Longitudinal Gradient Analysis to Identify Alterations in Functional Organization Associated with Repetitive Subconcussive Impacts in Collegiate Athletes

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INTRODUCTION

- Subconcussive impacts (SCI) are common in contact sports and may contribute to cumulative brain injury despite the absence of acute symptoms.[1]
- Prior mild traumatic brain injury (mTBI)/concussion may increase vulnerability to SCI, with the DMN representing a key region of interest due to its role as a transmodal hub and sensitivity to persistent functional disruption reported even after clinical recovery.[2,3]
- Gradient analysis captures functional organization along continuous axes of connectivity variation, avoiding the discrete network boundaries imposed by traditional approaches.[4]

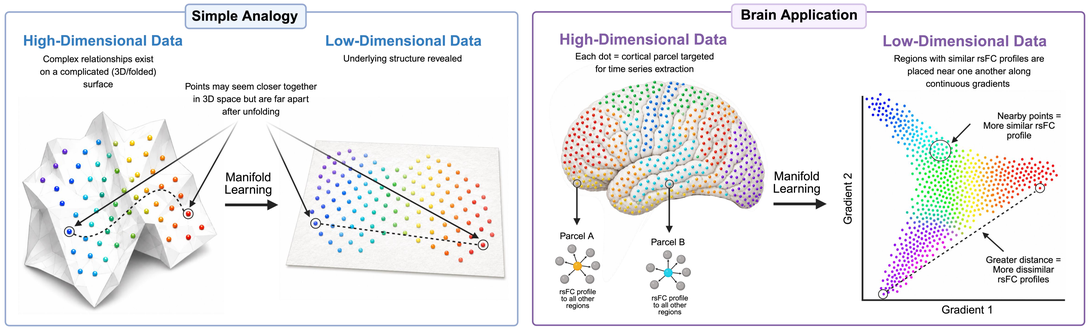

Figure 1: Conceptual overview of manifold learning and gradient analysis. High-dimensional data expressed into a lower-dimensional space, preserving local similarity relationships. Manifold learning positions cortical regions with similar connectivity profiles closer together along gradients. Gradient 1 reflects unimodal-to-transmodal axis. rsFC = resting-state functional connectivity.

Aim: Determine whether concussion history and contact-sport exposure are associated with altered functional brain organization across a competitive season.

METHODS

Study Participants & Timeline

- Queen's University Men's Football Team.
- Total Population N = 24; Prior concussion history (CH) N = 10; No concussion history (No CH) N = 14.
- 3 rs-fMRI Imaging Sessions: Pre-season (PRE); Post-training camp (PTC); Post-season (POST).

Preprocessing

- Standard preprocessing pipeline applied to T1-w/rs-fMRI data, including motion/distortion correction, ICA-AROMA denoising, nuisance regression, MNI normalization, and smoothing.

DMN ICA Network-Based Analysis

- Networks identified using FSL MELODIC group ICA.
- DMN components labelled by Dice overlap with Yeo-7/Atlas55+.[5,6]
- Within-DMN FC: pairwise Pearson correlation (Fisher z-transformed) between DMN IC masks mean BOLD time series.

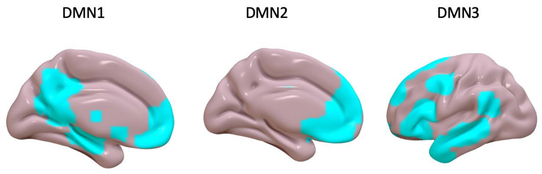

Figure 2: Atlas55+ DMN cortical projection.

Labelling	Subdivision	Anatomical Description
DMN1(DMN1a & DMN1b)	Subdivision 1	Medial orbital prefrontal cortex; Bilateral hippocampi; Precuneus/Posterior cingulate cortex
DMN2	Subdivision 2	Anterior cingulate cortex; Medial orbital prefrontal cortex; Medial superior prefrontal cortex
DMN3	Subdivision 3	Left inferior frontal gyrus; Temporal poles; Supplementary motor area; Medial superior prefrontal cortex; Left middle temporal gyrus; Left precentral gyrus

Table 1: Atlas 55+ DMN labels and anatomical locations.

Gradient Analysis: Subject-level Schaefer-400 functional connectivity matrices were embedded into cortical gradients via BrainSpace diffusion mapping and Procrustes-aligned to a reference template for cross-group comparison.[7-9]

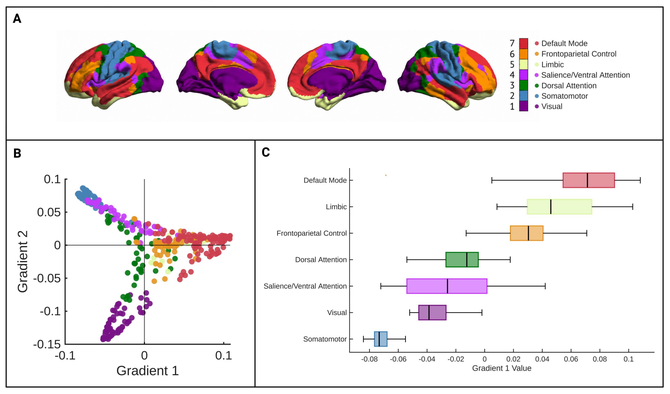

Figure 3: Cortical gradient decomposition across resting-state networks. (**A**) Yeo 7-network cortical projections; (**B**) Sample-derived Gradients 1-2 shown in Euclidean space; (**C**) Gradient 1 distributions across networks, ordered by median value, reflecting unimodal-to-transmodal hierarchy.

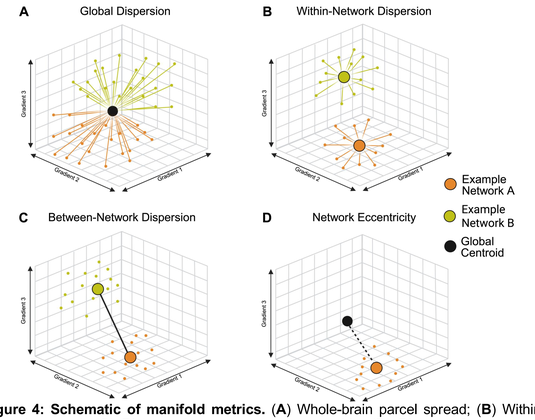

Figure 4: Schematic of manifold metrics. (**A**) Whole-brain parcel spread; (**B**) Within-network spread; (**C**) Distance between network centroids; (**D**) Distance from network centroid to global centroid.[10]

RESULTS

Statistics: LMMs included Session, CH, and Age as fixed effects with random subject intercepts; rmANCOVA was used for singular fits. Between-network tests were FDR-corrected. †p < .10; *p < .05; **p < .01. Points = estimated marginal means; error bars = 95% CIs.

ICA Network-Based Analysis

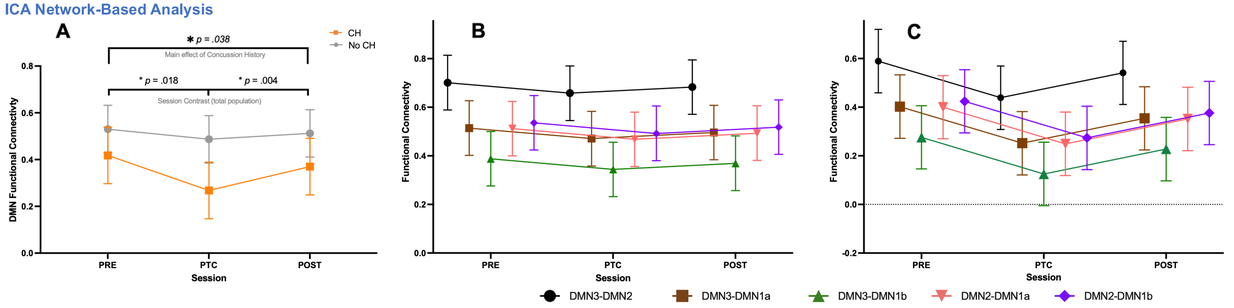

Figure 5. Within-DMN functional connectivity (Fisher z) across session by edge and CH group. (**A**) Total population; (**B**) No CH; (**C**) Prior CH.

Gradient Analysis

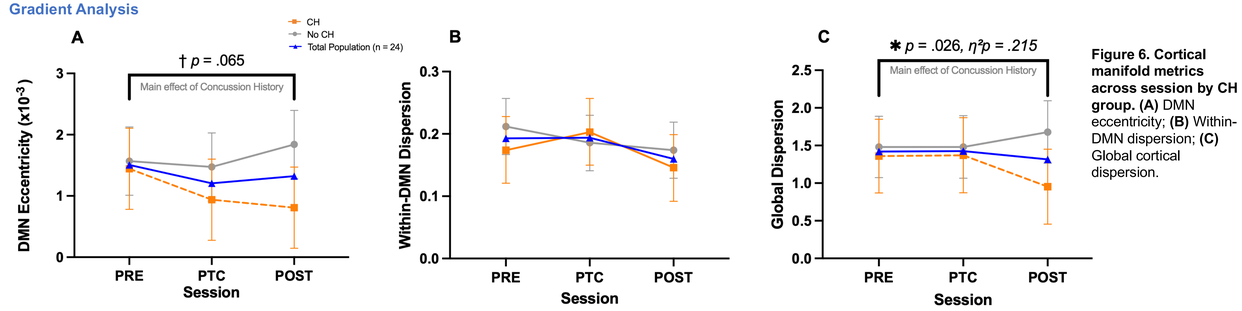

Figure 6. Cortical manifold metrics across session by CH group. (A) DMN eccentricity; **(B)** Within-DMN dispersion; **(C)** Global cortical dispersion.

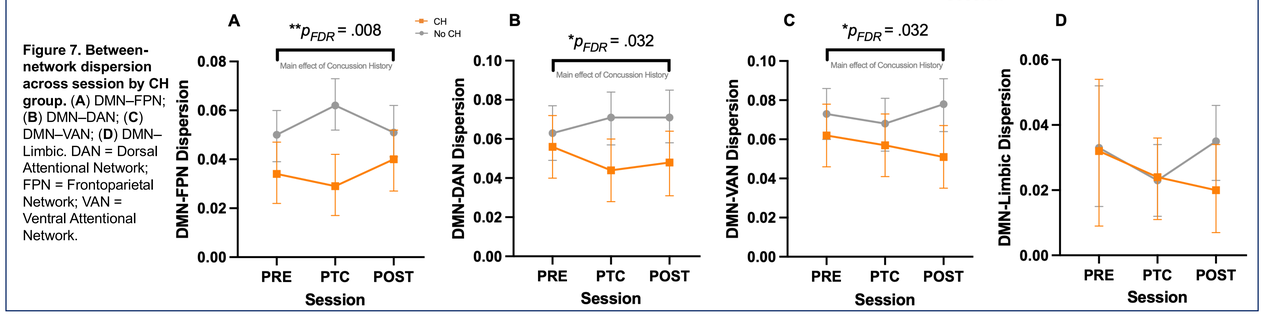

Figure 7. Between-network dispersion across session by CH group. (**A**) DMN–FPN; (**B**) DMN–DAN; (**C**) DMN–VAN; (**D**) DMN–Limbic. DAN = Dorsal Attentional Network; FPN = Frontoparietal Network; VAN = Ventral Attentional Network.

DISCUSSION

- Prior CH was associated with compressed manifold geometry, reduced between-network segregation, and lower within-DMN FC.
- Pre-season group differences suggest persistent alterations in functional organization that may exist before seasonal exposure to SCI.
- CH group displayed greater mid-season functional connectivity suppression and incomplete post-season recovery, suggesting a potential heightened vulnerability to SCI and impaired neural adaptation.
- Results from both analyses point toward pronounced mid-season changes amplified in CH athletes, suggesting that CH and not contact sport alone, may be a primary moderator of functional injury.
- Cortical gradient analysis demonstrated sensitivity to CH-related functional differences, highlighting its potential as a valuable neuroimaging tool in mTBI and SCI research.

Limitations:

- Manifold analysis lacks established normative benchmarks in concussion research; the directionality of gradient changes cannot be unambiguously characterized as adaptive or maladaptive.
- CH was self-reported with no control for number of prior concussions, recency of most recent injury, severity, or cumulative burden.

Future Directions:

- Larger samples are needed to confirm preliminary findings and provide power to detect interaction effects.
- Future work should quantify SCI exposure and incorporate it as a covariate to disentangle its contribution from prior CH effects.

REFERENCES