Cortical responses to a rectal balloon pain paradigm

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Background: The barostat balloon rectal distension paradigm is a gold standard in clinical settings for investigating visceral hypersensitivity, a widespread problem in gastrointestinal diseases such as Irritable Bowel Syndrome and Diverticular Disease. Visceral hypersensitivity occurs either because patients are peripherally sensitized by prior inflammation or because patients are hypervigilant. The relative contribution of these peripheral versus central factors is controversial and has implications for patient management. Several fMRI studies have investigated cortical activation in response to rectal distension, demonstrating that this elicits a widespread network of brain activity [1,2]. The clinical barostat paradigm comprises 30 to 40 s "ON" and "OFF" periods, in which the barostat balloon is applied at stepped pressure thresholds. However, the stimulus does not follow a classic box-car, as it takes a few seconds for the balloon to achieve the desired pressure in the rectum, meaning that the "ramp on" and "ramp off" times are slow. It is unclear which part of this varying distension curve is most relevant to the physiology. To date most fMRI studies have modelled the data using a simple "ON" box car stimulus waveform but cortical responses may better correlate with "ramp on" and "ramp off" periods. Here, the experiment was performed in fMRI to investigate the nature of the haemodynamic response, and repeated using magnetoencephalography (MEG) to provide neuromagnetic data which, given its direct nature, may provide further information on the cortical response to visceral sensation.

Materials and Methods: 15 healthy female volunteers (age 29.2±10.9 yrs) participated. A G&J Electronics Distender Series II barostat was used. The distension balloon was inserted rectally and the threshold of moderate pain determined using a tracking paradigm. The barostat paradigm comprised four stimuli: no stimulus, subliminal stimulus, perceived stimulus (first sensation) and painful stimulus (determined individually) with five repetitions of each. Each stimulus was 40 s followed by 30 s rest at 0 mmHg. Volunteers attended on one day for fMRI (using a 3T Philips Achieva scanner) and another for MEG (using a 275 channel CTF whole-head scanner). fMRI: 36 transverse double-gradient-echo (TE: 30 ms, 49 ms), EPI (64x64 matrix, voxel size 4x4x4 mm^3) images were acquired using an 8-channel SENSE coil every 2.6 sec (jittered). Following the fMRI experiment a T_2* map was formed from a multi-gradient-echo EPI data set (TE: 11, 30, 49, 68 and 87 ms). fMRI data were analysed using SPM5 and corrected for slice timing and realigned. T_2* maps were used to perform a weighted summation of the double echo fMRI data. These data were normalised to the EPI template and spatial smoothing (12 mm kernel), global scaling and temporal filtering (128 sec high pass filter) applied. A general linear model was formed to identify areas activated by the painful stimulus. This was modelled as (i) a box function of 40 s ON (Fig. 1a) or (ii) a box function of 5 s reflecting the "ramp-on" of the balloon (Fig.1b); each were convolved with a canonical HRF. The individual motion parameters were included as covariates of no interest. A random effects group of the analysis was performed. MEG data was source localised using synthetic aperture magnetometry (SAM) [3]. Data were analysed in α, β, γ and δ bands, with windows selected to contrast painful and baseline periods. Pseudo-T-statistical images showing the spatial distribution of power change between these windows were overlaid onto individual MR images.

Results: fMRI data show greater activation (number of activated voxels and t-scores) for the "ramp-on" model (Fig. 1d) than the 40 s "ON" (Fig. 1 c) distension model. Random effects group analysis for the "ramp-on" model (FWE P<0.05 corrected) showed significant activation in insula, anterior cingulate cortex, thalamus, parietal and somatosensory SII cortex. Time courses (Fig. 2) showed an initial peak response after the "ramp on" distension which declined rapidly, followed by a smaller BOLD response to the deflation of the balloon. MEG data (Fig. 3) showed significant event-related synchronisation in the anterior insula in α band, in the anterior cingulate in θ band and in the somatosensory cortex in δ and θ band.

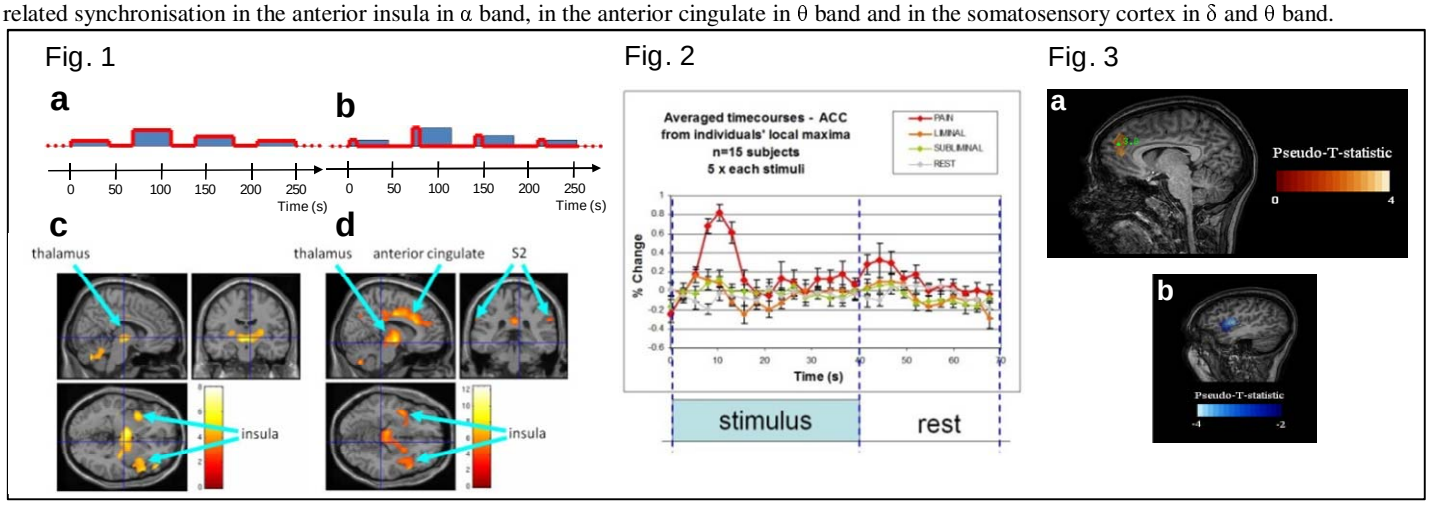

FIG. 1: Barostat distension paradigm modelled with 40 s "ON" barostat distension (a) or 5 s "ramp on" (b). fMRI maps for 40 s "ON" (c) and for the 5 s "ramp on" (d). FIG. 2: Average fMRI time courses from anterior cingulate for each stimulus level. FIG. 3: MEG activations with anterior cingulate cortex ERS in θ band (a) and insula cortex location of a ERD peak in β band (b).

Discussion: The fMRI data analysis shows the complexity of the barostat rectal distension stimulus, and that the cortical response occurs primarily during the ramps of the rectal distension. The paradigm detects activity in regions conventionally associated with sensory, cognitive and affective aspects of pain processing [4]. The brain areas identified with MEG largely matched those identified by fMRI. Given that no fMRI priors were used in MEG source localisation, this spatial agreement is compelling. The direct nature of MEG also gives it potential to provide insight into the timescale of electrical power changes in the cortical areas of interest identified using fMRI.

References: [1] Price et al. Pain 127:63-72, 2007. [2] Ladabaum et al. Neuroimage 34:724-32, 2007. [3] Robinson and Vrba, Recent advances in biomagnetism, Tohoku Univ. Press, 1998. [4] Peyron et al. Neurophysiol Clin 30:263-88, 2000.