# The pain trajectory of juvenile idiopathic arthritis (JIA): translating from adolescent patient report to behavioural sensitivity in a juvenile animal model

# Supplementary material

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# METHODS

## Part 1: Patient cohort

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All patients** | **Trajectory:** | **Statistical analysis** |
| **Low pain** | **Variable pain** | **High pain** | **F value/Chi-Square** | **P value** |
| Total no. of patients | 97 | 45 (46.4%) | 30 (30.9%) | 22 (22.7%) |  |  |
| ***Included disease activity markers*** |  |  |  |  |
| PGA (cm) | 2.40 (2.52) | 1.40 (2.11) | 3.11 (2.73) | 3.47 (2.31) | 7.64 | ***0.001*** |
| No. of: |  |  |  |  |  |  |
| Active joints | 0 (0-2) | 0 (0-1) | 1 (0-1) | 0 (0-2) | 2.06 | 0.13 |
| Swollen joints | 0 (0-2) | 0 (0-0) | 1 (0-2.25) | 1 (0-3.25) | 4.33 | ***0.016*** |
| Limited joints | 1 (0-2) | 0 (0-1) | 2 (0-3) | 2 (0-5) | 3.16 | ***0.047*** |
| ***Blood disease markers:*** |  |  |  |  |  |
| ESR | 11.98 (18.10) | 8.27 (11.97) | 16.13 (17.02) | 16.67 (29.74) | 1.54 | 0.22 |
| *No. of patients* | *61* | *33* | *16* | *12* |  |  |
| CRP | 3.75 (6.99) | 2.66 (3.96) | 5.77 (10.72) | 4.24 (7.93) | 0.90 | 0.41 |
| *No. of patients* | *50* | *28* | *13* | *9* |  |  |

Table 1 – JIA disease activity markers for each pain trajectory

Data is described as mean (standard deviation) for continuous data, number (% of patients with trajectory type) for categorical data or median (interquartile range) for discreet data (no. of active joints). Statistical comparison between trajectory groups were made using either one-way ANOVA or Chi-Square test. The number of patients with available information on blood disease markers is shown beneath each marker. PGA=Physician global assessment VAS.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Included patients** | **Excluded patients** | **Statistical analysis** |
| **≤2 pain VAS scores** | **Incorrect time intervals** | **F value/Chi-Square** | **P value** |
| No. of patients | 97 | 60 | 104 |  |  |
| PainVAS at study onset | 3.29 (2.89) | 2.78 (3.30) | 3.40 (3.08) | 2.78 | *0.064* |
| Age at JIA onset | 9.62 (4.86) | 9.13 (4.55) | 9.00 (4.93) | 0.48 | 0.62 |
| Age at study onset | 16.40 (1.21) | 17.39 (1.57)\* | 16.46 (1.34) | 10.51 | ***<0.001*** |
| Years since JIA onset | 6.78 (5.17) | 8.78 (4.83) | 8.15 (5.39) | 1.60 | 0.20 |
| Sex: |  |  |  | 2.47 | 0.29 |
| Female | 55 (56.7%) | 30 (50.0%) | 65 (62.5%) |  |  |
| Male | 42 (43.3%) | 30 (50.0%) | 39 (37.5%) |  |  |
| JIA subtype: |  |  |  | 8.14 | 0.23 |
| Polyarticular course | 54 (55.7%) | 25 (41.7%) | 61 (58.7%) |  |  |
| Oligoarticular | 6 (6.2%) | 9 (15.0%) | 11 (10.6%) |  |  |
| Enthesitis Related | 32 (33.0%) | 20 (33.3%) | 25 (24.0%) |  |  |
| Systemic | 5 (5.2%) | 6 (10.0%) | 7 (6.7%) |  |  |
| JIA activity markers: |  |  |  |  |  |
| PGA | 2.40 (2.52) | 1.63 (2.55) | 2.25 (2.63) | 1.78 | 0.17 |
| No. of active joints | 0 (0-2) | 0 (0-1) | 0 (0-2) | 1.15 | 0.32 |
| Medications: |  |  |  |  |  |
| No. taking DMARDs | 67 (69.1%) | 35 (58.3%) | 56 (53.8%) | 5.03 | *0.081* |
| No. taking Biologics | 40 (41.2%) | 19 (31.7%) | 41 (39.4%) | 1.53 | 0.47 |
| No. taking Steroids | 16 (16.5%) | 6 (10.0%) | 13 (12.5%) | 1.47 | 0.48 |

Table 2 – Patient characteristics of included and excluded patients

Data is described as mean (standard deviation) for continuous data, number (% of patients with trajectory type) for categorical data or median (interquartile range) for discreet data (no. of active joints). Statistical comparison between trajectory groups were made using either one-way ANOVA or Chi-Square test. PGA=Physician global assessment VAS. \* sig vs. included patients in post-hoc analysis.

# RESULTS

## Part 1: Pain in adolescent JIA patients



Figure 1 – Disability and quality of life as reported by patients with different levels of pain

Patients separated into low (n=45), variable (n=30) and high (n=22) pain trajectories via cluster analysis also experienced: **A**: differing levels of disability (as assessed by the Childhood Health Assessment Questionnaire [CHAQ]) (p<0.001) and **B**: varying levels of quality of life (as reported by the patient general evaluation VAS [PGE]) (p<0.001). \* p<0.05 between indicated groups.



Figure 2 – Ven diagrams examining proportions of patients with each type of joint

Venn diagrams examining the proportion of patients with active (green), swollen (blue) or limited joints (orange), or a combination of the three, within each trajectory type revealed a reduced number of patients with only active joints and an increase in the number of patients with swollen and limited joints in the variable and high pain trajectory groups (p=0.029).

## Part 2: Pain in a rodent model of joint inflammation

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All animals** | **Sex** | **Statistical Analysis** |
| **Female** | **Male** | **Chi-Square** | **P value** |
| No. of Animals | 25 | 10 | 15 |  |  |
| Trajectory: |  |  |  | 58.40 | ***<0.001*** |
| Low Sensitivity | 7 (28.0%) | 1 (10.0%) | 6 (40.0%) |  |  |
| Medium Sensitivity | 9 (36.0%) | 6 (60.0%) | 3 (20.0%) |  |  |
| High Sensitivity | 9 (36.0%) | 3 (30.0%) | 6 (40.0%) |  |  |

Table 3 – Animal numbers and the distribution of pain trajectories in female and male adolescent rats

Data is described as number (% of animals). Statistical comparison between trajectory groups were made using Chi-Square test.

|  |  |  |
| --- | --- | --- |
|  | **All animals** | **Animal groups** |
| **Saline+Saline** | **Saline+CFA** | **CFA+CFA** | CFA+CFA subgroups |
| **Low Sensitivity** | **High Sensitivity** |
| No. of animals | 67 | 24 | 22 | 21 | 12 | 9 |
| Age of onset: |  |  |  |  |  |  |
| P8 | 35 (52.2%) | 12 (50.0%) | 11 (50.0%) | 12 (57.1%) | 8 (66.7%) | 4 (44.4%) |
| P21 | 32 (47.8%) | 12 (50.0%) | 11 (50.0%) | 9 (42.9%) | 4 (33.3%) | 5 (55.6%) |
| Sex: |  |  |  |  |  |  |
| Female | 34 (50.7%) | 12 (50.0%) | 11 (50.0%) | 11 (52.4%) | 7 (58.3%) | 4 (44.4%) |
| Male | 33 (49.3%) | 12 (50.0%) | 11 (50.0%) | 10 (47.6%) | 5 (41.7%) | 5 (55.6%) |
| Pain behaviour at baseline: |  |  |  |  |  |
| % Weight bearing on inflamed limb | 49.11 (2.28) | 49.91 (1.74) | 49.91 (1.38) | 47.35 (2.64) | 49.06 (1.61) | 45.07 (1.92) |
| 50% log mechanical threshold | 1.12 (0.11) | 1.13 (0.10) | 1.10 (0.09) | 1.12 (0.13) | 1.13 (0.13) | 1.12 (0.15) |

Table 4 – Animal numbers and characteristics of animal groups receiving one or two bouts of monoarthritis

Data is described as mean (standard deviation) for continuous data or number (% of animals within group). Age of onset refers to the age monoarthritis was first induced: either postnatal day 8 or 21 (P8 or P21).