



International Association for the Study of Pain

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Working together for pain relief

S I G > N E W S L E T T E R

**Abdominal & Pelvic Pain**  
IASP Special Interest Group

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**In This Issue:**

- » [Happy New Year From Your "Leadership Team"](#)
- » [Summaries From Key Pelvic/Abdominal Pain Meetings](#)
- » [Opportunities for Collaborative Research](#)
- » [Recently Published Pertinent Articles](#)
- » [The U.S. NIH/NIDDK MAPP Research Network: Recent Findings and Future Directions](#)
- » [Notable Occurrences](#)

**Happy New Year From Your "Leadership Team"**

We have spent the year as a new leadership group reviewing the entire vision for the SIG, and one reality was a newsletter template had to be developed from scratch. In fact a major priority for our current term is to establish a permanent infrastructure so that projects like SIG workshops, SIG symposia, and newsletters become continuous work items rather than rebooted projects every time an annual meeting occurs.

If you would like to contribute to the SIGs development, please contact us, we need engagement! We do have a projected newsletter committee, one of two enumerated in the SIG by-laws. Under Katy and Qasim's guidance in 2016, they will be putting out this year's two newsletters. Current members of this committee include **William Rea**, **Kevin Hellman**, and **Sandy Hilton**.

>> **Frank Tu, Katy Vincent, and Qasim Aziz**

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**Summaries From Key Pelvic/Abdominal Pain Meetings**

... with apologies to many meetings--such as AUGS, AUA, or DDW--that we could not attend.

- **The second World Congress on Abdominal and Pelvic Pain took place June 11 -13, 2015, in Nice, France (courtesy Stephanie Prendergast, past president IPPS).**

This was the second conference of its type and followed from the discussions in Istanbul in 2011 where it was agreed that biannual meetings would occur and be jointly organized by the SIG on Abdominal and Pelvic Pain (formerly PUGO), the International Pelvic Pain Society (IPPS), and Convergences in pelviperineal pain (Convergences PP). The agreement was that each organization would take the lead in turn with the organizing and all three would be involved in the program. The Abdominal and Pelvic Pain SIG ran the first meeting in 2013 in Amsterdam. This year, Convergences PP took the lead in organizing the conference.

Convergences PP teamed up with the International Urogynecology Association (IUGA) to run simultaneous sessions at the Acropolis convention hall in Nice, France. Registrants of the IUGA conference were given passes to attend two lectures of their choice from the WCAPP conference. In addition, IUGA invited WCAPP speakers to speak at their general session on Friday, June 13. This was an amazing opportunity for WCAPP to increase awareness among the urogynecology community about pelvic pain disorders. The WCAPP lectures were very well attended by the IUGA participants, demonstrating the desire of the medical community to better understand how to evaluate and treat persisting pelvic pain.

The IPPS will host the third World Congress on Abdominal and Pelvic Pain, October 12-15, 2017, in Washington, D.C. One consideration we are exploring is to host a harmonization meeting to unify pelvic pain terminology for outcomes. More to come on this.

- **American Gastroenterological Association Freston lecture: A Renaissance in the Understanding and Management of Irritable Bowel Syndrome--August 29-30, in Chicago, Illinois.**

The AGA hosts some extremely focused topical meetings annually and SIG chair Dr. Tu “snuck” in as a non-GI speaker on cross-organ sensitization at the 2015 meeting, thus getting us some “ears on the ground.” It was quite a remarkable group to hear from, and beyond the scope of the newsletter to cover the terrain. However, I found several notable teams presenting that routinely are doing high-quality work in visceral pain.

First, the UCLA team headed by **Emeran Mayer** detailed some of the recent brain imaging findings that characterize visceral sensitivity and gave some really intriguing presentations on the use of network analysis to characterize whole brain processing of gut sensation. **Michael Snyder** from Stanford University, who has popularized the study of personalized genomics gave a glimpse of how to potentially apply this to gut microbiome. [Here](#) is an interesting article about this general area of work.

Last, I thought **Michael Camilleri** from Mayo Clinic (a key contributor in the field for some time) gave a very helpful update about the limitations and promise of biomarkers, reviewing how bowel transit times, dynamic serotonin levels, and immune regulatory markers in the gut might meaningfully subtype patients. I hope that for future meetings, the SIG will be able to designate reporters who can do a better job of capturing the fascinating content that many other presenters offered!

- **Society for Neuroscience--October 17-21, 2015, in Chicago, Illinois (courtesy of Kevin Hellman, PhD, NorthShore University HealthSystem and University of Chicago)**

Among all of the posters on visceral pain at the 2015 Society for Neuroscience meeting in Chicago, I would like to raise attention to two posters with translational implications:

The Traub lab investigated the effects of estradiol and testosterone in a model of stress induced visceral hypersensitivity (Poster 238.03). In their model, forced swim in rats was used to produce stress. The effects of stress on visceral sensitivity was examined with visceromotor responses (VMR) to colorectal distention in combination with evaluation of spinal cord expression. Dr. Traub's group noted estradiol facilitates and testosterone attenuates stress-induced visceral hypersensitivity by modulating spinal glutamate receptor expression independent of sex. These findings are line with Dr. Vincent's findings in women with dysmenorrhea and results for other types of pain studied in the Mogil lab. Thus, hormonal modulation of visceral pain may prove to be a clinically viable option.

Although stimulation methods are commonly used in pain management, approval is still being sought to for stimulation based bladder pain relief. The concurrent medication use can alter responses to stimulation and so prior to the development of a clinical trial, it is important to establish potential interactions. With support from Medtronic, the Ness lab examined the interaction between the GABA-B receptor agonist, baclofen, and acute bilateral electrical pudendal nerve stimulation on VMRs in a rat model of interstitial cystitis (poster 238.13). They found that even in hypersensitive rats that had received acute or chronic baclofen injections, pudendal nerve stimulation reduced VMRs. Thus their study suggests that in clinical trials baclofen will not interfere with electrical pudendal nerve stimulation.

- **International Pelvic Pain Society--October 22-25, 2015 (courtesy of Suzie As-Sanie University of Michigan and program chair)**

The keynotes for the annual meeting were given by **Kathy Sluka** and **Robert Dworkin**, both very seasoned pain researchers. Dr. Sluka has done some exceptional work how exercise influences pain initiation, both at the level of the brainstem and peripherally with regard to M1/M2 macrophage regulation. Robert's talk was very engaging, exposing some of the biases and underreporting issues with clinical trials in pain. **Rick Harris** discussed some recent findings of how acupuncture influences pain cortically by altering insular connections. The two award winning posters from UCLA were presented by **Laura Payne** and **Andrea Rapkin**, who have found in (1) dysmenorrhea – potential relationships between anxiety and disability with menstrual pain experience and (2) vulvodynia that in the NVA-funded vulvodynia registry that vulvar mucosal pain ratings have different potential mechanistic underpinnings, being linked namely to anxiety and provoked pain report while pelvic muscle pain ratings correlate instead with total comorbid pain conditions and history of abuse/trauma.

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## Opportunities for Collaborative Research

We need to have labs who are interested in this area really think about the possibility of doing collective webinars as IASP is interested in providing the multimedia space to conduct real time collaborations. We will be piloted this system this winter, and will be looking to host at least one other session this year. Those who believe their work might be of interest for this forum should contact the SIG leadership.

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## Recently Published Pertinent Articles

We invite SIG members to send in brief Twitter-length summaries (140 characters) of any papers they have published with the appropriate PUBMED links, and we will include them. We have included some selected PUBMED links here for relevant recent visceral pain articles from the leadership (we need some help so we can look through and summarize the rest of the literature), but we hope that a newsletter committee might assemble to tackle this task. In addition, we provide [this link](#) to the quarterly International Painful Bladder Foundation newsletter that **Jane Meijlink** personally collates and comments on.

- *World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project: II. Clinical and covariate phenotype data collection in endometriosis research.* Vitonis AF, Vincent K, Rahmioglu N, Fassbender A, Buck Louis GM, Hummelshoj L, Giudice LC, Stratton P, Adamson GD, Becker CM, Zondervan KT, Missmer SA; WERF EPHEct Working Group. *Fertil Steril.* 2014 Nov;102(5):1223-32. doi: 10.1016/j.fertnstert.2014.07.1244. PMID: 25256930
- *Altered brain connectivity in dysmenorrhea: pain modulation and the motor cortex.* Kutch JJ, Tu FF. *Pain.* 2016 Jan;157(1):5-6. doi: 10.1097/j.pain.0000000000000364. PMID: 26683107
- *Multimodal nociceptive mechanisms underlying chronic pelvic pain.* Hellman KM, Patanwala IY, Pozolo KE, Tu FF. *Am J Obstet Gynecol.* 2015 Dec;213(6):827.e1-9. doi: 10.1016/j.ajog.2015.08.038. PMID: 26299416
- *Cannabinoid hyperemesis syndrome: an important differential diagnosis of persistent unexplained*

vomiting. Ruffle JK, Bajgoric S, Samra K, Chandrapalan S, Aziz Q, Farmer AD. *Eur J Gastroenterol Hepatol*. 2015 Dec;27(12):1403-8. doi: 10.1097/MEG.0000000000000489. PMID: 26445382

- *Systematic review: instruments to assess abdominal pain in irritable bowel syndrome*. Mujagic Z, Keszthelyi D, Aziz Q, Reinisch W, Quetglas EG, De Leonardis F, Segerdahl M, Masclee AA. *Aliment Pharmacol Ther*. 2015 Nov;42(9):1064-81. doi: 10.1111/apt.13378. Epub 2015 Aug 20. PMID: 26290286
- *Rapid balloon distension as a tool to study cortical processing of visceral sensations and pain*. Lelic D, Nissen TD, Brock C, Aziz Q, Drewes AM. *Neurogastroenterol Motil*. 2015 Jun;27(6):832-40. doi: 10.1111/nmo.12557. PMID: 26011783
- *Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea*. Slattery SA, Niaz O, Aziz Q, Ford AC, Farmer AD. *Aliment Pharmacol Ther*. 2015 Jul;42(1):3-11. doi: 10.1111/apt.13227. Epub 2015 Apr 27. PMID: 25913530
- *A classification of chronic pain for ICD-11*. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Kosek E, Lavand'homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JW, Wang SJ. *Pain*. 2015 Jun;156(6):1003-7. doi: 10.1097/j.pain.0000000000000160. PMID: 25844555
- *Functional gastrointestinal disorders are associated with the joint hypermobility syndrome in secondary care: a case-control study*. Fikree A, Aktar R, Grahame R, Hakim AJ, Morris JK, Knowles CH, Aziz Q. *Neurogastroenterol Motil*. 2015 Apr;27(4):569-79. doi: 10.1111/nmo.12535. PMID: 25817057
- *Evidence of a role for GTP cyclohydrolase-1 in visceral pain*. Bulmer DC, Botha CA, Wheeldon A, Grey K, Mein CA, Lee K, Knowles CH, Winchester WJ, Aziz Q. *Neurogastroenterol Motil*. 2015 May;27(5):656-62. doi: 10.1111/nmo.12538.

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## The U.S. NIH/NIDDK MAPP Research Network: Recent Findings and Future Directions

Millions of Americans suffer from urologic pelvic pain syndrome (UCPPS)—an umbrella term that encompasses the symptomatically similar conditions of interstitial cystitis/bladder pain syndrome (IC/BPS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). UCPPS is characterized by chronic pain in the pelvis, bladder, pelvic floor myofascial tissues, or external genitalia, often accompanied by lower urinary tract symptoms. Despite past research, the pathophysiology, etiology, and risk factors associated with UCPPS remain unclear and there is a lack of generally effective treatments. To generate a more comprehensive understanding of UCPPS that will facilitate the design of future clinical trials and ultimately improve clinical management of UCPPS patients, the National Institute of Diabetes and Digestive and Kidney Diseases initiated the **Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network** in 2008.

**The MAPP Research Network Approach.** By bringing together a diverse set of researchers including urologists, gynecologists, neurobiologists, epidemiologists, and pain experts, among many others, the MAPP Research Network broadens UCPPS research beyond the traditional focus on the bladder and prostate to a systemic perspective with consideration of potential interactions between the genitourinary system and other local (pelvic) and systemic physiologic systems, such as the central nervous system. The MAPP Network leverages basic, translational, and clinical science studies to elucidate the pathophysiology of UCPPS and identify subgroups of UCPPS patients based on individual characteristics (phenotypes) including psychological factors, pain sensitivity, bladder symptoms, and brain structure and function. The primary research study conducted by the network was a prospective observational study of the treated natural history of UCPPS that aimed to:

- Assess the clinical characteristics of UCPPS at baseline and during a 12 month follow-up to derive new insights into clinical course and pathophysiology, including symptom variation and relationships with comorbid pain conditions.
- Assess structural and functional variation within the central nervous system between UCCPS patients and controls;
- Explore infectious agents as potential contributors to UCPPS etiology;
- Evaluate novel biomarkers associated with UCPPS; and

- Characterize symptom “flares” (periods of exacerbated symptoms) within UCPPS patients.

The primary clinical research study is complemented by animal model studies that aim to establish clinically relevant phenotypes that will improve translation between animal and human studies.

**Findings from MAPP I.** The first phase of the MAPP Research Network (MAPP I) involved a 12-month cohort study in which 424 individuals with UCPPS completed questionnaires every 2 weeks. Baseline findings suggest there are surprisingly few differences between men and women with UCPPS in terms of pelvic pain symptoms, quality of life impact, and presence of pain symptoms outside the pelvis. Individuals who experience pain with bladder filling or urgency may represent a distinct subset of patients with more severe UCPPS. Also, pain symptoms and urinary symptoms appear to have distinct longitudinal patterns, suggesting that these two types of symptoms should be measured and analyzed separately. Further, patients with UCPPS have objective, measurable physiologic differences. For example, a subset of individuals with UCPPS—who express a “centralized phenotype”—experience pain outside of the pelvis that correlates with increased global pain sensitivity. Additionally, brain imaging suggests individuals with UCPPS have different brain structure and function than individuals without UCPPS.

While analysis of longitudinal data from MAPP I is ongoing, initial assessment of pain body mapping data suggest individuals who experience ‘pelvic pain only’ fare better over time than those with pelvic pain accompanied by non-pelvic pain. Validation is being conducted to further examine this trend. Early review of symptom flare data indicate a “high symptom variability” UCPPS phenotype, which correlates with greater healthcare utilization. Current analysis of longitudinal flare data aims to uncover risk factors that correlate with flare occurrence.

**Future Directions for the MAPP Research Network.** To build on the success of MAPP I, a second phase of the MAPP Research Network (MAPP II) was launched in 2015. MAPP II will continue to follow men and women with UCPPS for an additional three years at less frequent intervals. In addition to gathering additional longitudinal data from neuroimaging and pain studies to better assess changes over time, MAPP II will focus on the relationship between patient characteristics (phenotype) and treatment outcomes.

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## Notable Occurrences

>> We are aware of four topical workshop submissions in the visceral pain area for the 2016 World Congress on Pain in Yokohama. We were grateful to see one of the two SIG-sponsored submissions was accepted, and **Janet Keast** from Australia, **Qasim Aziz** from the UK, and **Frank Tu** from the US will be giving a talk on autonomic regulation of viscera in pelvic pain states.

Based on IASP leadership feedback, we would encourage members to consider earlier planning for future topical workshop submissions and in particular to focus on mechanism-based workshops, ideally involving members from different continents.

>> On April 8-9, 2015, members of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS), including co-chair **Denniz Zolnoun** and **Sarah Fox** from IASP, organized an international meeting in order to reach a consensus on the terminology of vulvar pain. After discussions, a consensus terminology proposal was unanimously reached. It was decided by the three societies that the consensus terminology proposal would be brought to discussion and voted on by each society. The terminology has also been approved by ISSVD and ISSWSH.

For more information please follow [this link](#) to a brief explanation from the consensus committee. The new guidelines will be published in their entirety in several peer-reviewed journals.

Respectfully submitted,

Frank Tu, MD

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