UNIVERSITY OF LIVERPOOL

Alterations in resting-state brain activity of fibromyalgia patients

The Pain Relief Foundation

Dr Nick Fallon

Fibromyalgia syndrome

- Fibromyalgia syndrome (FMS) is a chronic pain disorder primarily associated with pain and tenderness, fatigue and psychological distress.
- Estimated to affect up to 5% of women.
- Challenging to treat, large socio-economic burden.

Previously considered to be central sensitisation syndrome, now peripheral factors are a major (and perhaps primary) consideration.

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Pathophysiological mechanisms in chronic musculoskeletal pain (fibromyalgia): the role of central and peripheral sensitization and pain disinhibition

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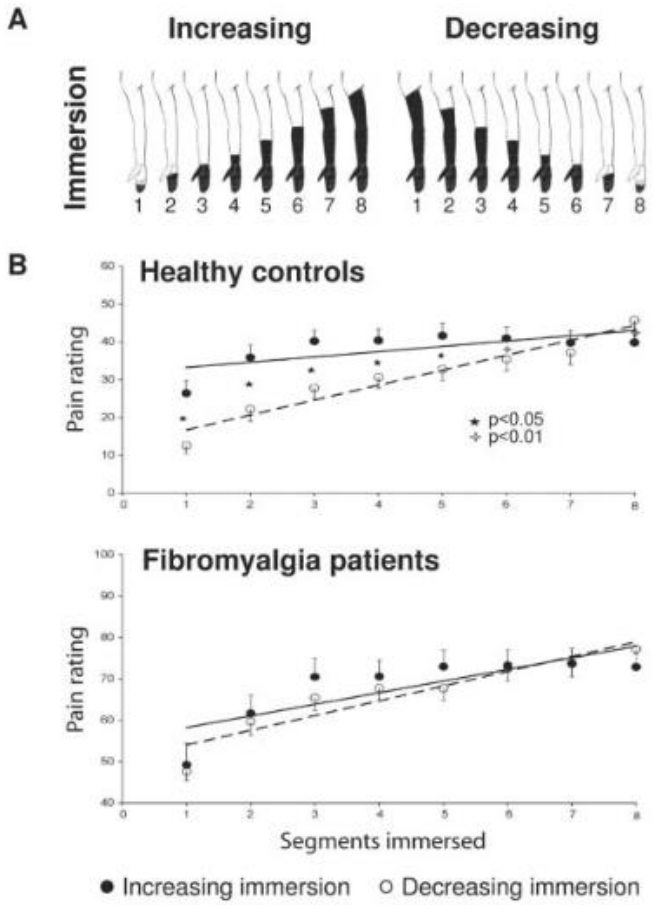
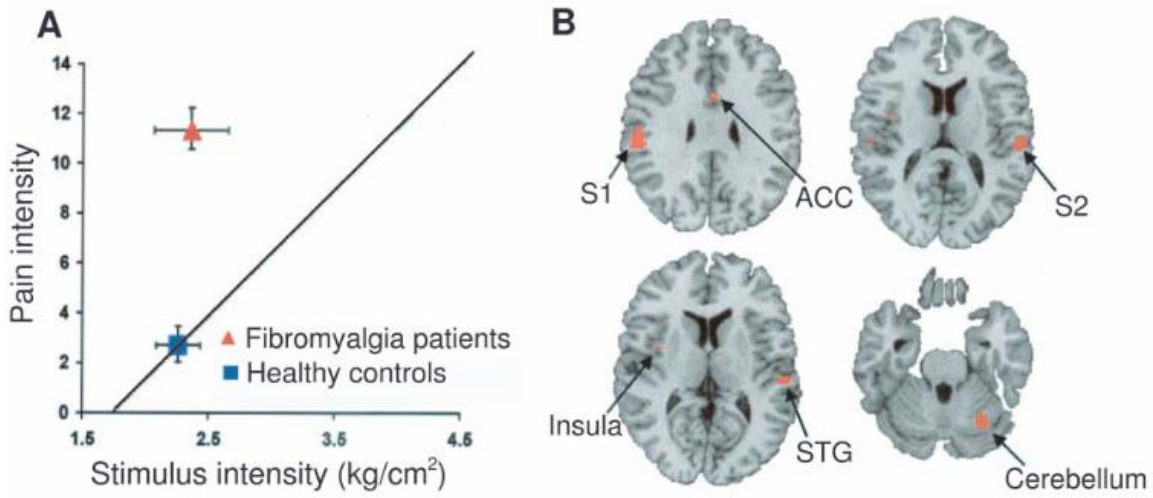
Central components of fibromyalgia?

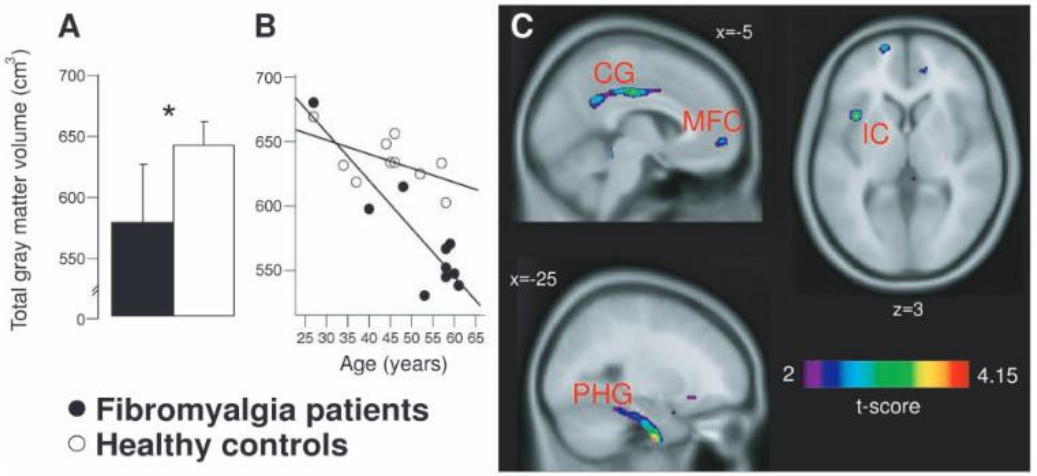
- Neuroimaging studies have frequently shown alterations to central structure or function in FM.



Reduced DNIC. Julien *et al.,* 2005



Enhanced activation profile to innocuous stimuli. Gracely *et al.,* 2002



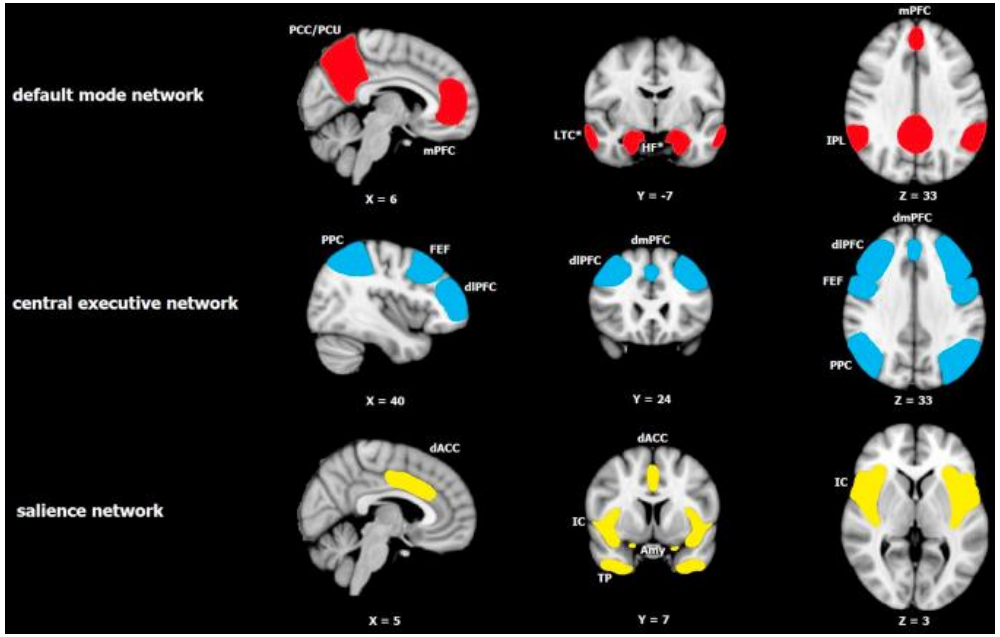
Grey matter reduction, and in pain-relevant regions. Kuchinad *et al.,* 2007

Resting-state analyses

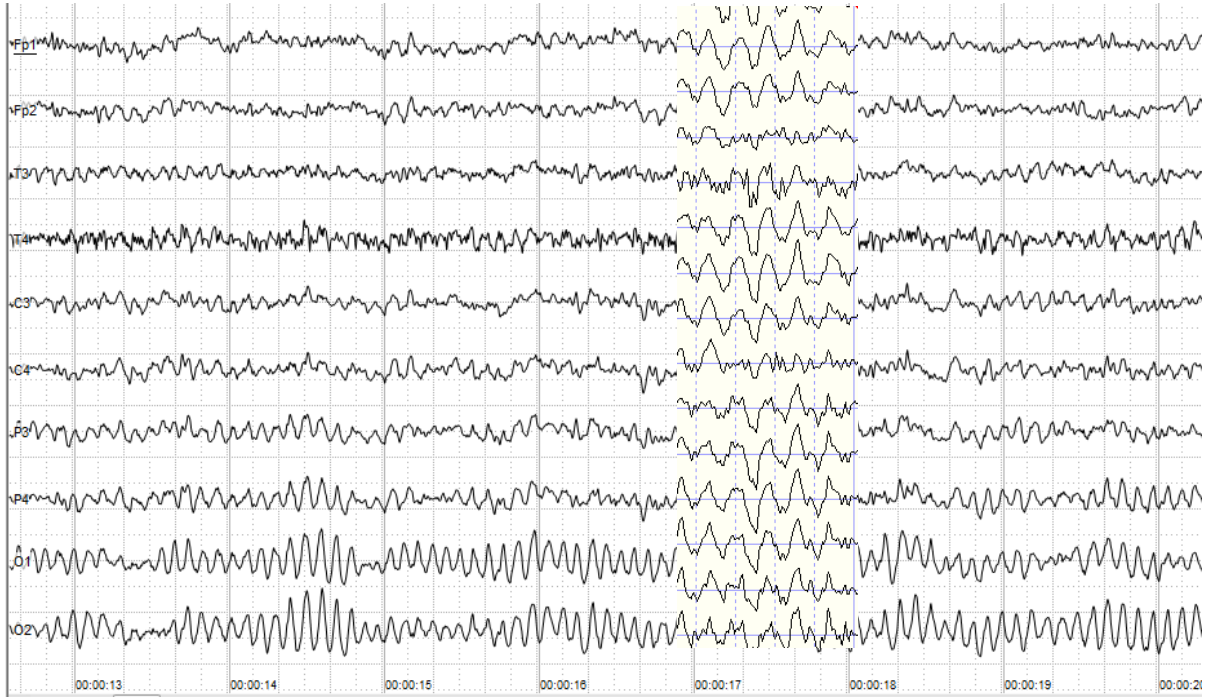
- Resting-state analyses consider the ongoing activity of the brain.

- This allows for investigations of spontaneous brain activity.

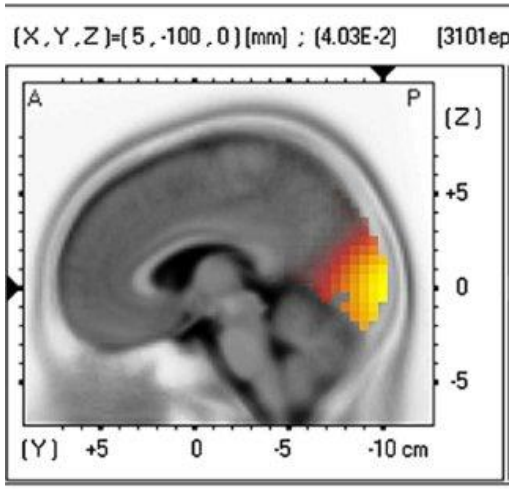
- Advantages:-
  - Investigation of brain networks.
  - Allows for a broader sampling of patients, e.g., those too impaired for task-based studies
  - Is not confounded by task performance, effort, practice effects, lab differences etc.
  - Increased signal-to-noise ratio (Fox & Greicius, 2010)



FM is associated with altered resting brain activity

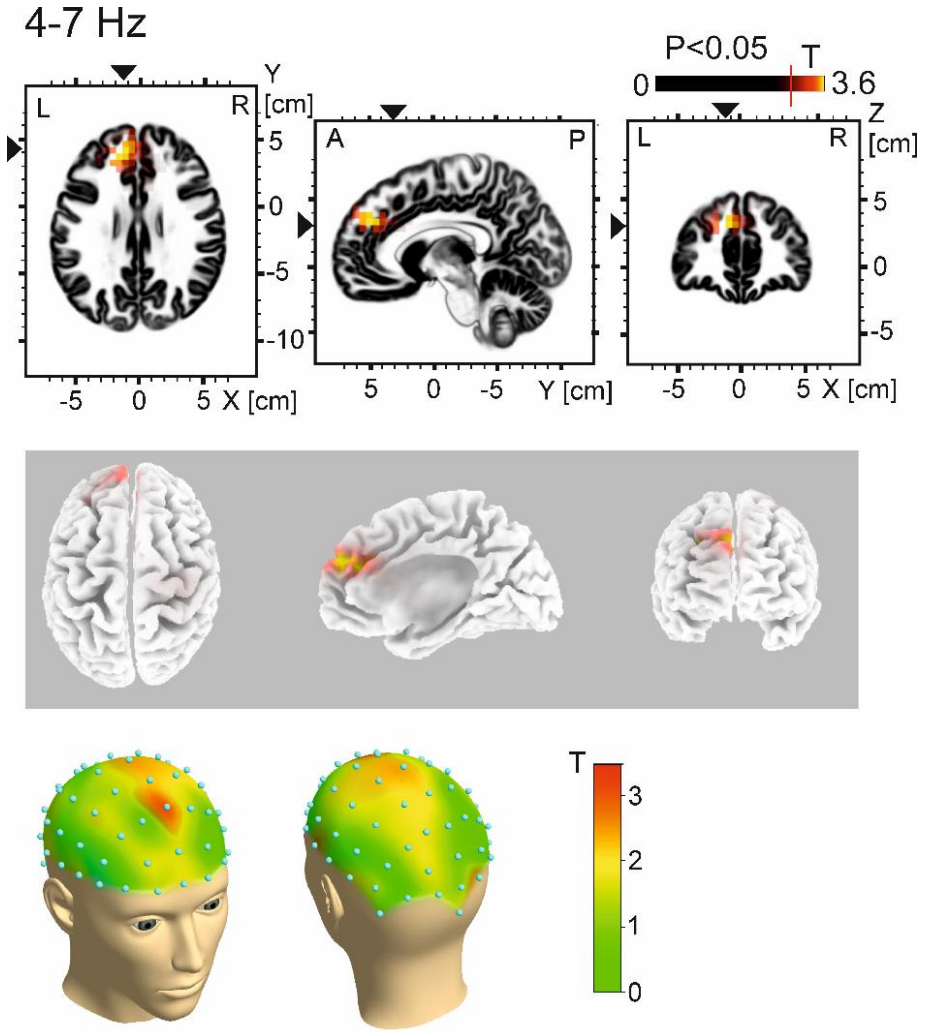


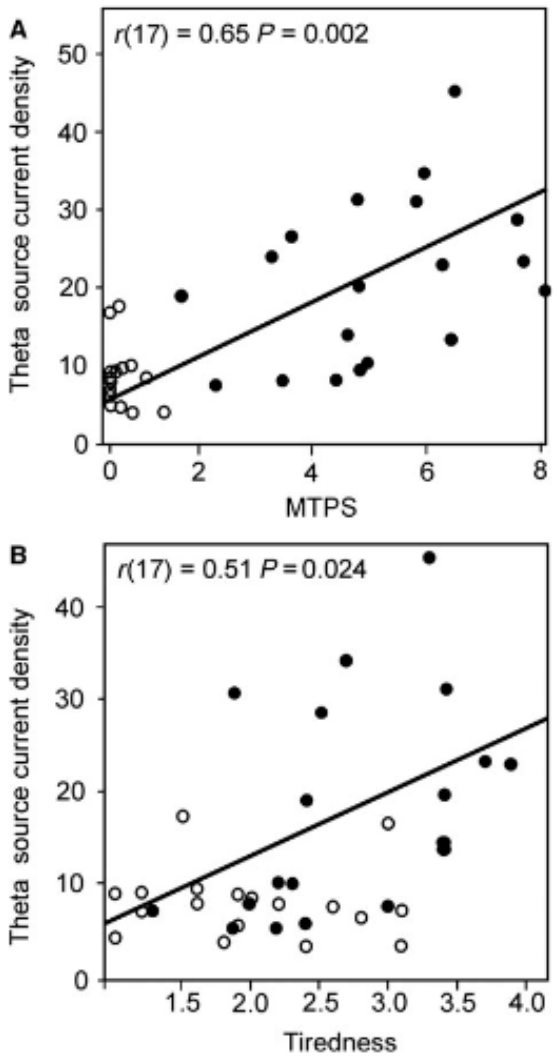
- We recruited 19 FM patients and compared to 18 healthy controls.
- We utilised EEG with a simple resting-state paradigm to consider the power of different oscillatory frequencies.
- The relative power of each frequency band of interested was calculated at scalp and source level.



FM is associated with altered resting brain activity

- FM patients demonstrate augmented frontal theta activity in both scalp electrodes and source analysis.
- Theta power in frontal regions significantly correlated with measures of tenderness and fatigue on the day of testing.
- Resting theta activity could offer some insight into fluctuating levels of chronic pain and other symptoms

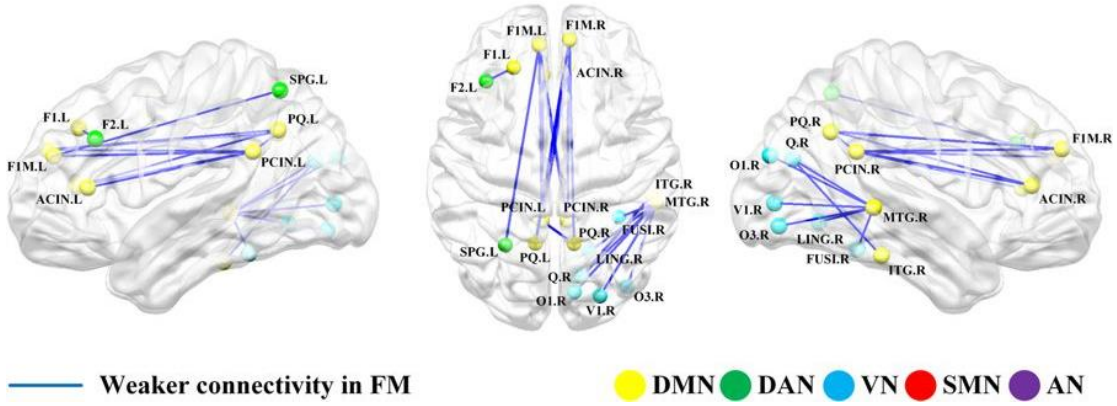




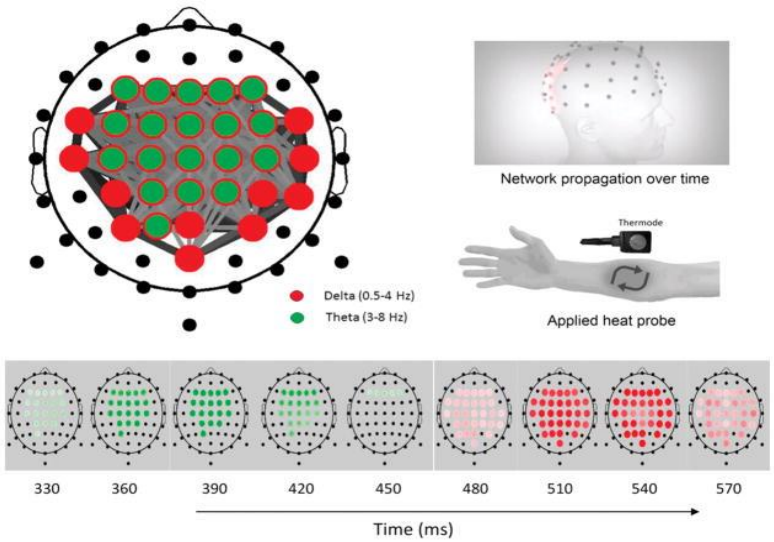
Fallon *et al.*, 2018 Eur J Pain.

Further support…

- Since our study, similar theta-band resting-state changes have been shown in FM patients using MEG (top right).
- Theta activity has been postulated as a potential biomarker or neural signature for pain using animal models (bottom right).
- Normalisation of theta network activity is a target outcome for tDCS for fibromyalgia (below)



(Choe, Lim, Kim, Lee, & Chung, 2018)



(Castillo-Saavedra et al., 2016)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Cortical theta is increased while thalamocortical coherence is decreased in rat models of acute and chronic pain

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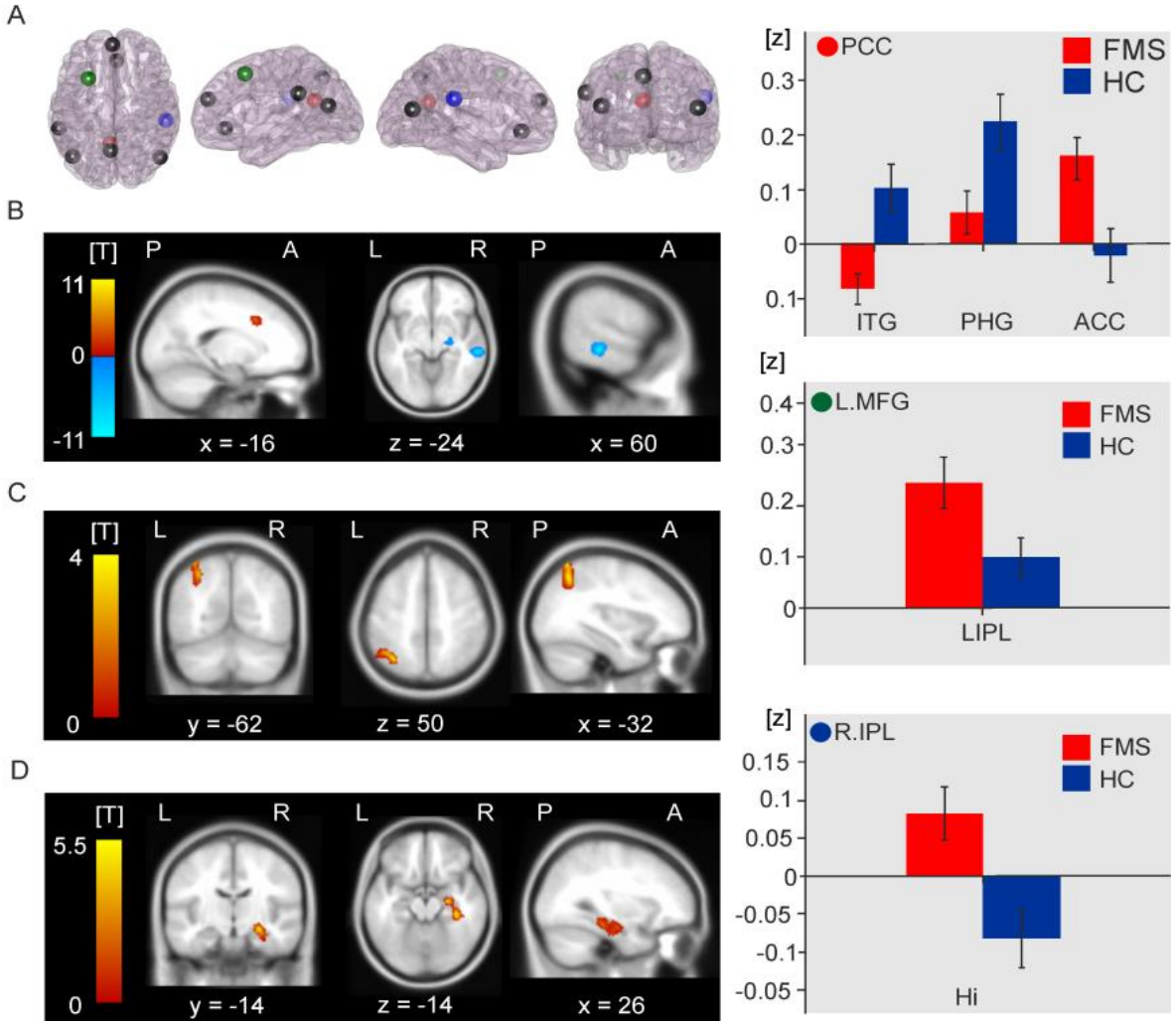
Further support (2)

- Previously we also identified demonstrated altered functional connectivity between resting brain networks using fMRI.
- Our results include connectivity seeds in middle frontal gyrus and ACC.
- Both of our resting-state studies indicate a relationship between alterations in resting brain activity and tonic pain levels from the day of testing.



Fallon., 2015. PLoS One

Conclusions

- It appears that alterations in resting brain activity of FM patients relate to fluctuating experience of symptoms.

- Central alterations could be downstream, or could interact with peripheral mechanisms.

- The direction and causal nature of such interactions is yet to be fully understood.

- Longitudinal analysis of resting-state analysis could prove to be an important tool
  - **Objectively evaluate novel treatments**

  - **Identifying patients** who are predisposed to develop chronic pain, or most likely to benefit from a particular type of treatment – i.e., personalised medicine.

Questions?

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