



# Chronic low back pain mechanistic phenotypes: association with clinical features

Roach, C.<sup>1</sup>, Scheffler, A.<sup>2</sup>, Ewing, S.<sup>2</sup>, Zheng, P.<sup>2</sup>, Hue, T. <sup>2</sup>, Lotz, J. <sup>2</sup>, Mehling, W. <sup>2</sup>, O'Neill, C.<sup>2</sup>



## Abstract

Subjects from a longitudinal observational e-cohort of adults with primary chronic low back pain (cLBP) were categorized into four mechanism-based categories. Multinomial logistic regression was utilized to identify associations between pain mechanism categories and twelve clinical features.

## Introduction

- Three pain mechanisms have been identified: nociceptive, neuropathic, and nociplastic.
- According to an expert consensus study<sup>1</sup> certain clinical features (notably inflammation, sleep disturbance, fatigue, and cognitive impairment) can help discriminate between these mechanisms.
- The objective of this study was to determine associations between clinical features and pain mechanism categories in a non-specific chronic LBP (cLBP) population.

## Methods

- Baseline data from a longitudinal observational cohort of U.S. adults with cLBP were analyzed. Back-dominant pain was required for inclusion. Survey data was collected via an on-line platform.
- Four pain mechanism categories (nociceptive, nociplastic, neuropathic, mixed) were defined using pain locations, number of chronic overlapping conditions, responses to the PAINDETECT questionnaire, and an expert consensus study<sup>1</sup>.
- The association of twelve clinical features (risk factors) with the pain mechanism categories were assessed using multinomial logistic regression.
- We tested the null hypothesis that the odds of mixed and nociplastic pain compared to nociceptive pain was equal as a function of each risk factor. We rejected the null hypothesis at a p-value of 0.05.

## Results

The frequency of neuropathic pain was 2.3%. Subjects with neuropathic pain (n=32) were excluded from further analysis.

Table 1: Subject characteristics

| Characteristic                                                                                            | mean (+/-SD) and n (%) |
|-----------------------------------------------------------------------------------------------------------|------------------------|
| <i>n</i>                                                                                                  | 1344                   |
| Age (years)                                                                                               | 55.0 ± 14.4            |
| Female sex                                                                                                | 904 (67.3 %)           |
| Inflammatory Pain<br>( <i>morning stiffness, better with exercise, night pain</i> )                       | 612 (45.5 %)           |
| Pain Mechanism                                                                                            |                        |
| Nociplastic                                                                                               | 615 (45.8%)            |
| Nociceptive                                                                                               | 544 (40.5%)            |
| Mixed                                                                                                     | 185 (13.8%)            |
| Current opioid use                                                                                        | 146 (10.9%)            |
| Pain, Enjoyment, and General Activity (PEG) score<br>( <i>range:0-10, higher=more pain interference</i> ) | 4.3 ± 2.2              |
| Fear avoidance score<br>( <i>range:0-24, higher=more avoidance</i> )                                      | 11.6 ± 5.9             |
| Pain catastrophizing score<br>( <i>range:0-12, higher=more catastrophizing</i> )                          | 4.5 ± 2.6              |
| PROMIS sleep disturbance t-score<br>( <i>range:31.7-76.1, higher=more disturbance</i> )                   | 54.7 ± 8.0             |
| PROMIS depression t-score<br>( <i>range:41.0-79.4, higher=more depressed</i> )                            | 52.5 ± 10.1            |
| Pain self-efficacy score<br>( <i>range:0-24, higher=more confidence</i> )                                 | 16.3 ± 5.4             |
| PROMIS anxiety t-score<br>( <i>range:40.3-81.6, higher=more anxiety</i> )                                 | 54.1 ± 10.1            |
| PROMIS cognitive function t-score<br>( <i>range:29.5-61.2, higher=more cognitive function</i> )           | 49.3 ± 7.5             |
| PROMIS physical function t-score<br>( <i>range:21.6-58.7, higher=more physical function</i> )             | 42.1 ± 7.5             |
| PROMIS fatigue t-score<br>( <i>range:33.7-75.8, higher=more fatigued</i> )                                | 1.0 ± 10.5             |

## Results

Odds ratios of mixed and nociplastic pain compared to nociceptive pain were generated for each clinical feature.

Table 2. Associations of Clinical Features with Pain Mechanism Categories

| Clinical Feature           | Mixed odds ratio (CI) | Nociplastic odds ratio (CI) |
|----------------------------|-----------------------|-----------------------------|
| PEG                        | 1.99 (1.81 - 2.20)    | 1.30 (1.22 - 1.38)          |
| Physical function          | 0.81 (0.78 - 0.84)    | 0.93 (0.91 - 0.94)          |
| Fatigue                    | 1.11 (1.09 - 1.13)    | 1.06 (1.05 - 1.07)          |
| Pain self-efficacy         | 0.82 (0.79 - 0.85)    | 0.92 (0.90 - 0.94)          |
| Sleep disturbance          | 1.13 (1.10 - 1.15)    | 1.08 (1.06 - 1.10)          |
| Pain catastrophizing score | 1.39 (1.30 -1.48)     | 1.09 (1.04 - 1.15)          |
| Anxiety                    | 1.09 (1.07 - 1.11)    | 1.05 (1.04 - 1.06)          |
| Depression                 | 1.09 (1.07- 1.11)     | 1.05 (1.03 - 1.06)          |
| Fear avoidance             | 1.13 (1.10 - 1.17)    | 1.03 (1.01 - 1.05)          |
| Cognitive function         | 0.92 (0.89 - 0.94)    | 0.96 (0.94 - 0.97)          |
| Current opioid use         | 6.3 (3.88 - 10.37)    | 2.06 (1.32 - 3.22)          |
| Age                        | 0.99 (0.98 - 1.00)    | 0.99 (0.98 - 1.00)          |

## Conclusion

Highly significant statistical associations (p <0.001) for all risk factors apart from age (p = 0.02) and inflammatory pain (p = 0.08) were observed.

## Discussion

- Contrary to expert consensus, our data does not support an association between inflammation and pain mechanism.
- Inflammatory back pain was common in our cohort, with a prevalence similar to what has been observed in other cLBP populations<sup>2</sup>. Given this high prevalence understanding the connection between inflammation and pain, which appears to be independent of currently defined mechanistic phenotypes, is critical. Features considered characteristic for nociplastic pain- sleep disturbance, fatigue, and cognitive impairment- were associated with pain mechanism, but given the odds ratios the usefulness of these features in discriminating between cLBP mechanistic phenotypes is questionable.
- As there are no gold standards for defining pain mechanisms the validity of methods for discriminating between them cannot be rigorously tested.
- Future work should focus on improving the validity of mechanistic phenotypes and defining the ability to predict treatment response.

## Acknowledgments

We express our gratitude to all patients participating in this study and the clinical staff facilitating data collection.

## Citations

- 1.Shraim MA, et al. Features and methods to discriminate between mechanism-based categories of pain experienced in the musculoskeletal system: a Delphi expert consensus study. Pain. 2022.
- 2.Weisman, et. The prevalence of inflammatory back pain: population-based estimates from the US National Health and Nutrition Examination Survey, 2009–10. Annals of Rheumatic Diseases. 2013.

## Affiliations

- <sup>1</sup>UCSF School of Medicine
- <sup>2</sup>UCSF Core Center for Patient-centric, Mechanistic Phenotyping in Chronic Low Back Pain (REACH)