Conclusion: The research shows that the most frequent symptoms among people with rheumatic diseases were depression and high levels of anxiety due to strong emotional stress. Psychological malaise caused direct effects in worsening the symptoms of rheumatic disease as well as other related effects, for example, insomnia. The forced isolation due to the lockdown has made people lack the social support that is fundamental for the psychological well-being especially for those suffering from some chronic pathology. Starting from the data collected, APMARR promptly activated a completely free psychological support service with 6 professional psychologists, two of them specialized in emergency psychology. The service is accessible online and is still going on for all who are not able to overcome the anxiety and fear related to the pandemic and its evolution. Thousands of accesses to the service have been measured to date.

References: S Mingolla1, A Celano1, M Santopietro2

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The origins of pain in RMDs

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Background: Modic type 1 changes (MC1) are vertebral bone marrow (BM) edema that associate with non-specific low back pain (LBP). Two etiologies have been described. In the infectious etiology the anaerobic aerotolerant Cutibacterium acnes (C. acnes) invades damaged intervertebral discs (IVDs) resulting in disc infection and endplate damage, which leads to the evocation of an immune response. In the autoinflammatory etiology disc and endplate damage lead to the exposure of immune privileged disc cells and matrix to leukocytes, thereby evoking an immune response in the BM. Different etiologies require different treatment strategies. However, it is unknown if etiology-specific pathological mechanisms exist.

Objectives: The aim of this study was to identify etiology-specific dysregulated pathways of MC1 and to perform in-depth analysis of immune cell populations of the autoinflammatory etiology.

Methods: BM aspirates and biopsies were obtained from LBP patients with MC1 undergoing spinal fusion. Aspirates/biopsies were taken prior screw insertion through the pedicle screw trajectory. From each patient, a MC1 and an intraparavertebral level were taken. If C. acnes in IVDs adjacent to MC1 were digested, CD45 BM mononuclear cells isolated with fluorescence activated cell sorting (FACS), and 10000 cells were sequenced (10x Genomics). Seurat R toolkit was used for quality-control, clustering, and differential expression analysis. Transcriptomic changes (n=5) of CD45 BM neutrophils isolated from CD66b+ expression with flow cytometry. CD66b+ and CD66b- BM neutrophils were compared with paired t-test.

Results: Comparing MC1 to control in total bulk RNAseq, 204 DEG in the autoinflammatory and 444 DEG in the infectious etiology were identified with only 67 shared genes (Fig. 1a). GO enrichment revealed “T-cell activation” (p = 2.50E-03) in the autoinflammatory and “complement activation, classical pathway” (p=1.1E-25) in the infectious etiology as top enriched upregulated biological processes (BP) (Fig 1b). ScRNAseq of autoinflammatory MC1 showed an over-representation of T-cells (p=1.00E-34, OR=1.54) and myelocytes (neutrophil progenitor cells) (p=4.00E-05, OR=2.27) indicating an increased demand of these cells (Fig 1c). Bulk RNAseq analysis of neutrophils from the autoinflammatory etiology revealed an activated, pro-inflammatory phenotype (Fig 1d), which was confirmed with more CD66b+ neutrophils in MC1 (n=13) ± 2.71%, p=0.02) (Fig 1e).

Conclusion: Autoinflammatory and infectious etiologies of MC1 have different pathological mechanisms. T-cell and neutrophil activation seem to be important in the autoinflammatory etiology. This has clinical implication as it could be explored for diagnostic approaches to distinguish the two MC1 etiologies and supports developing targeted treatments for both etiologies.

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Persistent knee osteoarthritis pain at 24-months: data from the OSTEOArthritis INITIATIVE

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Background: In the UK, 10% of men and 18% of women over the age of 60 suffer from symptomatic osteoarthritis (OA), and rising. OA knee pain can worsen without significant radiographic changes and pain remains a major problem for up to 20% of patients after total knee joint replacement. Chronic knee OA pain is...
altered by central pain mechanisms, including central sensitisation. Measures of the level of central involvement in pain could inform clinical decision making. Self-report characteristics of depression, anxiety, cognitive difficulties, catastrophising, sleep disturbance, fatigue, and widespread pain distribution together contribute to a Central Mechanisms Trait which is associated with central sensitisation and OA knee pain.

**Objectives:** Using self-report questionnaire data from the Osteoarthritis Initiative Cohort Study (OAI) we aimed to evaluate the prognostic performance of baseline CMT for pain at 24-months.

**Methods:** OAI participants with knee OA or at risk of knee OA with pain in the same knee at both index time point (48-months) and one year prior to that date were included (n=1984). Knee pain was measured using the Western Ontario and McMahons University Osteoarthritis Index (WOMAC) pain sub-scale, by reference to the index knee (the knee with the highest WOMAC pain sub-scale score at baseline). Questionnaire items were selected to assess the 7 available characteristics identified by Akin-Akinoye et al.[1], from which a single CMT factor was calculated by confirmatory factor analysis. Anxiety, fatigue and cognitive difficulties were assessed by single items, depression and sleep disturbance represented by multiple items, and catastrophising by using the Coping Strategies Questionnaire – Catastrophising sub-scale. Pain distribution was defined as a sum of other painful joints at or below the hip. A CMT factor was derived from the 7 characteristics using confirmatory factor analysis. The association between the CMT factor score and 24-month pain (adjusted for baseline pain, radiographic OA (Kellgren-Lawrence (KL) scale) and demographic confounders) was investigated using generalised linear regression with a negative binomial link function.

**Results:** At baseline, participants had a mean (SD) age 65(9) years, a BMI 26 (4) kg/m², 60% were female, 19.8% were African American, KL score was 1.92(1.35) indicating that the majority of the cohort had radiographic OA. Model diagnostics informed the CMT model, with the final model having an RMSEA of 0.073 (90%CI 0.070-0.076). Data were consistent with a single factor model for CMT. In the multivariable model, higher baseline CMT scores were significantly associated with 24-month WOMAC pain scores, with or without adjustment for baseline pain and other covariates, including KL score (multivariable model; std beta=0.164 (SE=0.038), p<0.001). Adjusted regression coefficients and associated p-values are shown in Table 1.

**Table 1. Adjusted regression coefficients for analysed variables against WOMAC pain at 24-months**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Std beta (SE)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>-0.096 (0.101)</td>
<td>0.344</td>
</tr>
<tr>
<td>Age, y</td>
<td>-0.001 (0.006)</td>
<td>0.881</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>0.017 (0.010)</td>
<td>0.088</td>
</tr>
<tr>
<td>Index Knee Kellgren-Lawrence Score</td>
<td>0.164 (0.038)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CMT Factor Score</td>
<td>0.173 (0.060)</td>
<td>0.004</td>
</tr>
<tr>
<td>Baseline Pain</td>
<td>0.857 (0.035)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

n=1421, rows in bold indicate significant association (p<0.05), associations adjusted for race and ethnicity.

**Conclusion:** CMT predicts worse pain prognosis with a similar magnitude to radiographic OA even after adjustment for other factors. A self-report tool which included items relevant to the characteristics included in the CMT may help to select people with OA knee pain with unfavourable pain prognosis. Poor outcomes related to central pain mechanisms or to joint structural damage might be amenable to treatments addressing central or peripheral pain mechanisms respectively.

**REFERENCES:**


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**OP0085**

**ALTERED EXPRESSION OF NEUROTROPHINS AND THEIR RECEPTORS IN THE SKIN OF PATIENTS WITH COMPLEX REGIONAL PAIN SYNDROME (CRPS)**

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**Background:** Complex regional pain syndrome (CRPS) is a rare painful condition that usually appears after trauma or surgery of the extremities. Symptoms include pain, sensory, sudomotor and vasomotor disturbances, trophic changes and impaired motor function. The course varies from mild to chronic disease with a high impact on daily functioning and quality of life. Neuroplasticity processes together with reduced epidural nerve fibers are reported. Neurotrophins and their receptors are mediators in cell-to-cell communication and key mediators of pain signaling.

**Objectives:** The aim of this study was to identify differential expression of neurotrophins and their receptors in the skin and skin fibroblasts of patients with CRPS.

**Methods:** Healthy controls (HC) and patients with acute CRPS with symptoms for less than 6 months fulfilling the Budapest criteria were recruited. Pain scores were evaluated by numeric rating scale (0=no pain, 10=maximal) and body perception was assessed using the Bath Body Perception Disturbance Scale (BBPDS) (0=no perception disturbance, 57=maximal perception disturbance).

Skin biopsies of the affected and/or non-affected side were taken. Immunohistochemistry on formalin-fixed, paraffin-embedded skin tissue slides was used to show NT3 expression in skin tissues. Blinded analysis was done by an experienced dermato-pathologist determined staining gradient by 0=none, 1=sparse, 2=moderate, 3= dense.

Skin fibroblasts were isolated from skin biopsies by outgrowth cultures (CRPS, affected side, n=6 and HC, n=5). Cells (passage 3-6) were starved and subsequently stimulated with TNFα (10 ng/ml) or TGFβ (10 ng/ml) for 24 h to mimic active disease and total RNA was isolated by miRNeasy kit. Gene expression of neurotrophins (NGF, BDNF, and NT3) and neurotrophin receptors (NGFR, TrkA, TrkB and TrkC) was measured by quantitative real time PCR and quantified using the ΔΔCq method with GAPDH as a reference gene. ELISA was used to analyze NT3 protein expression in cell culture supernatants.

**Results:** In 5 of 9 patients with CRPS immunohistochemical staining of NT3 showed an higher expression (from low to moderate) in the affected side versus the non-affected side. In 4 of 9 patients the expression of NT3 was high in the non-affected side (mild/delayed) and stayed high in the affected side.

On interest, the patients with increasing expression of NT3 in the affected side showed increased pain scores (max pain 80+/-10.95, n=5 vs 48.16+/-18.16, n=4, p=0.059 and changed body perception 26.8+/-8.68 n=5 vs 6.5+/-3.91, n=4, p=0.016). Isolated skin fibroblasts from the affected side of patients with CRPS compared to healthy skin fibroblasts showed higher basal gene expression of NT3 (log fold-change= 1.9+/-0.4, p=0.005) and NGFR (log fold-change= 3.6 +/- 2.1, p=0.014). TNFα stimulated CRPS skin fibroblasts showed higher expression for NT3 (log fold-change= 2.1 +/- 1.2, p=0.002) compared to HC. TGFβ stimulated skin fibroblasts of patients with CRPS showed higher expression of NT3 (log fold-change= 1.4+/-0.8, p=0.019), NGFR (log fold-change= 2.6 +/- 1.8, p=0.036) and TrkC (log fold-change= 2.3 +/- 1.8, p=0.032) compared to HC.

On protein level, NT3 showed a tendency of upregulation in unstimulated fibroblasts from CRPS patients comparing to HC (CRPS mean= 8.0 +/- 2.2 pg/ml, HC 2.1, p=0.036) and TrkC (log fold-change= 2.3 +/- 1.8, p=0.032) compared to HC.

**Disclosure of Interests:** None declared.