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.

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The origins of pain in RMDs

OP0083

INFECTIOUS AND AUTOINFLAMMATORY MODIC TYPE 1 CHANGES HAVE DIFFERENT PATHOMECHANISMS

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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 intra-patient control aspiration/biopsy from the adjacent vertebral level was taken. If *C. acnes* in IVDs adjacent to MC1 were detected by anaerobic bacterial culture, patients were assigned to the infectious, otherwise to the autoinflammatory etiology.

Total RNA was isolated from aspirates and sequenced (Novaseq) (infectious n=3+3, autoinflammatory n=5+5). Genes were considered as differentially expressed (DEG) if p-value < 0.01 and log2fc > ± 0.5. Gene ontology (GO) enrichment was performed in R (Goseq), gene set enrichment analysis (GSEA) with GSEA software.

Changes in cell populations of the autoinflammatory etiology were analyzed with single cell RNA sequencing (scRNAseq): Control and MC1 biopsies (n=1+1) were digested, CD45⁺CD66b⁺ 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+5) of CD45⁺CD66b⁺ neutrophils isolated with flow cytometry from aspirates were analyzed as for total bulk RNAseq. Neutrophil activation (n=3+3) was measured as CD66b⁺ expression with flow cytometry. CD66b^{high} and CD66b^{low} fractions in MC1 and control 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^{high} neutrophils in MC1 (+11.13 ± 2.71%, p=0.02) (Fig. 1e).

Figure 1. (a) Venn diagram of DEG from total bulk RNAseq (b) Top enriched upregulated BP of autoinflammatory (left) and infectious (right) etiology (c) Cell clustering of autoinflammatory MC1 BM (d) Enrichment of "inflammatory response" gene set in autoinflammatory MC1 neutrophils (e) Representative histogram of CD66b⁺ expression in MC1 and control neutrophils.

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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OP0084

CENTRAL MECHANISMS TRAIT PREDICTS 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

augmented 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, catastrophizing, 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 McMaster Universities 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-Akinyosoye 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 29.6(5.1) 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=0.173 (SE=0.027), p=0.004). Association of baseline CMT was of similar strength, and over and above association of KL score with 24-month pain (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

Variables	Std beta (SE)	P
Sex	-0.096 (0.101)	0.344
Age, y	-0.001 (0.006)	0.881
BMI, kg/m ²	0.017 (0.010)	0.088
Index Knee Kellgren-Lawrence Score	0.164 (0.038)	<0.001
CMT Factor Score	0.173 (0.060)	0.004
Baseline Pain	0.857 (0.035)	<0.001

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.

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OP0085

ALTERED EXPRESSION OF NEUROTROPHINS AND THEIR RECEPTORS IN THE SKIN OF PATIENT 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. In skin tissue, sustained inflammatory, fibrotic processes together with reduced epidermal 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, 100=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 dermatopathologist determined staining graduated by 0= none, 1= sparse, 2=moderate, 3= dense.

Skin fibroblast 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 TNF α (10ng/ml) or TGF β (10ng/ml) for 24h 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 $\Delta\Delta Cq$ 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 immunohistological 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 (moderate/dense) and stayed high in the affected side.

Of interest, the patients with increasing expression of NT3 in the affected side showed increased pain scores (max pain 80+/-10.95, n=5 versus 48.16+/-18.16, n=4, p=0.059 and changed body perception 26.8+/-8.68 n=5 versus 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 (log₂ fold-change= 1.9 +/- 0.4, p=0.005) and NGFR (log₂ fold-change= 3.6 +/- 2.1, p=0.014). TNF α stimulated CRPS skin fibroblasts showed higher expression for NT3 (log₂ fold-change= 2.1 +/- 1.2, p=0.002) compared to HC. TGF β stimulated skin fibroblasts of patients with CRPS showed higher expression of NT3 (log₂ fold-change= 1.4+/-0.8, p=0.019), NGFR (log₂ fold-change= 2.6 +/- 1.8, p=0.036) and TrkC (log₂ 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