interleukin-1 and interleukin-6, affect serotonin transporters in the brain and promote low stress tolerance and depression².

Objectives: To investigate the effect of orthopaedic surgery on the mental condition of patients with RA by assessing the Beck depression inventory II (BDI-II) and to investigate the factors associated with changes in the BDI-II.

Methods: A prospective cohort study was performed in 294 sites of primary elective surgery in 276 patients with structural damage due to RA. The average (range) age was 64^{19–89} years old, and the average (range) disease duration was 16^{1–60} years. The surgical site was the shoulder in 6 patients, elbow in 26, wrist in 74, hand in 63 (with wrist in 18), hip in 13, knee in 50, ankle in 12, and forefoot in 50. The BDI-II, EuroQol 5 dimensions (EQ-5D), Japanese version of the Stanford Health Assessment Questionnaire (J-HAQ), and disease activity score 28 using C-reactive protein⁴ (DAS28-CRP⁴) were assessed at the baseline and at 12 months after surgery. During the observational period, the number of patients using methotrexate (MTX), prednisolone (PSL), and biological disease-modifying anti-rheumatic drugs (bDMARDs) did not change significantly. The mean dose of MTX and PSL was reduced by 0.4 mg/w and 0.2 mg/d, respectively, at 12 months after surgery.

Results: In total, the mean BDI-II significantly improved from 13.0 to 11.5 at 12 months after surgery ($p<0.01$). The number of patients with depression (BDI-II ≥ 14) decreased from 42.8% to 34.8% (figure 1). A significant improvement in the BDI-II was noted in the elbow, wrist, hand, and forefoot surgeries ($p<0.05$). EQ-5D, J-HAQ, and DAS28-CRP⁴ also improved significantly ($p<0.01$)³. A multiple regression analysis showed that the magnitude of decrease in the BDI-II (Δ BDI-II) was independently related to the Steinbrocker's stage (95% confidence interval [CI]: 0.42, 2.39, $p=0.005$) and pain-visual analogue scale (VAS) (95% CI: 0.01, 0.10, $p=0.02$) at baseline and inversely related to matrix metalloproteinase-3 (MMP-3) (95% CI: -0.01 , -0.001 , $p=0.03$) at baseline. The BDI-II was correlated with the EQ-5D ($\gamma=-0.049$, $p<0.01$) and J-HAQ ($\gamma=0.387$, $p<0.01$) at 12 months after surgery.

Abstract THU0156 – Figure 1. Distribution of BDI-II at baseline and a postop. 12mos.

Conclusions: Depression was ameliorated by surgical intervention in patients with RA. The mental condition is associated with the quality of life and physical function.

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THU0157 ALTERED DNA-METHYLATION IN CHILDREN BORN TO MOTHERS WITH RHEUMATOID ARTHRITIS DURING PREGNANCY

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Background: Exposures during early life are associated with later-life health, which is referred to as the Developmental Origins of Health and Disease hypothesis¹. Epigenetic processes are thought to be one of the mechanisms underlying this hypothesis. DNA-methylation is the best studied and understood epigenetic modification. DNA-methylation of the fetus *in utero* may be influenced by multiple factors, including maternal disease².

Objectives: To determine whether the DNA-methylation profile of children born to women with RA is different from children born to women from the general

population. Furthermore to determine which pathways are associated with the significantly differentially methylated CpG sites.

Methods: For the current study, blood from 80 children with a mean age of 6.82 (SD=1.28) born to women with RA, who were followed prospectively during pregnancy and postpartum in the PARA-study³, was used to measure genome-wide DNA-methylation using the Infinium Illumina Human-Methylation 450 k BeadChip. DNA from 345 children with a mean age of 6.04 (SD=0.39) born to women from the population-based Generation R study⁴ were used as controls, also followed prospectively during pregnancy and postpartum. Linear mixed models were used to analyse differences in methylation between these groups. The models were corrected for age, BMI (SDS) and sex of the child, gestational age at delivery, maternal age, folic acid use during pregnancy, socioeconomic status, maternal smoking during pregnancy, white blood cell subtypes and technical batch.

Results: In total 770 CpGs were significantly different between the 2 groups at Bonferroni threshold $p=1.08 \times 10^{-7}$ (see table 1. for top 10 sites). In addition, pathway analysis resulted in 4 statistically significant enriched pathways. The top 2 pathways were the FOXO signalling pathway consisting of 16 genes ($p=3.39 \times 10^{-4}$) and mTOR signalling pathway consisting of 17 genes ($p=5.65 \times 10^{-4}$). These pathways are known for regulating the glucose and lipid metabolism, respectively.

Table 1 Top 10 methylation sites from the linear mixed model

CpG	P-value	Beta	SE	Nearby gene (± bp)	Chr	Bp	Location*
(Effect size)							
cg07786668	4.75*10 ⁻³³	0.027	0.002	ZFXH3(-10142)	16	73092391	-
cg06642177	1.29*10 ⁻²⁹	0.028	0.002	SLC2A12(-122529)	6	134496341	-
				SGK1(+142878)			
cg08867893	5.68*10 ⁻²⁷	0.017	0.001	ZNF365(+221)	10	64134160	-
cg20116574	4.89*10 ⁻²³	0.024	0.002	NCOA5(+435)	20	44718168	Promoter
cg06778273	9.33*10 ⁻²³	0.021	0.002	TNFRSF18(+4995)	1	1137117	-
				TTL10(+27808)			
cg21160472	8.45*10 ⁻²²	0.015	0.001	ATF3(+119)	1	212782112	Promoter
cg01067849	4.09*10 ⁻²⁰	0.011	0.001	WRNIP1(-102)	6	2765587	Promoter
cg06656994	5.88*10 ⁻¹⁹	0.051	0.005	FAM163A(+903)	1	179713176	Enhancer
cg14810343	1.36*10 ⁻¹⁸	0.013	0.001	CXXC5(-127)	5	139028149	-
cg01458961	3.47*10 ⁻¹⁸	0.032	0.003	PPP3CA(-822)	4	102269425	-

* Location in promoter, gene, enhancer or other/unknown (-)

SE= standard error; bp=base pair; Chr= chromosome

Conclusions: This study demonstrates that children born to women with RA have a different methylation profile compared with children born to mothers from the general population.

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THU0158 INCREASED PROGRESSION OF ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IS PARTIALLY REFLECTED BY DISEASE SEVERITY AT THE TIME OF DIAGNOSIS- 11-YEAR PROSPECTIVE FOLLOW-UP

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Background: Patients with Rheumatoid arthritis (RA) have increased mortality and morbidity due to cardiovascular disease (CVD) compared to general population. While it has been established that atherosclerosis is increased, there is much yet to reveal about the underlying cause. Contributing factors, such as