual-level comparisons (two-sample t -test) of structure-function coupling between TN and HC, $*p < 0.05$, FDR corrected.

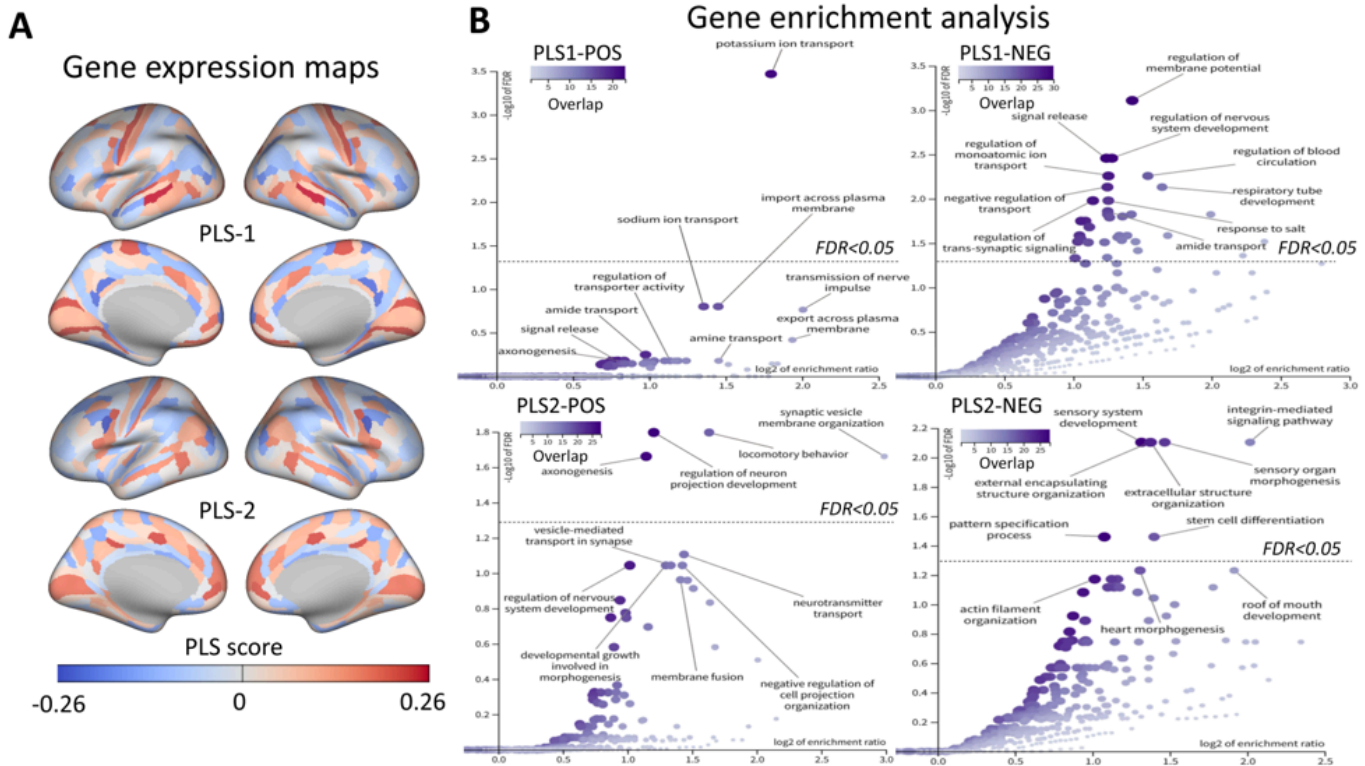


Figure 4

Cortical gene expression correlates of gradient alterations in TN. Cortical transcriptomic correlates. The association between gene expression and gradient changes was assessed via PLS regression. (A) PLS-1 and PLS-2 expression maps (weighted average of 10,027 genes). (B) Enrichment volcano plots: PLS-1 genes enriched in ion transport, axon signaling, membrane potential regulation; PLS-2 genes enriched in nervous system development. Color indicates gene count per biological process. PLS, partial least squares.

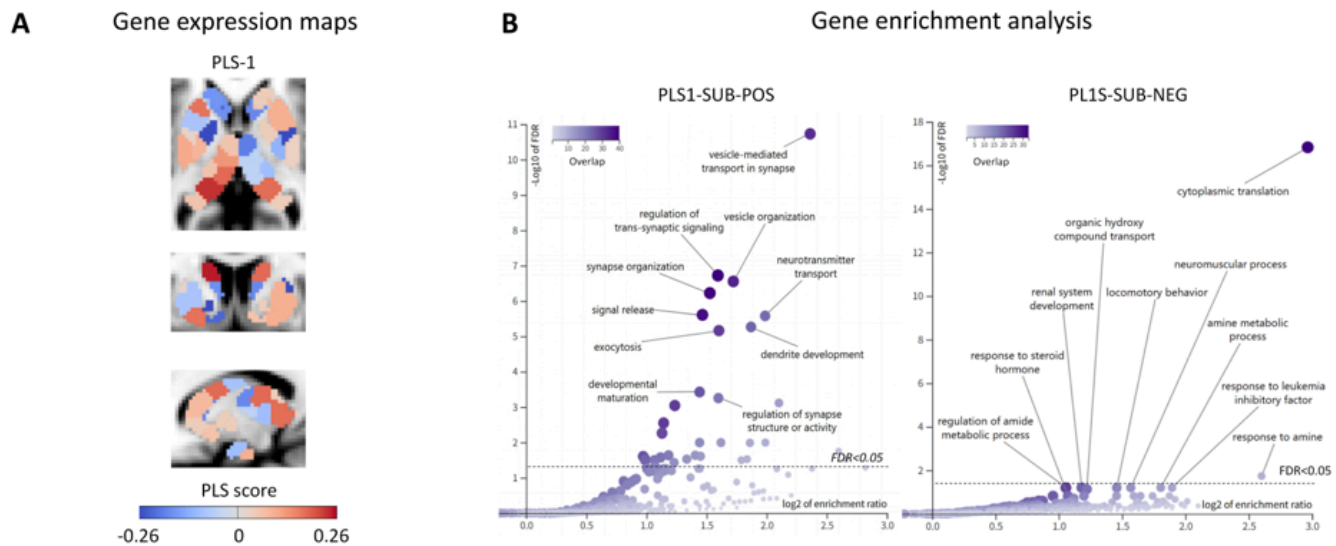


Figure 5

Subcortical transcriptomic correlates of gradient alterations in TN. The association between gene expression and gradient changes was assessed via PLS regression. (A) Gene expression map within subcortical regions. The color bar indicates PLS-1 scores, representing the weighted average expression level of 10,027 genes. (B) Gene enrichment analysis: genes associated with PLS-1 were significantly enriched in vesicle transport and cytoplasmic translation.

Supplementary Files

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- [SupplementaryMaterials.docx](#)