Fibromyalgia and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): An interoceptive predictive coding model of pain and fatigue expression

Harriet EC Sharp[1], Kristy Themelis [1,3], Marisa L Amato[1], Andrew Barritt[1,2], Kevin A Davies[1,2], Neil A Harrison[1,4], Hugo D Critchley[1], Sarah N Garfinkel [1,5], Jessica A Eccles [1, 2]

[1]Brighton and Sussex Medical School, Brighton, [2]Brighton and Sussex University Hospitals NHS Trust [3]University of Warwick , [4]University of Cardiff , [5]University College London, UK

Introduction

- Fibromyalgia and ME/CFS exhibit a wide variety of symptoms, including chronic pain and fatigue
- Aetiology is poorly understood but may include:
  - Inflammatory processes
  - Autonomic dysregulation
  - Interoception (sensing of internal bodily signals)
- Interoception has been conceptualised as a predictive coding process, comparing:
  - Top-down prediction signals
  - Bottom-up afferents signals
  - 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.

Aim

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

Methods

- 65 patients with fibromyalgia and/or ME/CFS diagnosis and 26 matched controls recruited
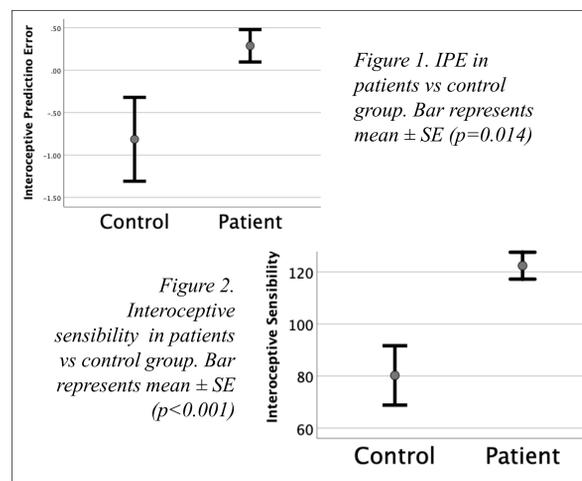
	Pain +	Pain -
Fatigue +	Fibromyalgia + ME/CFS	ME/CFS
Fatigue -	Fibromyalgia	Control

- Baseline assessment:
  - Pressure-pain thresholds
  - Self-report symptom questionnaires (pain & fatigue)
- Randomised, double-blind, crossover design:
  - Inflammatory challenge with typhoid injections or placebo (saline injection)
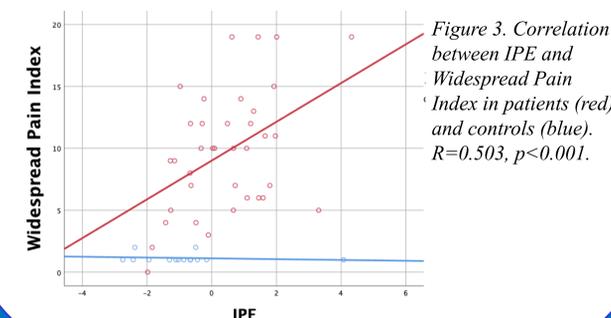- Followed by heartbeat tracking tasks (assessing interoceptive accuracy)

Interoceptive dimension	Measured by:
Subjective interoceptive sensibility	Porges Body Perception Questionnaire
Objective interoceptive accuracy	Heartbeat tracking task
Metacognitive interoceptive awareness	Correlation between confidence (VAS) and accuracy measures
Interoceptive prediction error (IPE)	Discrepancy between accuracy and sensibility

Results

- Patients with fibromyalgia and ME/CFS had:
  - Significantly higher interoceptive sensibility
  - Significantly higher IPE (suggesting tendency to overestimate interoceptive ability)
  - No differences in interoceptive accuracy

Figure 1. IPE in patients vs control group. Bar represents mean ± SE (p=0.014)

Figure 2. Interoceptive sensibility in patients vs control group. Bar represents mean ± SE (p<0.001)

- Interoceptive sensibility and IPE correlated:
  - Positively with all self-report fatigue and pain measures
  - Negatively with pain thresholds

Figure 3. Correlation between IPE and Widespread Pain Index in patients (red) and controls (blue). R=0.503, p<0.001.

- After inflammatory challenge: IPE correlated negatively with the mismatch between subjective and objective measures of pain induced by inflammation.
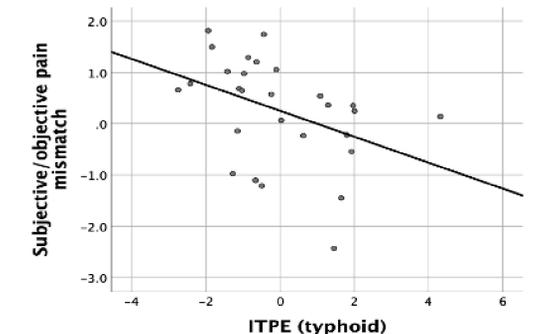

Figure 4: Correlation between IPE and subjective/objective pain mismatch (r=0.408, p=0.031)

Conclusion

- This is the first study revealing altered interoception in patients with fibromyalgia and ME/CFS
- We found elevated IPE in patients, correlating with subjective experiences of pain and fatigue
- We hypothesise a predictive coding model, where mismatch between expected and actual internal bodily states results in prediction error signalling which could be metacognitively interpreted as chronic pain and fatigue.
- Interoceptive processes may represent a new potential target for diagnostic and therapeutic intervention