

Supplementary Information

A multi-modal MRI study of the central response to inflammation in rheumatoid arthritis

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Supplementary Table 1 Clinical Characteristics for 54 rheumatoid arthritis patients

| | Baseline visit | 6 month visit |
|--|----------------|---------------|
| | Mean, s.d. | |
| RA disease activity ^a | 3.62±1.30 | 3.39±1.36 |
| ESR (mm/hr) | 19.39±14.66 | 17.76±14.92 |
| CRP (mg/L) | 7.78±8.54 | 7.52±10.81 |
| Fatigue ^b | 4.59±2.19 | 4.91±2.01 |
| Number of painful sites ^d | 6.48±4.64 | 6.59±3.94 |
| Pain ^f | 3.81±2.38 | 2.91±1.92 |
| Cognitive performance (%) ^g | 82.48±18.71 | 84.79±16.45 |

^aDisease activity score 28; ^bCurrent fatigue 0-10 numerical rating scale (NRS); Widespread Pain Index of the 2011 fibromyalgia survey; Current pain NRS; ^g percentage of correct paced auditory serial addition test responses

Supplementary Table 2 Frequency and percentage of treatment with anti-inflamamtory drugs

| Medication N (%) | Baseline | 6 month visit |
|---------------------|----------|---------------|
| Methotrexate | 29 (54) | 30 (56) |
| Sulphasalazine | 6 (11) | 6 (11) |
| Lefunomide | 5 (9) | 7 (13) |
| Hydroxychloroquine | 5 (9) | 5 (9) |
| Rituximab | 7 (13) | 7 (13) |
| Tociluzimab | 4 (7) | 5 (9) |
| Adalumimab | 7 (13) | 7 (13) |
| Etanercept | 7 (13) | 6 (11) |
| Certoluzimab | 7 (13) | 8 (15) |

Supplementary Table 3 The network based statistic inflammation configuration

| Edge | Node 1 | Network | Node 2 | Network |
|-----------|--------|--------------------------------|--------|--------------------------------|
| 13 to 28 | 13 | Uncertain | 28 | Sensory/somatomotor Hand |
| 13 to 34 | 13 | Uncertain | 34 | Sensory/somatomotor Hand |
| 13 to 47 | 13 | Uncertain | 47 | Cingulo-opercular Task Control |
| 25 to 116 | 25 | Sensory/somatomotor Hand | 116 | Default mode |
| 28 to 264 | 28 | Sensory/somatomotor Hand | 264 | Dorsal attention |
| 34 to 47 | 34 | Sensory/somatomotor Hand | 47 | Cingulo-opercular Task Control |
| 34 to 264 | 34 | Sensory/somatomotor Hand | 264 | Dorsal attention |
| 39 to 47 | 39 | Sensory/somatomotor Hand | 47 | Cingulo-opercular Task Control |
| 39 to 112 | 39 | Sensory/somatomotor Hand | 112 | Default mode |
| 39 to 202 | 39 | Sensory/somatomotor Hand | 202 | Fronto-parietal Task Control |
| 39 to 213 | 39 | Sensory/somatomotor Hand | 213 | Salience |
| 39 to 215 | 39 | Sensory/somatomotor Hand | 215 | Salience |
| 39 to 216 | 39 | Sensory/somatomotor Hand | 216 | Salience |
| 43 to 177 | 43 | Sensory/somatomotor Mouth | 177 | Fronto-parietal Task Control |
| 43 to 212 | 43 | Sensory/somatomotor Mouth | 212 | Salience |
| 43 to 215 | 43 | Sensory/somatomotor Mouth | 215 | Salience |
| 47 to 48 | 47 | Cingulo-opercular Task Control | 48 | Cingulo-opercular Task Control |
| 49 to 116 | 49 | Cingulo-opercular Task Control | 116 | Default mode |
| 55 to 177 | 55 | Cingulo-opercular Task Control | 177 | Fronto-parietal Task Control |
| 68 to 82 | 68 | Auditory | 82 | Default mode |
| 68 to 177 | 68 | Auditory | 177 | Fronto-parietal Task Control |
| 69 to 177 | 69 | Auditory | 177 | Fronto-parietal Task Control |
| 70 to 177 | 70 | Auditory | 177 | Fronto-parietal Task Control |
| 75 to 199 | 75 | Default mode | 199 | Fronto-parietal Task Control |
| 75 to 256 | 75 | Default mode | 256 | Dorsal attention |
| 75 to 260 | 75 | Default mode | 260 | Dorsal attention |
| 86 to 177 | 86 | Default mode | 177 | Fronto-parietal Task Control |
| 86 to 207 | 86 | Default mode | 207 | Salience |

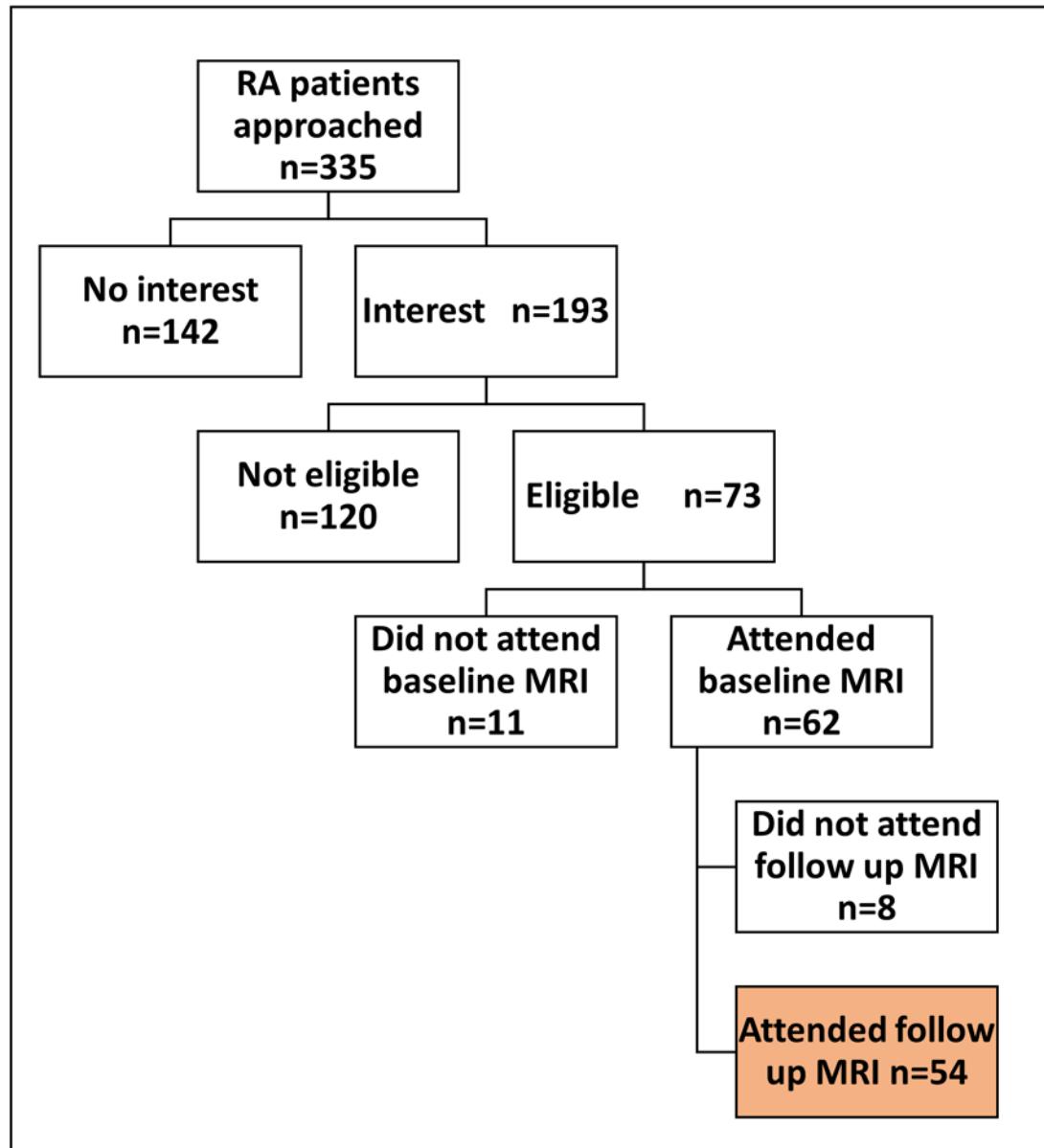
| | | | | |
|------------|-----|------------------------------|-----|------------------------------|
| 86 to 227 | 86 | Default mode | 227 | Subcortical |
| 87 to 208 | 87 | Default mode | 208 | Salience |
| 87 to 259 | 87 | Default mode | 259 | Dorsal attention |
| 90 to 190 | 90 | Default mode | 190 | Fronto-parietal Task Control |
| 95 to 190 | 95 | Default mode | 190 | Fronto-parietal Task Control |
| 95 to 192 | 95 | Default mode | 192 | Fronto-parietal Task Control |
| 95 to 258 | 95 | Default mode | 258 | Dorsal attention |
| 116 to 144 | 116 | Default mode | 144 | Visual |
| 116 to 165 | 116 | Default mode | 165 | Visual |
| 116 to 190 | 116 | Default mode | 190 | Fronto-parietal Task Control |
| 116 to 192 | 116 | Default mode | 192 | Fronto-parietal Task Control |
| 116 to 197 | 116 | Default mode | 197 | Fronto-parietal Task Control |
| 116 to 199 | 116 | Default mode | 199 | Fronto-parietal Task Control |
| 116 to 200 | 116 | Default mode | 200 | Fronto-parietal Task Control |
| 116 to 256 | 116 | Default mode | 256 | Dorsal attention |
| 116 to 258 | 116 | Default mode | 258 | Dorsal attention |
| 116 to 259 | 116 | Default mode | 259 | Dorsal attention |
| 116 to 264 | 116 | Default mode | 264 | Dorsal attention |
| 122 to 150 | 122 | Default mode | 150 | Visual |
| 122 to 227 | 122 | Default mode | 227 | Subcortical |
| 150 to 206 | 150 | Visual | 206 | Salience |
| 151 to 187 | 151 | Visual | 187 | Fronto-parietal Task Control |
| 151 to 192 | 151 | Visual | 192 | Fronto-parietal Task Control |
| 160 to 187 | 160 | Visual | 187 | Fronto-parietal Task Control |
| 177 to 215 | 177 | Fronto-parietal Task Control | 215 | Salience |
| 196 to 206 | 196 | Fronto-parietal Task Control | 206 | Salience |

All identified connections and putative networks from the network based statistic analysis of higher erythrocyte sedimentation rate and whole brain connectivity. Nodes are identified by their parcellation according to the Power Atlas.

Supplementary Table 4 Eigenvector centrality hubs at baseline

| ROI | Approximate structure |
|-----|----------------------------|
| 13 | L precuneus |
| 15 | L SMA paracentral lobule |
| 25 | R postcentral |
| 26 | R postcentral |
| 28 | R precentral |
| 30 | L postcentral |
| 31 | R SMA medial frontal |
| 32 | R postcentral |
| 34 | L postcentral |
| 40 | R SMA medial frontal |
| 47 | L SMA medial frontal |
| 53 | R SMA sup frontal |
| 54 | R SMA medial frontal |
| 59 | L mid cingulate |
| 89 | R precuneus |
| 94 | mid cingulate |
| 112 | L frontal sup medial |
| 113 | L dorsal ACC |
| 134 | L precuneus |
| 135 | R precuneus |
| 136 | R precuneus |
| 157 | R mid occip |
| 159 | R cuneus |
| 166 | L precuneus |
| 174 | L precentral |
| 188 | L mid frontal BA |
| 190 | R IPL |
| 191 | L IPL superior |
| 192 | R IPL |
| 194 | R IPL |
| 195 | L IPL |
| 199 | R IPL |
| 202 | L medial sup frontal |
| 203 | R PCC paracentral mid cing |
| 204 | R supramarginal |

| | |
|-----|--------------------------------|
| 205 | R middle frontal precentral |
| 213 | L mid cing SMA |
| 214 | L mid frontal |
| 215 | midline dorsal ACC |
| 216 | R mid cing |
| 251 | R precuneus |
| 255 | R postcentral |
| 256 | R precuneus |
| 258 | R sup parietal |
| 260 | L precuneus mid occip |
| 261 | L mid frontal precentral |
| 263 | L sup parietal |
| 264 | R mid frontal |



Supplementary Figure 1. Study flow chart.