#3083 Title: Fibromyalgia and myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): an interoceptive predictive coding model of pain and fatigue expression

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Introduction:
The aetiology and pathophysiology of fibromyalgia and ME/CFS are poorly characterised but altered inflammatory, autonomic and interoceptive processes have been implicated. Interoception has been conceptualised as a predictive coding process; where top-down prediction signals compare to bottom-up afferents, resulting in prediction error signals indicating mismatch between expected and actual bodily states. Chronic dyshomeostasis and elevated interoceptive prediction error signals have been theorised to contribute to the expression of pain and fatigue in fibromyalgia and ME/CFS.

Objectives/aims:
To investigate how altered interoception and prediction error relates to baseline expression of pain and fatigue in fibromyalgia and ME/CFS and in response to an inflammatory challenge.

Methods:
Sixty-five patients with fibromyalgia and/or ME/CFS diagnosis and 26 matched controls underwent baseline assessment: self-report questionnaires assessing subjective pain and fatigue and objective measurements of pressure-pain thresholds. Participants received injections of typhoid (inflammatory challenge) or saline (placebo) in a randomised, double-blind, crossover design, then completed heartbeat tracking task (assessing interoceptive accuracy). Porges Body Questionnaire assessed interoceptive sensibility. Interoceptive prediction error (IPE) was calculated as discrepancy between objective accuracy and subjective sensibility.

Results:
Patients with fibromyalgia and ME/CFS had significantly higher IPE (suggesting tendency to over-estimate interoceptive ability) and interoceptive sensibility, despite no differences in interoceptive accuracy. IPE and sensibility correlated positively with all self-report fatigue and pain measures, and negatively with pain thresholds. Following inflammatory challenge, IPE correlated negatively with the mismatch between subjective and objective measures of pain induced by inflammation.

Conclusions:
This is the first study to reveal altered interoception processes in patients with fibromyalgia and ME/CFS, who are known to have dysregulated autonomic function. Notably, we found elevated IPE in patients, correlating with their subjective experiences

of pain and fatigue. We hypothesise a predictive coding model, where mismatch between expected and actual internal bodily states (linked to autonomic dysregulation) results in prediction error signalling which could be metacognitively interpreted as chronic pain and fatigue. Our results demonstrate potential for further exploration of interoceptive processing in patients with fibromyalgia and ME/CFS, aiding understanding of these poorly defined conditions and providing potential new targets for diagnostic and therapeutic intervention.