White matter abnormalities associated with visceral pain: Preliminary data from the Multi-disciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Network

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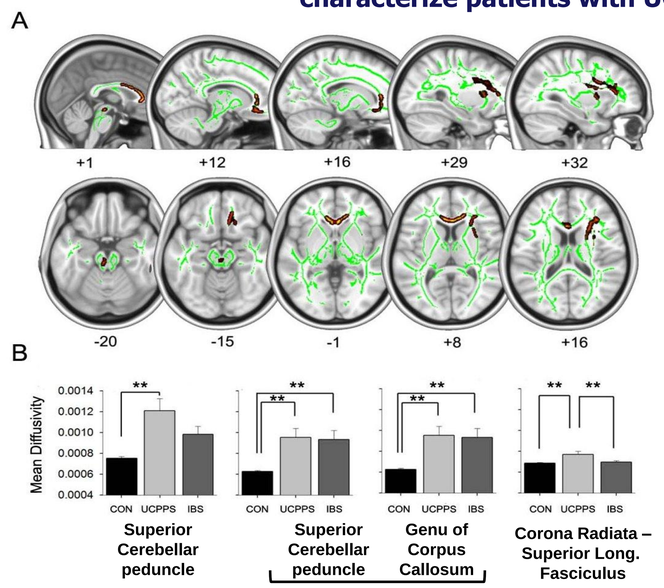
INTRODUCTION

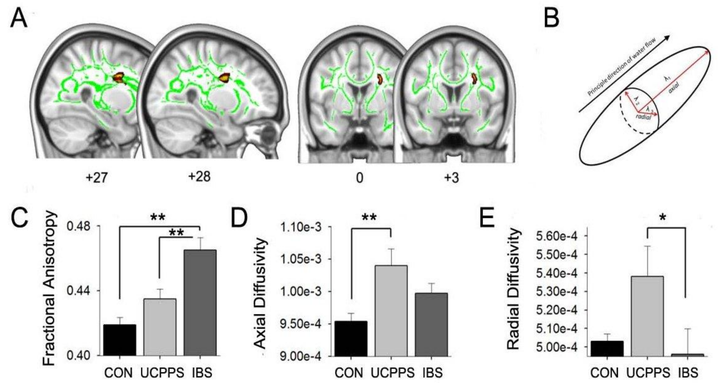
- Chronic visceral pain is characterized by diffuse, dull, or throbbing pelvic, bladder, and/or abdominal pain, and is associated with negative affect and autonomic changes.
- Visceral pain is clinically diagnosed as urological chronic pelvic pain syndrome (UCPPS)—including chronic prostatitis pain syndrome (CPPS) in men and interstitial cystitis (IC) in men and women—as well as irritable bowel syndrome (IBS).
- Etiological hypotheses have focused on peripheral pathology, which does not reliably correlate with symptom severity.
- Accumulating evidence suggests that chronic pain conditions may be associated with brain reorganization, including altered white matter microstructure
- To investigate the role of white matter properties across types of visceral pain, we conducted a diffusion tensor imaging study as part of the MAPP Research Network initiative.

1 Regional white matter mean diffusivity abnormalities characterize patients with UCPPS



- UCPPS, IBS and control contrasts yielded four significant clusters with mean diffusivity differences
  - superior cerebellar peduncle, midline to anterior thalamic radiation, bilaterally
  - genu of corpus callosum
  - tract linking R superior and anterior corona radiata to superior longitudinal fascilulus
- Each cluster showed distinct patterns of specificity

3 Fractional diffusivity properties of SLF uniquely distinguish UCPPS from controls



UCPPS + IBS > Controls
(specific for visceral pain)

Axial diffusivity
UCPPS > Controls
(no specificity for IBS)

Radial diffusivity
UCPPS > IBS

METHODS

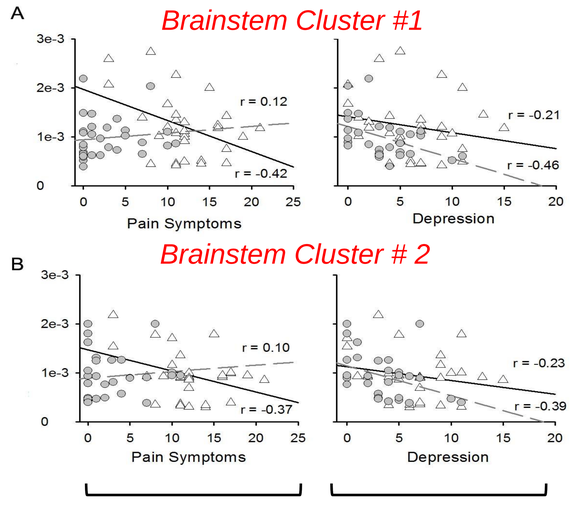
- Diffusion-weighted (DTI) and high resolution T1-weighted images collected at Northwestern University and University of California at Los Angeles using comparable data acquisition parameters on 3 Tesla Siemens scanners.
- Participants included 32 men and women with UCPPS, 30 men and women with IBS, and 34 age- and sex- matched healthy men and women.
- Data was eddy current- and head motion-corrected with FMRIB's Diffusion Toolbox (FDT) and skull extracted. A diffusion tensor model was fit to determine voxel-wise fractional anisotropy (FA) and statistically evaluated with tract-based spatial statistics (TBSS) from FSL to create a mean group skeleton.
- A one-way ANOVA was calculated to determine between group mean and FA diffusivity differences, using permutation methods to threshold statistical maps. Post-hoc t tests were conducted to identify directionality of effects.
- Clinical parameters were correlated with subject mean diffusivity values to expand on their clinical significance.

2 Clinical Pain and Affective Characteristics

	Controls mean(*SD*)	UCPPS mean(*SD*)	IBS mean(*SD*)
Age	38.59 (12.88)	40.63(15.38)	34.93 (10.81)
SYMPQ			
Pain/pressure/discomfort	0	4.17 (2.65)	1.41 (2.06)
Urgency	0.5 (1.05)	4.23 (3.04)	1.76 (2.01)
Severity of urination	0.72 (1.55)	4.4 (3.04)	1.69 (1.88)
Frequency of urination	1.22 (0.42)	2.27 (0.94)	1.41 (0.67)
Severity urologic symptoms	0	4.2 (2.63)	1.03 (1.84)
Severity non-urologic symptoms	0.13 (0.42)	3.1 (2.48)	2.45 (2.29)
Gracely intensity	0	10.07 (4.37)	6.89 (4.67)
Gracely unpleasantness	0.87 (4.17)	8.75 (3.93)	5.89 (4.25)
McGill Pain Questionnaire (total)	0.17 (0.49)	11.63 (7.2)	5.74 (4.67)
Sensory subscale	0.17 (0.49)	9.29 (5.64)	4.59 (3.65)
Affective subscale	0	2.07 (2.36)	1.15 (1.69)
Anxiety (HADS)	3.19 (3.12)	7.69 (3.30)	5.07 (4.79)
Depression (HADS)	1.87 (1.63)	6.38 (3.87)	3.45 (2.93)
Genitourinary Pain Index (total)	1.06 (1.45)	24.7 (8.43)	7.97 (7.51)
Pain	0.11 (0.66)	12.05 (4.11)	2.83 (3.49)
Urinary	0.64 (1.06)	4.97 (3.22)	1.83 (2.00)
Quality of life	0.31 (0.57)	7.69 (2.99)	3.31 (3.29)

- UCPPS patients reported greater symptom severity than positive (IBS) or healthy controls.

4 Regional mean diffusivity reflects distinct clinical parameters in UCPPS vs. IBS



- UCPPS patients with lower regional mean diffusivity reported **less pelvic pain**
- IBS patients with lower regional mean diffusivity reported **less anxiety**

CONCLUSIONS

- These novel findings constitute the first description of clinically relevant brain white matter changes unique to UCPPS, suggesting that **condition-specific axonal reorganization contributes to chronic pelvic pain**.
- White matter mean diffusivity in a tract stretching between the corona radiata and superior longitudinal fasciculus shows highest specificity for UCPPS.
- Examination of multiple diffusivity patterns can reveal high specificity for distinct types of visceral pain, suggesting that **UCPPS and IBS white matter alterations are anatomically and phenotypically distinct.**
- However, distinct types of visceral pain may **differentially modulate common axonal circuitry.**
- **Pelvic pain resides in the brain.**

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