

Condylar Position-Dependent Cerebellar Connectivity Changes in Painful Temporomandibular Disorder: A Brief Report

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Short Report

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Abstract

The cerebellum contributes to sensory, cognitive, emotional, and pain-modulatory processes beyond motor coordination. In temporomandibular disorders (TMD), alterations in spontaneous cerebellar neural activity and strengthened functional connectivity with limbic structures have been reported, suggesting involvement of central neuroplastic mechanisms. Mandibular displacement and occlusal imbalance may further modulate brain networks related to motor regulation, sensory integration, and pain-related emotional processing.

In this study, magnetic resonance imaging(MRI) and diffusion tensor imaging(DTI) was used to examine cerebellar connectivity across different mandibular positions in a patient with painful TMD. Functional MRI and diffusion tensor imaging were acquired in three conditions: centric occlusion, centric relation, and stabilization splint. Cerebellar regions of interest were defined using SUIT parcellation, and position-dependent structural–functional connectivity was assessed using diffusion-based tractography and Δ -metrics ($\Delta = \text{MNI} - \text{COUNT}$).

No measurable cerebellar connectivity was detected in the centric occlusion condition. In contrast, both centric relation and splint positions demonstrated heterogeneous cerebellar connectivity patterns with substantial variability (centric relation: mean Δ 43.64, SD 101.48; splint: mean Δ 47.32, SD 106.89). Similarity between centric relation and splint connectivity profiles was low ($r = 0.28$; cosine similarity = 0.39), while large Euclidean distance and mean absolute difference values indicated marked divergence in network organization.

These findings indicate that mandibular position is associated with distinct cerebellar connectivity patterns in painful TMD, consistent with position-dependent neuroplastic adaptation. Integration of functional and diffusion MRI may help to characterize central nervous system involvement in TMD and support the development of individualized therapeutic strategies.

BACKGROUND

The cerebellum contributes to sensory integration, affective regulation, and pain modulation in addition to motor coordination^{1–4}. Neuroimaging studies in temporomandibular disorders (TMD) have reported altered spontaneous cerebellar activity and strengthened functional connectivity with limbic regions, supporting the concept of central neuroplastic involvement in chronic orofacial pain⁵. In parallel, mandibular displacement and occlusal imbalance have been associated with changes in brain networks related to motor regulation, sensory processing, and pain-related emotional appraisal^{6–8}.

However, it remains unclear whether clinically relevant mandibular positions used in TMD management are accompanied by distinct cerebellar connectivity patterns within the same individual^{9–11}.

To address this gap, we compared DTI MRI-derived cerebellar connectivity^{12,13} across three mandibular conditions—centric occlusion, centric relation, and stabilization splint—in a patient with painful TMD,

using SUIT-based cerebellar parcellation¹⁴ and diffusion-based tractography metrics integrated with functional mapping.

Methods

Magnetic resonance imaging was performed in a single patient with painful temporomandibular disorder under three mandibular conditions: centric occlusion, centric relation, and stabilization splint. Brain MRI included MRI and diffusion tensor imaging acquired during each condition. A neutral rest position was not scanned because brief discontinuation of splint use provoked symptom exacerbation.

Cerebellar regions of interest were defined using the Spatially Unbiased Infratentorial Template (SUIT) atlas in standard MNI space. Diffusion-based deterministic tractography was performed to generate cerebellar connectivity matrices representing streamline counts and endpoint distributions. Structural–functional integration was assessed using Δ -metrics calculated as the difference between MNI-based endpoint measures and streamline count–based connectivity (Fig. 1).

For each mandibular condition, Δ matrices were analyzed to quantify position-dependent similarity and divergence using Pearson correlation, cosine similarity, Euclidean distance, and mean absolute difference. Dimensionality reduction was performed using principal component analysis to characterize dominant sources of variance across cerebellar regions. All analyses were conducted in MATLAB (R2024a); tractography was performed in DSI Studio.

Results

Cerebellar connectivity differed across mandibular positions. In the centric occlusion (CO) condition, no reliable ROI-to-ROI cerebellar connections were detected, resulting in all-zero Δ matrices (Δ = MNI – COUNT). As illustrated by the correlation matrix and heatmap, the CO condition showed no measurable connectivity structure (Fig. 2,3).

Consequently, similarity metrics between CO and the other mandibular conditions could not be meaningfully computed. In contrast, both centric relation (CR) and stabilization splint conditions demonstrated measurable cerebellar connectivity with substantial heterogeneity (Fig. 4,5).

Heatmap visualization and ROI-to-ROI correlation matrices demonstrated organized but heterogeneous cerebellar functional connectivity in the splint condition (Fig. 4). The correlation matrix revealed stable positive associations across multiple cerebellar regions, including vermal and bilateral hemispheric ROIs, extending beyond the diagonal and indicating non-random functional coupling. Several clusters of moderate correlations were observed, while large uniformly zero or near-zero regions were absent, supporting the presence of structured cerebellar connectivity.

The corresponding Δ -matrix (Δ = MNI – COUNT) showed marked spatial heterogeneity across cerebellar ROI pairs (Fig. 3). Both positive and negative Δ values were present, with region-specific deviations

rather than a global directional shift. The distribution of Δ values varied across rows and columns, indicating differential divergence between tractography-based streamline counts and spatial endpoint-based connectivity measures among cerebellar regions. Notably, high-magnitude Δ values were confined to localized ROI combinations, whereas large portions of the matrix exhibited moderate values, consistent with distributed rather than focal connectivity differences.

Together, the correlation matrix and Δ -heatmap provide complementary representations of cerebellar connectivity in the centric relation condition, capturing both functional coupling patterns and region-specific structural–functional divergence without evidence of uniform or homogeneous network organization

For the CR condition, the mean Δ value was 43.64 (SD = 101.48), whereas the splint condition showed a mean Δ of 47.32 (SD = 106.89). Heatmap visualization and correlation matrices confirmed heterogeneous and spatially distributed Δ patterns in both conditions (Fig. 5).

Heatmap visualization and ROI-to-ROI correlation matrices demonstrated organized cerebellar functional connectivity in the centric relation condition (Fig. 5). The correlation matrix showed stable positive associations across multiple cerebellar regions beyond the main diagonal, indicating non-random functional coupling. Moderate correlation values were distributed across bilateral hemispheric and vermal regions, with preservation of left–right symmetry for homologous ROIs. Large contiguous regions of near-zero correlations were not observed.

The corresponding Δ -matrix ($\Delta = \text{MNI} - \text{COUNT}$) revealed marked spatial heterogeneity across cerebellar ROI pairs in the centric relation condition (Fig. 4). Both positive and negative Δ values were present, without evidence of a uniform directional shift across the matrix. High-magnitude Δ values were confined to localized ROI combinations, whereas the majority of entries demonstrated moderate values. The distribution of Δ values varied across rows and columns, reflecting region-specific divergence between tractography-based streamline counts and spatial endpoint-based connectivity measures.

Together, the correlation matrix and Δ -heatmap provide complementary representations of cerebellar connectivity in the centric relation condition, capturing structured functional coupling alongside heterogeneous structural–functional correspondence across cerebellar regions (Fig. 5).

Analysis of the ten ROI pairs with the largest absolute CR–Splint correlation differences revealed that these high-magnitude changes involved a restricted set of cerebellar regions. The most frequently represented regions were Left_VI and Left_CrusI, followed by Left_V, Left_IX, and Left_VIIIa. Additional regions appearing within the top-10 pairs included Left_CrusII, Left_X, Vermis_X, Right_VI, and Right_CrusI. Collectively, these regions span anterior, intermediate, and posterior cerebellar lobules as well as vermal territories, indicating that the largest correlation differences across conditions were distributed across multiple cerebellar subdivisions rather than confined to a single lobule

According to the SUI cerebellar atlas, the regions involved in the top-10 CR–Splint correlation differences encompass multiple functional subdivisions of the cerebellum.

Lobule VI (Left_VI, Right_VI) is located in the anterior–intermediate cerebellum and is primarily associated with sensorimotor integration, orofacial motor control, and pain-related sensorimotor processing. This lobule represents a transitional zone linking classical motor cerebellar territories with higher-order functional regions.

Crus I and Crus II (Left_CrusI, Right_CrusI, Left_CrusII) belong to the posterolateral cerebellar hemispheres and are predominantly involved in cognitive, associative, and affective functions. These regions are strongly connected with prefrontal, parietal, and limbic cortical areas and are implicated in cognitive control, emotional modulation, and higher-order integration of sensory information.

Lobule V (Left_V) forms part of the anterior cerebellar lobe and is classically related to primary motor functions, including coordination of voluntary movements and sensorimotor timing, particularly for orofacial and upper limb musculature.

Lobule VIIa (Left_VIIa) is situated in the posterior cerebellum and is associated with sensorimotor processing, motor execution, and integration of proprioceptive feedback, often considered part of the secondary motor representation within the cerebellum.

Lobule IX (Left_IX) is located in the inferior posterior cerebellum and has been linked to vestibular, autonomic, and multimodal integration processes, with additional involvement in affective and default-mode–related networks.

Lobule X (Left_X), corresponding to the flocculonodular lobe, plays a key role in vestibular processing, balance control, and visuomotor coordination. Its functional profile is closely tied to eye–head coordination and spatial orientation.

Finally, Vermis X (Vermis_X) represents the midline component of the flocculonodular lobe and is involved in axial motor control, vestibular integration, and autonomic regulation, reflecting the integrative role of the cerebellar vermis across motor and non-motor domains.

Pairwise comparison between CR and splint connectivity patterns revealed low similarity. Pearson correlation analysis yielded $r = 0.28$, and cosine similarity was 0.39. Divergence metrics further indicated marked differences between conditions, including a Euclidean distance of 2434.26 and a mean absolute difference of 72.37. These quantitative results are consistent with the visually distinct connectivity patterns observed in the corresponding correlation matrices and heatmaps.

Principal component analysis (PCA) demonstrated that cerebellar connectivity variability was distributed across multiple regions rather than dominated by a single component. In the CR condition, the first two principal components explained 25.15% and 23.00% of the variance, respectively, whereas in the splint condition they accounted for 16.40% and 15.35%. When PCA was restricted to the most variable

cerebellar regions, the first two components together explained more than 75% of the total variance, indicating that a limited subset of ROIs captured the dominant position-dependent differences (Fig. 5).

BRIEF DISCUSSION

This brief report demonstrates that cerebellar connectivity patterns vary markedly across clinically relevant mandibular positions in a patient with painful temporomandibular disorder. The absence of measurable cerebellar connectivity in centric occlusion contrasted with the presence of heterogeneous but distinct connectivity profiles in centric relation and stabilization splint conditions. These findings indicate that mandibular position is associated with position-dependent modulation of cerebellar structural–functional organization².

The low similarity between centric relation and splint connectivity patterns suggests that cerebellar engagement may not be uniformly expressed across occlusal conditions and may depend on the biomechanical and proprioceptive context of mandibular positioning^{9,10,11,14}.

Notably, the centric relation condition was associated with more coherent cerebellar organization alongside clinical pain reduction, whereas the splint condition showed persistent heterogeneity despite improved joint congruency on TMJ MRI. This dissociation underscores the potential relevance of central neural responses, in addition to peripheral joint alignment, in understanding treatment effects in TMD^{3,4,6–8}.

Several limitations should be acknowledged. This analysis is based on a single patient, precluding generalization. A neutral resting mandibular position could not be assessed due to symptom exacerbation, limiting comparison with an unstrained baseline. In addition, diffusion-based tractography is methodologically sensitive and its cerebellar application should be interpreted cautiously; therefore, the absence of detectable connectivity in centric occlusion warrants conservative interpretation^{12,13,17,18}. Despite these limitations, the present findings highlight the potential value of neuroimaging for probing central mechanisms associated with mandibular repositioning in TMD^{3,6,8}.

Declarations

Ethics approval

The study was conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments. Ethical approval was obtained from the Commission on Ethics and Academic Integrity of the Shupyk National Healthcare University of Ukraine (protocol No. 13/10, 17 December 2024). Registration card of research registration number: 0125U003930.

Consent for publication

Written informed consent to participate in the study was obtained from the patient

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to patient privacy considerations but are available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions (CRediT taxonomy)

N.O. Savychuk:	Methodology; Data Curation; Supervision
V.V. Pekhno:	Conceptualization; Formal analysis; Investigation; Data Curation; Writing – original draft preparation; Project administration
R.V. Sulik:	Formal analysis; Visualization;
I.B. Riabko:	Software; Validation; Investigation; Visualization

Authors' information

Not applicable

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Figures

```

% Symmetrize the matrices and set diagonal to zero
MNI = (MNI + MNI') / 2;
COUNT = (COUNT + COUNT') / 2;
diag_idx = 1:size(MNI,1)+1:numel(MNI);
MNI(diag_idx) = 0;
COUNT(diag_idx) = 0;

% Compute  $\Delta$  as the difference between MNI-based and COUNT-based connectivity
Delta = MNI - COUNT;

% ... (further analysis and visualization steps)

```

Figure 1

MATLAB r2024 script for $\Delta = \text{MNI} - \text{COUNT}$

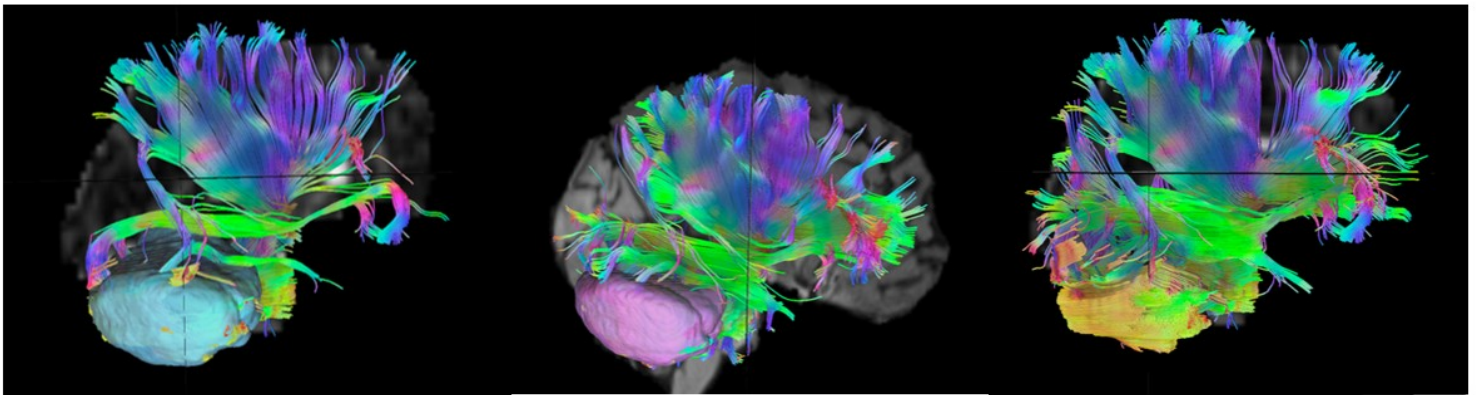


Figure 2

Cerebellar tractography/connectometry renderings across mandibular conditions.

(A) Centric occlusion (closed-mouth condition, CO).

(B) Occlusal appliance ("Splint") condition

(C) Centric relation (CR).

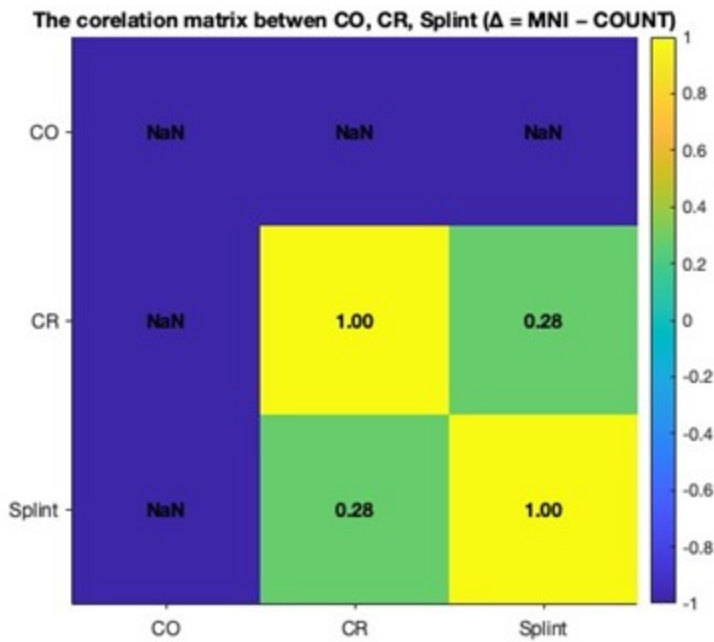


Figure 3

The correlation matrix across mandibular positions ($\Delta = \text{MNI} - \text{Count}$)

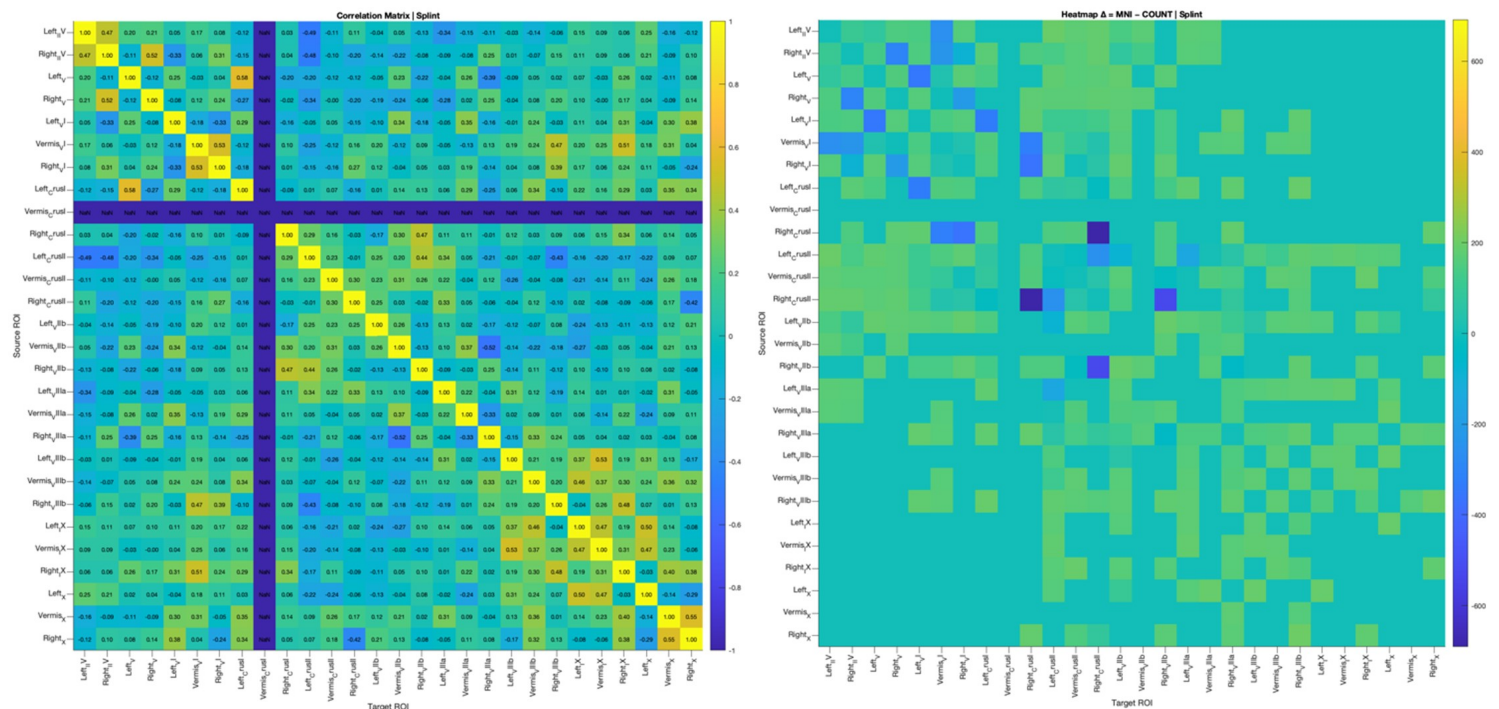


Figure 4

Cerebellar connectivity matrices for the splint condition

(A) ROI-to-ROI correlation matrix demonstrating heterogeneous but organized functional connectivity across cerebellar regions.

(B) Δ -matrix (MNI – COUNT) illustrating region-specific divergence between structural tractography-based and spatial endpoint-based connectivity measures.

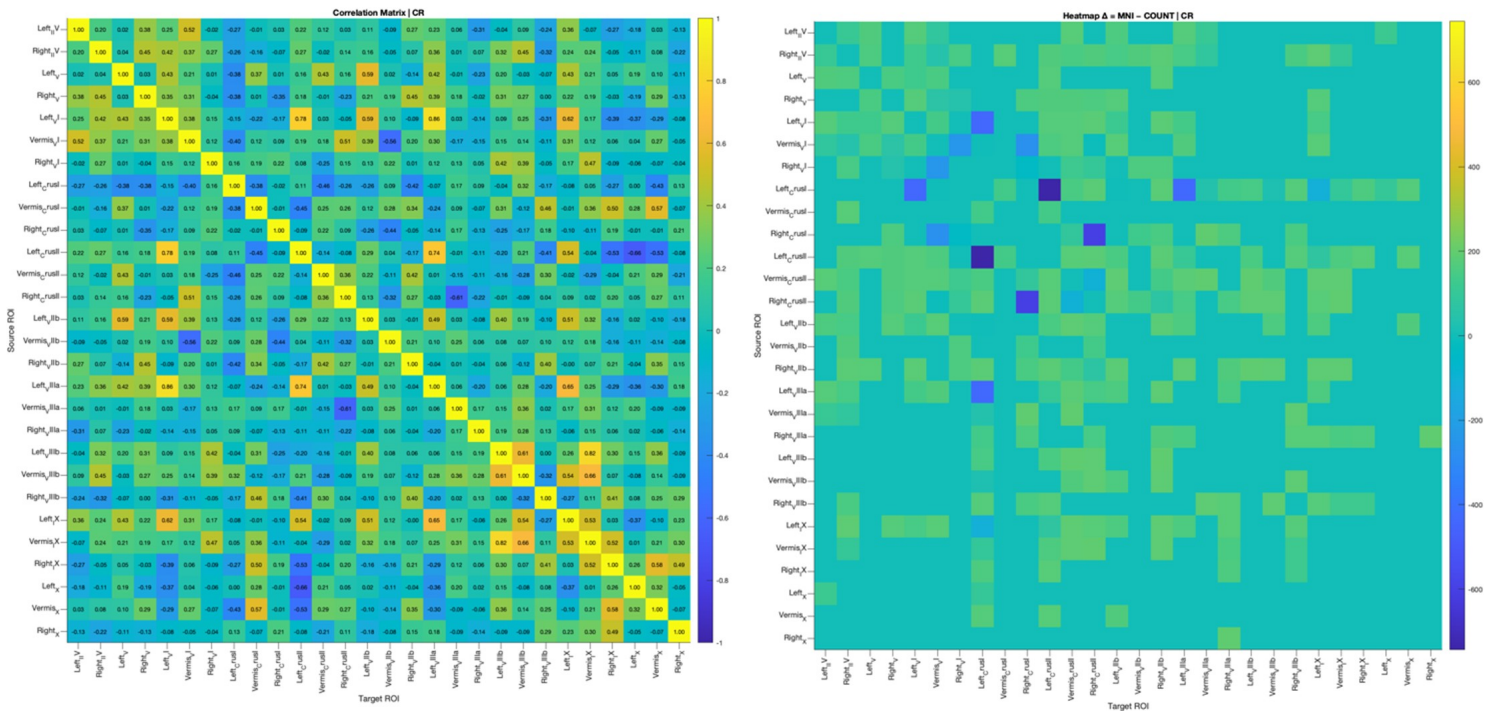


Figure 5

Cerebellar connectivity matrices for the CR condition

(A) ROI-to-ROI correlation matrix showing organized, non-random functional connectivity across cerebellar regions.

(B) Δ -matrix (MNI – COUNT) depicting region-specific heterogeneity between tractography-based streamline counts and spatial endpoint-based connectivity measures.

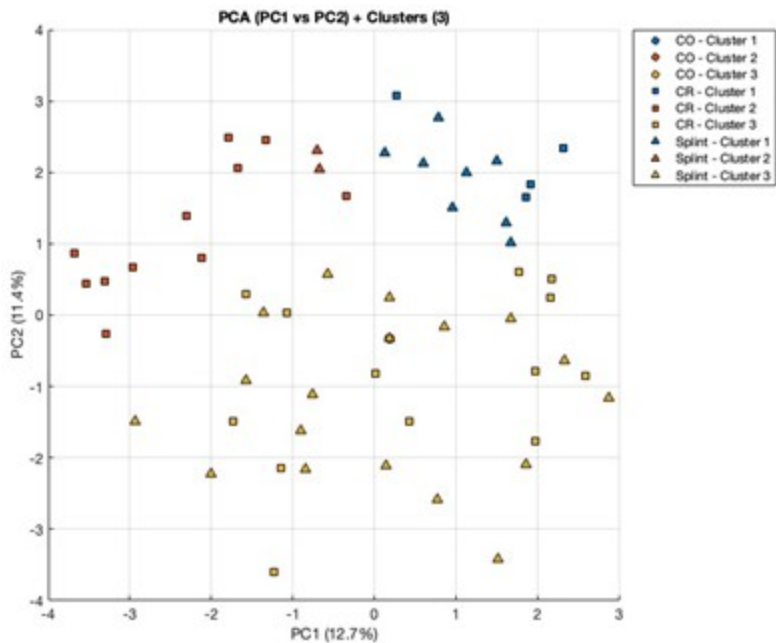


Figure 6

Principal component analysis (PCA) across mandibular positions.

