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NEUROGENIC PAIN RELATED LYSOPHOSPHATIDYLCHOLINE IS INCREASED IN THE SPINAL FLUID OF PATIENTS WITH HUNNER TYPE INTERSTITIAL CYSTITIS

Hypothesis / aims of study
Typical histopathological finding of Hunner type interstitial cystitis (HIC) is infiltration of inflammatory cells and it cause acute nociceptive pain. However, it is often seen that the pain become chronic and refractory to NSAIDs and opioids, and those medicines for neuropathic pain such as pregabalin and amytriptyline show better effect on pain relief, instead.
Lysophosphatidilcholine (LPC) is a demyelinating and signaling molecule involved in neuropathic pain, hyperalgia and allodynia. Our aim was to investigate the relationship between LPC and its related mediators and pain plasticity in patients with interstitial cystitis.

Study design, materials and methods
A total of 13 HIC patients and 22 non-IC controls who underwent spinal anaesthesia were enrolled to this study. Diagnosis of IC and differential diagnosis of HIC and NHIC were made according to the clinical guidelines for interstitial cystitis and hypersensitive bladder syndrome and controls were patients without chronic pain and hospitalized for other reason than IC (e.g. URS for urolithiasis, TUR of tiny bladder cancer). Self-assessment questionnaire for IC, OAB and pain (O'Leary and Sants' symptom index and problem index (OSSI, OSPI) and VAS scores were measured before hospitalization. Spinal fluid samples were collected when these patients underwent spinal anaesthesia and then investigated for the amount of LPC by using mass spectrometry. The mass spectrometry method has been developed and validated to quantify LPC species (LPC 14:0, LPC 16:0, LPC 16:1, LPC 18:0, LPC 18:1, LPC 18:2 and LPC 20:4, LPC 22:6) in human spinal fluid. A paired samples t-test was used to compare the difference in these species between HIC and non-IC group.

Results
Table 1 shows the patient demography. The background of the control cases as follows; 8 URS cases, 12 TUR-BT, 1 TUR-P, 1 TVM. All the patients in control group did not have any history of pelvic pain nor discomfort. The symptom scores OSSI, OSPI, OABSS and VAS scores showed symptomatic severity was significantly higher in HIC group, compared to control.
All the LPC species, except 14:0 LPC showed significant elevation in HIC group, compared to the control group. (Figure 1)

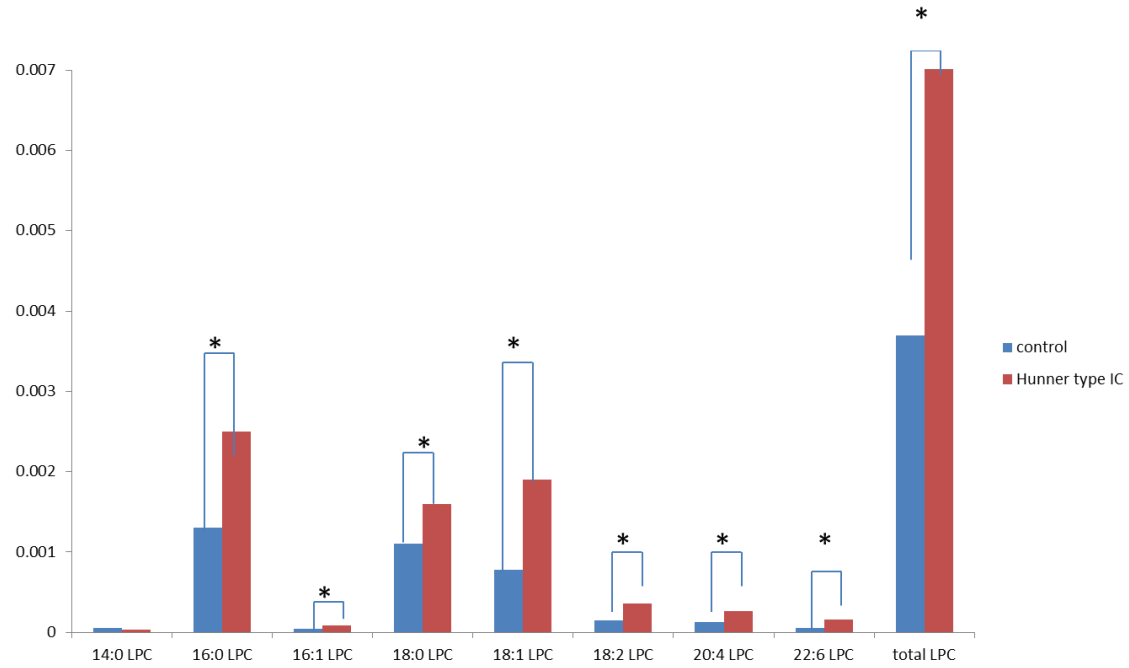
Interpretation of results
We demonstrate LPC was significantly increased in the spinal fluid of HIC.
LPC is known to cause demyelination of sensory nerves which leads to neurogenic pain, hyperalgia, allodynia.
Recently, Foster et. al. demonstrated primary afferent neurons associated with the bladder exhibit increased chemokine receptor signalling following sciatic nerve injury with LPC in rodent model, suggesting the somatic nerve injury may induce neurogenic inflammation.
Although the major pathophysiology of pain in HIC is nociceptive, prolonged HIC pain may have induced neural cross talk, causing neural plasticity.

Concluding message
Neurogenic pain related LPC was increased in the spinal fluid of HIC. This finding suggests that cross talk of nociceptive neurons may have occurred in HIC and is attributed to chronification of bladder pain.

Table 1. Patient demography

	Control n=22	Hunner type IC n=13	P value
Gender M:F	17:5	12:1	
Age	65.5 ±12.1	66.0 ±9.4	0.9
OSSI	8.7 ±5.5	15.2 ±3.6	<0.001
OSPI	7.6 ±4.9	12.2 ±3.7	0.036
OABSS	5.6 ±4.7	12.0 ±5.2	0.013
VAS Score	2.7 ±2.6	8.9 ±3.7	0.005

Figure 1.



References

1. Foster, R., Jung, J., Farooq, A., McClung, C., Ripsch, M. S., Fitzgerald, M. P., & White, F. A. (2011). Sciatic nerve injury induces functional pro-nociceptive chemokine receptors in bladder-associated primary afferent neurons in the rat. Neuroscience, 183, 230-237.

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