

IN BRIEF

CONNECTIVE TISSUE DISEASE

Predicting progression to disease in an at-risk cohort

A prospective observational study investigated whether two interferon-stimulated gene expression scores could predict progression to autoimmune connective tissue disease in at-risk individuals (antinuclear antibody-positive). Of 118 patients, 19 progressed to disease. Both interferon scores were increased in these at-risk individuals who went on to develop disease. Patients who progressed to disease did not have different baseline clinical characteristics or ultrasonography findings compared with patients who did not progress to disease. These interferon scores may enable early intervention for disease prevention.

ORIGINAL ARTICLE Md Yusof, M. Y. et al. Prediction of autoimmune connective tissue disease in an at-risk cohort: prognostic value of a novel two-score system for interferon status. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2018-213386> (2018)

AUTOIMMUNITY

Is there a link between stress and autoimmunity?

Researchers conducted a population-matched, sibling-matched retrospective Swedish cohort study to identify whether a link exists between stress-related disorders (including post-traumatic stress disorder (PTSD) and acute stress reaction) and subsequent autoimmune disease. Patients with stress-related disorders were at increased risk of developing autoimmune disease compared with population-matched individuals (HR 1.36 (95% CI 1.33–1.40)). Treatment with selective serotonin reuptake inhibitors during the first year following a diagnosis of PTSD was associated with attenuated relative risk of autoimmune disease.

ORIGINAL ARTICLE Song, H. et al. Association of stress-related disorders with subsequent autoimmune disease. *JAMA* **319**, 2388–2400 (2018)

PSORIATIC ARTHRITIS

Pain relief with secukinumab treatment

Secukinumab has excellent effects on the signs and symptoms of psoriatic arthritis (PsA). McInnes and colleagues further analysed the effects of this drug on pain relief in the FUTURE 2 cohort. Pain was measured using three patient-reported measures (a pain visual analog scale, Short Form-36 bodily pain domain scores and EuroQol 5-Dimension 3-Level Questionnaire pain item scores). Secukinumab led to rapid and sustained pain relief, starting at week 3 and sustained through to 2 years. Improvements in pain were similar in patients who had or had not been exposed to TNF inhibitors.

ORIGINAL ARTICLE McInnes, I. B. et al. Secukinumab provides rapid and sustained pain relief in psoriatic arthritis over 2 years: results from the FUTURE 2 study. *Arthritis Res. Ther.* **20**, 113 (2018)

SPONDYLOARTHRITIS

Understanding immunopathology of sacroiliitis

Few studies have investigated the pathogenesis of sacroiliitis in axial spondyloarthritis (axSpA) and it is not well understood. Clinical, laboratory and imaging data were collected from 193 patients with axSpA at baseline and during follow-up. The most common feature in early sacroiliitis was subchondral pannus formation. Pannus invasion was found to be central to pathological degeneration of the cartilage. The researchers concluded that cartilage pannus invasion or endochondral ossification at baseline can predict radiological structural damage during follow-up.

ORIGINAL ARTICLE Wang, D. M. et al. Pannus inflammation in sacroiliitis following immune pathological injury and radiological structural damage: a study of 193 patients with spondyloarthritis. *Arthritis Res. Ther.* **20**, 120 (2018)

RHEUMATOID ARTHRITIS

Inflammation rewires the brain

A functional and structural MRI study of patients with rheumatoid arthritis (RA) now published in *Nature Communications* may begin to explain how chronic systemic inflammation changes brain function. “Two regions of the brain, the inferior parietal lobule and the medial prefrontal cortex, become more strongly connected to multiple brain networks in patients with higher levels of inflammation,” says corresponding author Andrew Schrepf.

Inflammation is known to affect brain connectivity and patients with chronic inflammatory conditions are susceptible to fatigue and hyperalgesia. However, previous analyses of the link between inflammation and brain function were reliant on animal models or acute inflammatory induction by lipopolysaccharide injection into human volunteers. “We naturally wanted to know what happens to the brain in a chronic inflammatory condition,” explains Schrepf. For this purpose, patients with RA are ideal candidates, as natural fluctuations in the degree of systemic inflammation can be used as correlates, without the need to ‘artificially’ induce acute inflammatory responses with immunogens.

The researchers measured erythrocyte sedimentation rate and serum C-reactive protein concentration as markers of inflammation in 54 patients with RA. These patients then underwent functional MRI and structural neuroimaging while they performed a basic cognitive test of continuously adding numbers. Data at baseline were compared against a 6-month follow-up.

The authors visualized a decrease in grey matter in the inferior parietal lobule by voxel-based morphometry, but the data were not statistically significant and the loss was not detected in the medial prefrontal cortex; longer term follow-up may be needed.

Using seed-based correlation analyses to infer functional



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connections, the researchers found strong linkage to some well characterized seed networks, including the default mode network, dorsal attention network, salience network, and the medial visual network.

“We looked at a huge number of possible connections – every connection between every pair of regions after dividing up the brain into 264 areas,” explains Schrepf.

Aside from linking inflammation with increased connectivity to these networks, intriguingly, the researchers also noticed odd patterning correlations with patient-reported fatigue and severity of pain. “It looked as if the brains of patients with higher inflammation were drawing on resources from the default mode network,” specifies Schrepf, “which is usually thought of as being ‘quiet’ during tasks like the one patients were performing.” He thinks this unusual requisition of the brain’s computing power might be necessary for these patients to complete the mathematical task given, which hints at a basis for explaining cognitive dysfunction in patients with chronic inflammatory diseases.

“We are planning analyses in several other cohorts of patients with autoimmune disease and chronic pain to see how these findings hold up,” says Schrepf “but to really understand these mechanisms we need to see if they change with successful treatment.”

Nicholas J. Bernard

ORIGINAL ARTICLE Schrepf, A. et al. A multi-model MRI study of the central response to inflammation in rheumatoid arthritis. *Nat. Commun.* **9**, 2243 (2018)