Alterations in resting state oscillations and connectivity within sensory and motor networks in women with interstitial cystitis/painful bladder syndrome

Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS)

- IC/PBS is a chronic pelvic pain condition associated with urinary urgency and frequency that may affect over 7 million women in the United States.¹

- The specific pathophysiology remains incompletely understood, but is thought to involve a central disturbance in the processing of pain and viscerosensory signals.²,³

¹Berry et al (2011) J Urol
²Clemens (2008) J Urol
³Mayer & Bushnell (2009)
Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network

- MAPP is a multi-site effort to identify epidemiological and neuroimaging parameters that will advance clinical phenotyping and treatment efforts for urological chronic pelvic pain, including IC/PBS.

- Neuroimaging data was collected at 5 sites and included structural MRI, diffusion tensor imaging and resting scan fMRI.
Resting Scan fMRI

- Resting scan fMRI capitalizes on the fact that a wealth of information can be extracted from the intrinsic fluctuations in the blood oxygen-level dependent (BOLD) signal without the need of an external stimulus.

- Advantages of resting scan over task-based fMRI include a greater degree of standardization across research centers.

- In addition, brain responses to acute, experimental pain in the laboratory may have limited utility for understanding chronic pain.
Aim of Study

- Using resting scan fMRI, we aimed to identify differences in intrinsic brain activity and connectivity between female IC/PBS patients and healthy controls.
- We hypothesized that IC/PBS patients show altered oscillation frequency and functional connectivity in viscero- and sensorimotor regions.
Subjects

- 85 female healthy controls (HC) and 82 female IC/PBS patients collected from 5 MAPP discovery sites.

- To meet IC/PBS symptom criteria, patients had to report an unpleasant sensation of pain, pressure or discomfort perceived to be related to the bladder and/or pelvic region associated with lower urinary tract symptoms.

- IC/PBS symptoms must have been present for most of the time during any 3 months in the previous 6 months and for most of the time during the most recent 3 months.
Methods: Data Acquisition

- Scanning was performed at multiple sites using different scanner technology (3T Siemens Trio (NWU and UCLA), 3T Phillips Ingenia (UM), 3T Philips Achieva (UAB), and 3T GE Discovery (SU)).

- Standardized acquisition parameters were used to collect 10 minute resting fMRI scans. During the scan subjects rested with eyes closed.

- Data was collected, quality controlled and archived according to multi-site imaging procedures developed collaboratively between the MAPP Research Network, the UCLA PAIN repository and the UCLA Laboratory of Neuroimaging.
Methods: Analyses

- Alterations in frequency distribution were determined by transforming the BOLD signal time course data of each brain voxel into the frequency domain and computing the fractional amplitude of frequency power in 3 frequency bands
  - LF (0.01-0.027 Hz; aka slow-5)
  - MF (0.027-0.073 Hz; aka slow-4)
  - HF (0.073-0.198 Hz; aka slow-3)

- Regions demonstrating altered frequency distribution were further examined for altered functional connectivity by computing band-specific correlation maps.
Altered insular frequency distribution and functional connectivity in women with IC/PBS compared to healthy women.

Posterior insula (pINS) shown in blue displayed decreased LF power and decreased functional connectivity with the mid insula (mINS) shown in green in IC/PBS patients.
Altered sensorimotor frequency distribution and functional connectivity in women with IC/PBS compared to healthy women.

Sensorimotor regions shown in red displayed increased LF power and increased connectivity with the regions in yellow in IC/PBS patients.
Altered connectivity was greatest in patients endorsing pain during bladder filling.

The connectivity between sensorimotor cortices and midbrain/cerebellular regions was greatest in patients endorsing pain during bladder filling.
Conclusions

- IC/PBS patients demonstrated alterations in viscerosensory regions which may reflect tonically increased viscerosensory input to the brain and altered integration of interoceptive information into subjective awareness.

- Several regions with known involvement in bladder function and pelvic floor muscle control demonstrated altered frequency distribution and connectivity in IC/PBS patients. Connectivity alterations were greatest in patients reporting pain during bladder filling. Although no assessment of pelvic floor dysfunction was performed in the current study, these alterations may be related to pelvic floor dysfunction as several clinical observations support the concept of altered pelvic floor activity in IC/PBS.
Conclusions

- Overall, these results suggest that women with IC/PBS have a sensorimotor component to their pathology involving alterations in a cortico-cerebellar pathway previously associated with bladder and pelvic floor function.
The PAIN Repository is targeting collection of MRI scans from 1,000 subjects for Big Data Analysis

- Diverse chronic pain conditions and healthy controls
- Structural, DTI and resting state functional scans
- Both standardized data for multisite combination and non-standardized for meta-analysis

Funded by NIDA, NCCAM R01AT007137 (Tillisch/Naliboff)

PAINRepository.org
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Funding for the MAPP Research Network was obtained under a cooperative agreement from National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH) (DK82370, DK82342, DK82315, DK82344, DK82325, DK82345, DK82333, and DK82316.). In addition, this work was supported in part by: R01 DK04835 and K01 DK085133