Self-report central mechanisms trait predicts knee pain persistence in the Knee Pain In the Community (KPIC) cohort

Kehinde Akin-Akinyosoye^{1,3}, Nadia Frowd^{1,3}, Laura Swaithes^{1,3}, Joanne Stocks^{1,3}, Aliya Sarmanova^{1,3}, Gwen Fernandes^{1,3,5}, Ana Valdes^{1,2,3}, Daniel F McWilliams^{1,2,3}, Weiya Zhang^{1,2,3}, Michael Doherty^{1,2,3}, Eamonn Ferguson^{1,4}, David A Walsh^{1,2,3}.

³Division of Rheumatology, Orthopaedics, and Dermatology, School of Medicine, University of Nottingham

⁴School of Psychology, University of Nottingham

⁵Arthritis Research UK Centre for Sports, Exercise, and Osteoarthritis

Emails:

Miss Kehinde Akin-Akinyosoye: kehinde.akin@nottingham.ac.uk

Mrs. Nadia Frowd: nadia.frowd@nihr.ac.uk

Mrs Laura Swaithes: l.swaithes@keele.ac.uk

Dr. Joanne Stocks: joanne.stocks@nottingham.ac.uk

Dr. Aliya Sarmanova: aliya.sarmanova@bristol.ac.uk

Dr. Gwen Sascha Fernandes: gwen.fernandes@bristol.ac.uk

Associate Professor Ana Valdes: ana.valdes@nottingham.ac.uk

Dr. Daniel McWilliams: <u>dan.mcwilliams@nottingham.ac.uk</u>

Professor Weiya Zhang: weiya.zhang@nottingham.ac.uk

Professor Michael Doherty: michael.doherty@nottingham.ac.uk

Professor Eamonn Ferguson: Eamonn.Ferguson@nottingham.ac.uk

Professor David Walsh: david.walsh@nottingham.ac.uk

¹ Arthritis Research UK Pain Centre

²NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals, NHS Trust

Background: In the UK, approximately 25% of individuals aged over 55 have chronic knee pain, often due to osteoarthritis. Knee pain originates from the joint due to structural changes or inflammation (peripheral mechanisms), and is often intensified by processing of afferent signals by the central nervous system (central mechanisms). We aimed to investigate whether baseline measures associated with central sensitization, including a simple self-report 'central mechanism' trait score and Pressure Pain Detection Thresholds (PPT), predict future pain outcomes in individuals with knee pain.

Methods: Data from participants consenting to the Knee- Pain In the Community (KPIC) study were analysed. 1471 participants reported knee pain at baseline and responded to a 1-year follow-up questionnaire. Of these, 204 participants underwent further radiographic and PPT assessments at baseline. A summary score for a latent 'central mechanisms' trait was derived from baseline scores for 8 questionnaire items, representing component traits of anxiety, depression, catastrophizing, neuropathic-like pain, fatigue, sleep-disturbance, pain-distribution, or cognitive-impact. Presence/absence of pain persistence (pain present at baseline and year 1) served as the primary pain outcome. In those reporting pain persistence, persistent pain severity (residualized pain severity change scores) served as the secondary pain outcome. Prediction of pain outcomes by baseline scores for the central mechanisms trait and PPTs used logistic and linear regression models. Receiver-operator-characteristic (ROC) curves and areas-under-the-curve (AUC) compared the predictive strength of the central mechanisms trait to other predictors of pain persistence.

Results: 976 (66%) individuals reported pain persistence, of whom 118 individuals underwent further assessments at baseline. The central mechanisms trait score was a significant predictor for pain outcomes (Pain persistence: Relative Risk, RR=1.73, n=1471, p<0.001; Persistent pain severity: β =0.47, n=976, p<0.001), even after adjustment for age, sex, BMI, radiographic OA and symptom duration (Pain persistence: RR=2.14, n=204, p=0.001; Persistent pain severity: β =0.47, n=118; p<0.002). Lower medial joint-line PPT was associated with persistent pain severity (β =0.32, n=118, p=0.007). The central mechanisms trait score model showed good discrimination power in distinguishing pain persistence cases from resolved pain cases (AUC = 0.70; n=1471). The discrimination power of other predictors, including radiographic OA (AUC = 0.62; n=204), age, sex and BMI (AUC range = 0.51 to 0.64; n=1471), improved significantly (p<0.04) when the central mechanisms trait was included in each logistic regression model (AUC range = 0.69 to 0.74).

Conclusion: A simple self-report 'central mechanisms' trait score, consisting of 8 self-report items, shows prognostic value in identifying individuals more likely to report knee pain persistence at follow-up. This might indicate a contribution of central mechanisms to poor knee pain prognosis. Ongoing work seeks to validate a newly developed questionnaire based on these 8 items for use in clinical practice and epidemiological research settings.

Word count (Without headings): 443/450 words

Funding statement: This work was supported by Arthritis Research UK (Centre initiative grant number=20777), and University of Nottingham as Sponsor and host institution.