An Intrinsic Pathway In the Brain Underlying the Relationship Between Pain Catastrophizing and Chronic Pain in Temporomandibular Disorders

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BACKGROUND

- Pain catastrophization (PC), involving rumination, magnification, and helplessness[1], is a common psychological factor that contributes to Temporomandibular Disorders (TMDs), characterized by pain and dysfunction of the TMJ[1]. TMD patients with high-level PC have greater pain severity and interference than those with low-level PC[1].
- However, it is unknown how PC changes the way pain is processed in the brain. Previous studies report altered functional connectivity in regions such as: the **posterior cingulate cortex (PCC)**[2], **anterior insula (aINS)**[2], and **periaqueductal grey (PAG)**[2].
- The purpose of this study is to examine whether PCC-aINS-PAG represents a functional pathway underlying the relationship between PC and pain severity and interference in TMD patients.

METHODS

- All study procedures were approved by the University of Maryland, Baltimore IRB (HP-00068315) as part of a parent study on placebos in TMD. TMD diagnosis was verified by a dental clinical at the UMB School of Dentistry using Axis I Diagnostic Criteria (DC/TMD).
- **Phase 1** (Aug 2016 to Jan 2020): Total sample included 397 TMD participants. Participants completed questionnaires including:
  - Graded Chronic Pain Scale (GCPS) to measure pain severity and interference
  - Jaw Functional Limitation Scale (JFLS-20)
  - Pain Catastrophizing Scale (PCS) including subscales rumination (Rum), magnification (Mag), and helplessness (Help)
  - Depression, Anxiety, and Stress Scale (DASS-21)
  - Positive and Negative Affect Scale (PANAS)
  - Revised Life Orientation Test (LOT-R) to measure optimism
  - Neo Five Factors Inventory Form S (NEO-FFI) to measure extraversion
- **Phase 2**: Data collection began in May 2021 and is on-going, but 71 of the original 397 TMD participants have completed the resting state functional magnetic resonance imaging (rsfMRI) scan. Participants also repeated the GCPS and PCS.
  - 4 participants were removed for missing Phase 2 PCS scores (*n* = 66 for behavioral data)
  - To date, 48 participants imaging data has been preprocessed using fMRIPrep, and 6 participants were removed for excessive head motion (*n* = 38 for imaging data)

BEHAVIORAL RESULTS

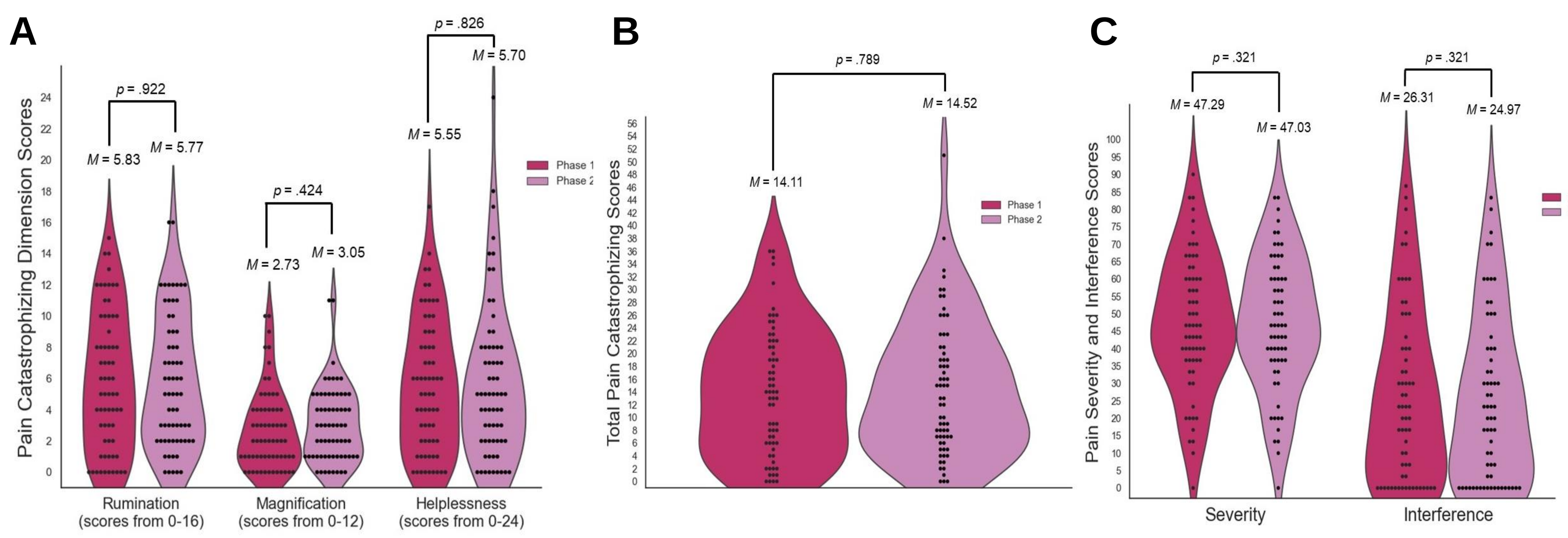
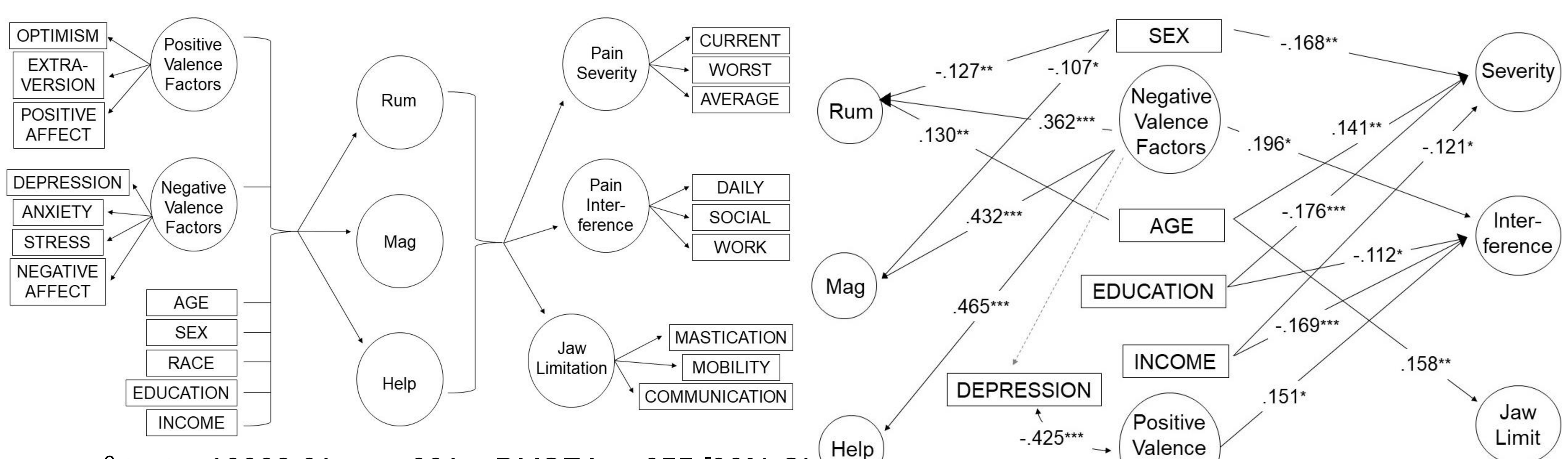


Figure 1. PC, severity, and interference scores were compared from Phase 1 (pre-COVID-19 pandemic) to Phase 2 (during the pandemic) in the 66 participants that completed Phase 2 using *t*-tests. There was no significant difference in **A)** PC dimension scores, **B)** total PC, nor **C)** severity or interference from Phase 1 to 2. Although not significant, magnification, helplessness, and total PC increased, while rumination, severity, and interference decreased from Phase 1 to 2.



χ^2 test = 10003.61, p < .001; RMSEA = .055 [90% CI .05 to .059]; SRMR = .049; CFI = .934; TLI = .922

Figure 2. Structural equation modeling was used to determine the importance of PC on pain severity and interference taking into account related sociodemographic and psychological variables from Phase 1 using structural equation modeling (SEM). Mediating effects of each dimension of PC was calculated via a 2000 bootstrapped sample. Hypothesized SEM is left, and the final SEM with only significant paths is right. Overall model fit was within an acceptable to excellent range. Education was the strongest predictor of severity; negative valence factors was the strongest predictor of interference; and age was the only predictor of jaw limitation. The dimensions of PC did not individually mediate the relationship between any predictor variables and any outcome variables.

DISCUSSION

- This TL1 project sheds light on clinical and mechanistic aspects of PC in TMD. PC dimensions do not vary over time (Phase 1 to Phase 2), and PC does not predict pain severity and interference as well as education and negative valence factors.
- Preliminary functional connectivity results support PCC-aINS connectivity but not aINS-PAG connectivity. Correlational analyses confirm the behavioral results, suggesting that other factors such as negative valence factors need to be taken into account to understand the neural mechanisms of pain severity and interference in TMD.
- However, analysis of the full dataset is required before drawing any conclusions.

MEDIATION RESULTS

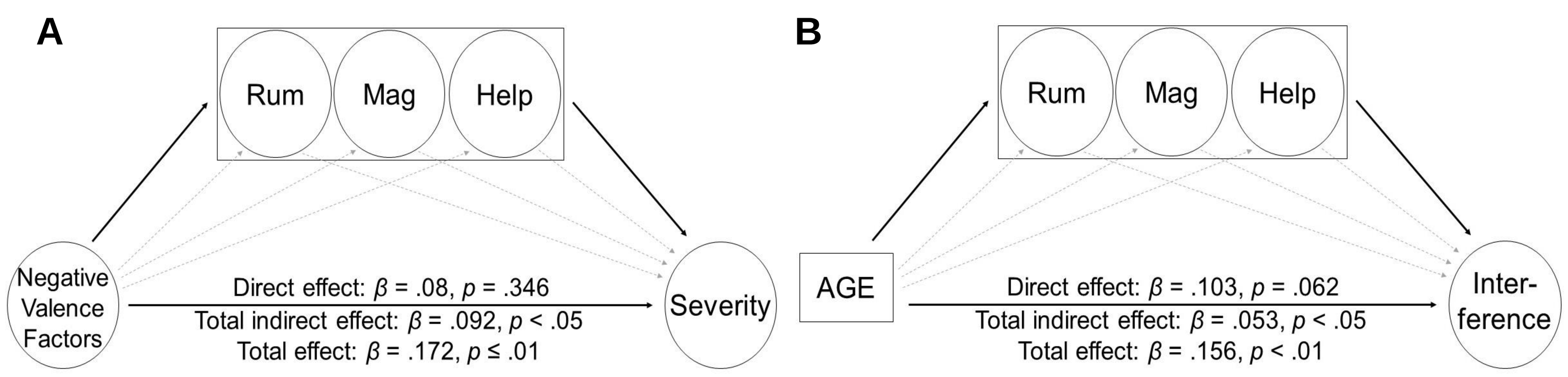


Figure 3. Mediation analyses were conducted to explore the role of PC dimensions. Rather than acting as individual mediators, there was a significant **total** indirect effect between **A)** negative valence factors and severity, and **B)** age and interference, suggesting that the dimensions of PC do not differentially influence TMD pain outcomes.

BRAIN IMAGING PRELIMINARY RESULTS

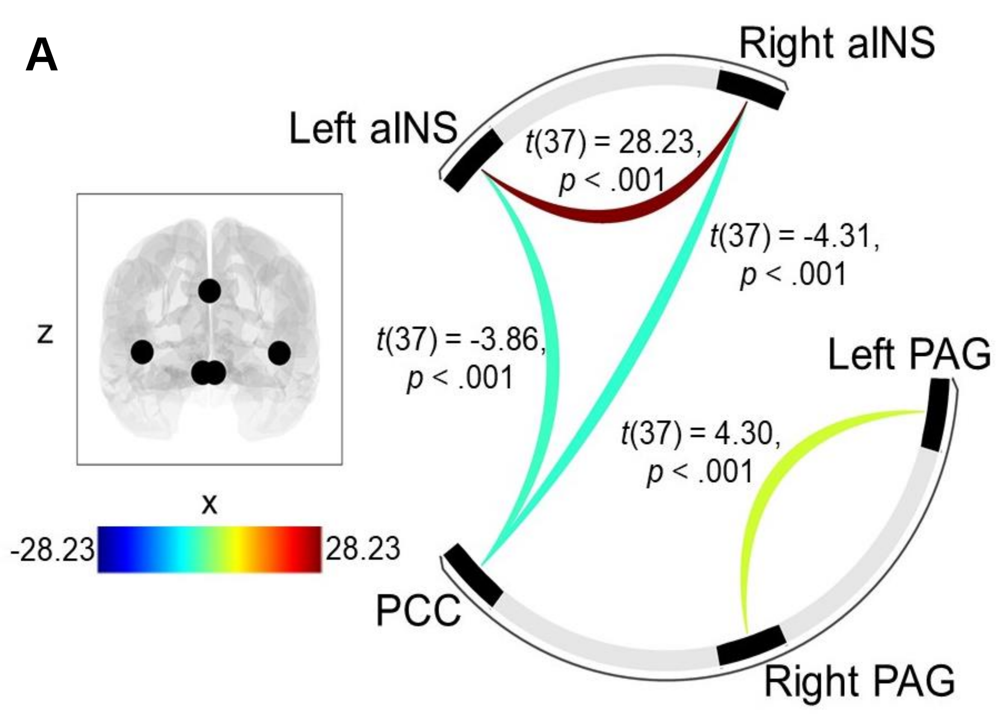
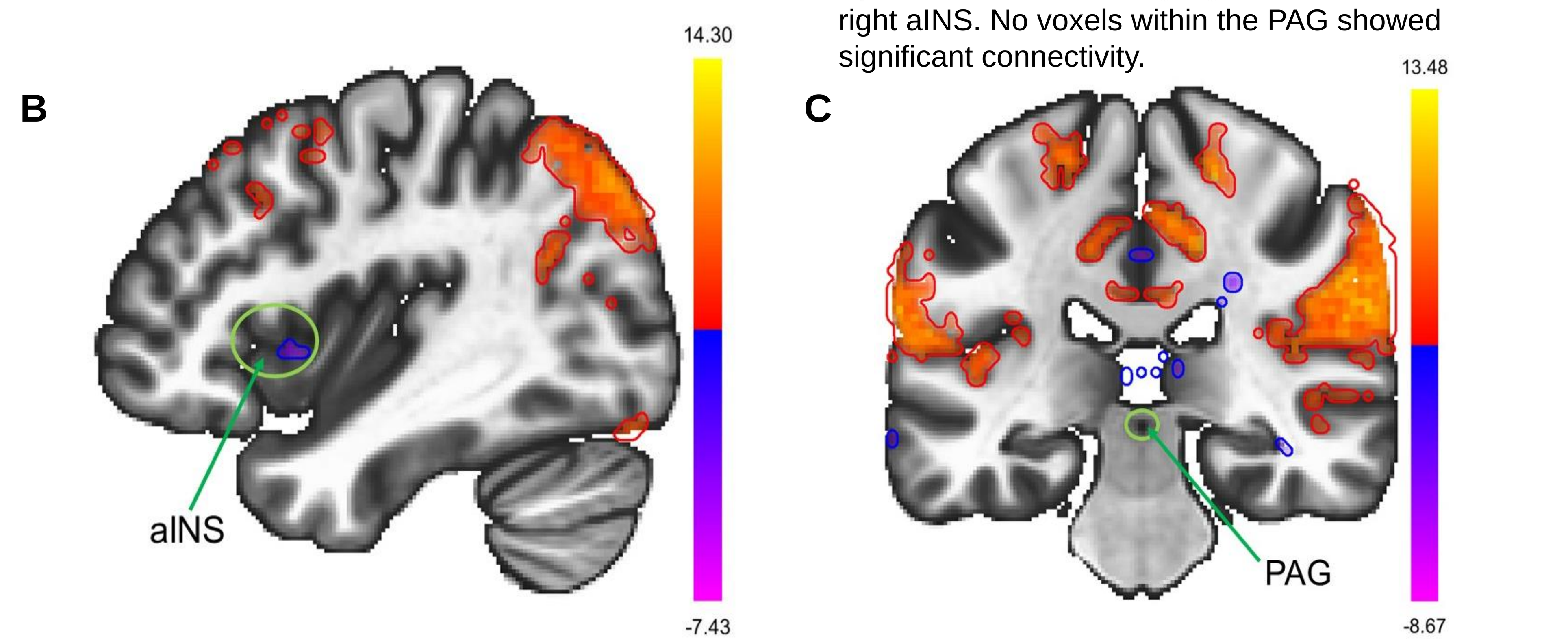


Figure 4. Functional connectivity was assessed using a seed-based analysis. PAG region of interest (ROI) was created using a sphere at peak voxels as reported in other studies[3]. CONN toolbox's network ROI's were used for PCC and aINS. All analyses were uncorrected *p* < .01 at the voxel level and FDR-corrected *p* < .05 at the cluster level. **A)** T-scores for connectivity between ROI's, noted by black dots on the glass brain. The color of the connection denotes the strength of the connectivity. The PCC showed small but significant functional connectivity with the bilateral aINS. Neither PCC nor aINS showed connectivity to bilateral PAG.
B) Sagittal slice showing significant voxels for the PCC. There is a small cluster in the aINS that showed connectivity to the PCC.
C) Coronal slice showing significant voxels for the right aINS. No voxels within the PAG showed significant connectivity.



	Rum	Mag	Help	Total	Sev	Intf	Age
Rumination	-						
Magnification	.657***	-					
Helplessness	.781***	.599***	-				
Total	.929***	.775***	.934***	-			
Severity	-.019	.150	-.103	-.025	-		
Interference	.137	.091	.141	.144	-.063	-	
Age	-.310[a]	-.226	-.231	-.287	-.105	.110	-
PCC with							
Left aINS	.054	.232	-.036	.055	.183	.461**	.002
Right aINS	-.116	.315	-.130	-.074	.131	.405*	.120
Left PAG	.103	.173	.183	.169	0	.020	.024
Right PAG	.160	.178	.140	.172	.037	.081	-.209
Left aINS with							
Right aINS	.276	.320[b]	.160	.259	-.176	.149	-.447**
Left PAG	-.272	-.161	-.336*	-.309[a]	.130	-.237	.046
Right PAG	-.123	-.149	-.224	-.191	-.117	.051	-.162
Right aINS with							
Left PAG	-.020	-.179	-.165	-.127	-.043	-.155	-.089
Right PAG	-.042	-.129	-.232	-.158	.108	.022	-.016
Left PAG with							
Right PAG	.083	.128	.076	.098	.071	.358*	.010

Preliminary results. Pearson's correlations for behavioral data with functional connectivity strength. Strength of connectivity was transformed to standardized Fisher's *z*-scores from Pearson's *r*-values. Significant correlations are denoted with red stars, **p* < .05, ***p* < .01, ****p* < .001. [a]trending *p* = .059, [b]trending *p* = .051. No measures of PC significantly correlated with pain severity (Sev) or interference (Intf). The strength of connectivity between PCC and bilateral aINS correlated with interference. Although the connectivity between the left aINS and left PAG did not reach significance, its strength correlated with helplessness and trended with total PC, but the full dataset analyses are needed to draw conclusions.

REFERENCES & ACKNOWLEDGEMENTS

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