α-Fucose increased in the brain of Chronic Pelvic Pain Syndrome patients with inflammation at onset recorded by 2D L-COSY

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Purpose: Chronic Pelvic Pain Syndrome (CPPS) is a common but poorly understood condition affecting men. CPPS is the most common form of prostatitis and accounts for 90-95% of cases[3]. CPPS is sub classified into non-inflammatory (type IIIA) or inflammatory (type IIIB)[3]. Fucose is suggested to play a role in the inflammatory process with fucosylated epitopes, e.g. sialyl Lewis x, shown to increases during the early events of inflammation[4 5]. This study aimed to characterize changes in free and bound fucose, in patients with CPPS, using in vivo 2D localized correlation spectroscopy (L-COSY) at 3T.

Methods: In vivo two dimensional localised correlation spectroscopy was acquired from the posterior cingulate gyrus (PCG) using a 3T MR scanner (Siemens TIM Trio) with a 12 channel head coil, on nine patients diagnosed with CPPS (four with inflammatory (type IIIB) and five non-inflammatory (type IIIA)) and nine healthy age and sex matched controls. Localised shimming was performed prior to data acquisitions using automatic adjustment of first and second order shim gradients, followed by manual shimming of the zero-order shim gradient to achieve a peak width of water at half-maximum that was 14Hz or better. Data was acquired from the PCG with a 3x3x3 cm^3 voxel using the following parameters: RF carrier frequency at 2.0 ppm; TR 1.5 s; spectral width of 2000 Hz; increments size of 0.8 ms in 96 t1 increments giving an indirect spectral width of 1250 Hz; 12 averages per increment; and 1024 data points. The WET water-suppression sequence was applied prior to data acquisition [6]. Scan time for the 2D COSY was 29 minutes.

Raw 1D COSY spectra was transferred to MATLAB for signal combination followed by row concatenation into a 2D matrix. Felix 2007 was used for the processing and analysis of the 2D COSY data. The data was processed in Felix using the parameters detailed by Ramadan et al[2]. Water suppression was applied using Felix: CNV solvent suppression, sine convolution function, function width 40 and linear extrapolation. The creatine methyl resonance (3.02-3.02ppm) was used as the internal chemical control for both chemical shift and cross-peak volume [7]. Cross and diagonal peaks were assigned and peak volumes measured using Felix NMR 2007. Average peak volume concentrations were calculated for each assigned metabolite and statistical significance was calculated using a Mann-Whitney test (due to non-normal distribution) in Stata.

Results: The chemical shift assignments for the region containing free and bound fucose is shown in Figure 1[1-2]. The average chemical shift assignment for alpha-fucose in CPPS patients was calculated to be 4.19-1.11 (SD: 0.027 – 0.033). A comparison between controls and inflammatory (type IIIB) /non-inflammatory (type IIIA) CPPS is shown in **Table 1**. The mean cross peak volumes for all groups is shown in **Table 2**. A significant increase in the cross peak volumes assigned to α-Fucose between healthy controls and CPPS type IIIB was recorded. Additionally there was a 105% decrease in the composite cross-peak Fucose I/threonine (Thr/FucI) in CPPS (type IIIB). The increases in α- fucose is large such that a cohort size of 5 or less is sufficient to reach the significance level of P=0.05 with a power of 90% from the Altman Nomogram[8].

Table 1 - Cross peak volumes of CPPS vs. Healthy Controls

	CPPS (type IIIA) vs. cont.		CPPS (type IIIB) vs. cont.	
F2-F1	% Difference	p-value	% Difference	p-value
Lactate (4.10-1.30)	30%	0.10	45%	0.28
α-Fuc(4.20-1.22)	37%	0.95	**68%**	**0.02**
Thr/Fuc I (4.26-1.39)	-68%	0.32	-105%	0.06
Fucose II (4.28-1.25)	12%	0.13	27%	0.76
Fuc III (4.30-1.41)	-23%	0.46	-14%	0.64
Fuc IV (4.38-1.31)	-33%	0.39	25%	0.54

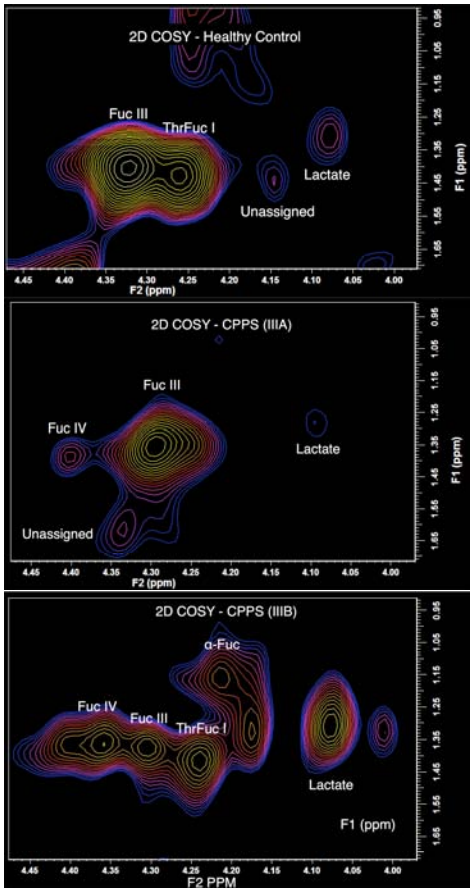

Figure 1 - Typical L-COSY from a healthy control and patients with CCPS IIIA and CPPS IIIB (F2 3.95–4.50 ppm, and F1 0.90–1.73 ppm, with assignments from [1] and [2]. Contour threshold: 0.03. Lev Mult: 1.05

Conclusion: L-COSY was undertaken on the brains of patients with CPPS compared with a healthy control population. We report a statistically significant increase of 68% in α-fucose in the CPPS IIIB group with inflammation at onset. There is a concomitant 105% decrease in the composite Thr/Fuc I suggesting an altered pathway.

References:

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Table 2 – Mean cross peak volumes for CPPS patients and healthy volunteers

	CPPS (type IIIA)			CPPS (type IIIB)			Healthy Control		
	Mean	95% Conf. Interval		Mean	95% Conf. Interval		Mean	95% Conf. Interval	
α-Fuc(4.20-1.22)	3.75E-03	-1.34E-03	8.83E-03	7.45E-03	3.50E-04	1.46E-01	2.37E-03	7.27E-04	4.02E-03
Thr/Fuc I (4.26-1.39)	8.24E-03	8.75E-04	1.56E-02	6.76E-03	2.73E-03	1.08E-02	1.38E-01	6.13E-03	2.16E-01
Lactate (4.10-1.30)	4.46E-03	2.30E-03	6.62E-03	5.70E-03	-1.64E-03	1.30E-02	3.14E-03	1.60E-03	4.68E-03
Fucose II (4.28-1.25)	2.71E-03	1.54E-03	3.89E-03	3.28E-03	-3.97E-03	1.05E-02	2.40E-03	2.05E-04	4.59E-03
Fuc III (4.30-1.41)	1.23E-02	1.46E-03	2.32E-01	1.32E-02	1.61E-03	2.48E-02	1.51E-01	1.04E-02	1.98E-02
Fuc IV (4.38-1.31)	5.41E-03	9.81E-04	9.84E-03	9.56E-03	-3.38E-04	1.95E-02	7.19E-03	4.71E-03	9.67E-03