Versus Arthritis 4th Annual Pain Research in the UK conference

Date: 27th of June 2022

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Overview from Conference Chair

The 4th Annual Versus Arthritis conference successfully brought together researchers from diverse pain-related disciplines within the excellent facilities of the Great Hall, Kings College, London. The meeting was the culmination of extensive efforts from our secretariat, Organising Committee, Versus Arthritis, Pain Centre Versus Arthritis at the University of Nottingham and, most of all, everyone who participated in the conference. We identified the most influential directions in pain research and encouraged the exchange of views, ideas, and inspiration to promote further advancement in these areas. The Elevator Pitch Speakers provided succinct overviews of recent and ongoing pain research at academic and commercial institutions across the UK, together painting the bigger picture of the pain research that is so much more than just the sum of its constituent parts. Participants were from institutions across the UK, although future meetings might need to be even larger if they are to fully represent all that is happening in UK pain research. Our interactive workshops focussed on four themes with particular current importance to researchers and patients: Psychosocial aspects of pain, Nociplastic pain, 'Omics' in pain, Peripheral mechanisms of chronic pain, and Comorbidities and chronic pain. Workshops delivered effective small-group discussions and inclusive participation. The conference provided opportunities to early-career as well as established researchers, with approximately equal representation among participants. Participants provided very helpful post-conference feedback on what worked well, and next year we will further enhance the poster sessions to maximise its value for networking, scientific discussion and professional development for early career researchers. We will consider ways in which we can further address specific skills and techniques in pain research, promoting the exchange of experiences and competencies. I am grateful to everyone for participating and I am looking forward to seeing everyone at our 5th Pain Research in the UK Conference in 2023.

David Walsh

Conference Chair, co-director, Pain Centre Versus Arthritis at the University of Nottingham.

Workshop conference report

The main aim of the workshops was to facilitate discussions in small groups on specific topics relating to pain, to develop collaborations, share and learn from other's experiences.

Workshop No	Workshop Theme	Co-chair	Co-chair	Facilitator
1	**Psychosocial aspects of pain**	Dr Lauren Heathcotes (King's College Lonson)	Dr Whitney Scott (King's College Lonson)	Dr Rebecca Lee (University of Manchester)
2	**Nociplastic pain**	Dr Michael Lee (University of Cambridge)	Dr Anushka Soni (University of Oxford)	Wendy Chaplin (University of Nottingham)
3	**'Omics' in pain**	Dr Gopuraja Dharmalingamm (Eli Lilly)	Prof Geoff Woods (University of Cambridge)	Afroditi Kouraki (University of Nottingham)
4	**Peripheral mechanisms of chronic pain**	Prof Ewan St John Smith (University of Cambridge)	Prof Camilla Svensson (Karolinska Institutet)	Dr George Goodwin (King's College London)
5	**Comorbidities and chronic pain**	Prof Weiya Zhang (University of Nottingham)	Dr Katy Vincent (University of Oxford)	Dr Sara Hestehave (University College London)

Workshop 1 – Psychosocial aspects of pain

Questions for discussion:

Q1. What are the key psychosocial mechanisms which should be measured in all studies?

Q2. What are the understudied psychosocial mechanisms?

Q3. What are the major challenges facing psychosocial pain research?

Q4. Do/can psychosocial factors impact pain? Or just functioning?

Key take-home messages and priorities:

- Current terminology and how we conceptualise psychosocial mechanisms can lead to confusion.
- Measurement of the dynamic nature of psychological factors over time is limited by cross-sectional nature of previous studies and methodological weaknesses in questionnaire studies

- Other than ‘catastrophizing’ or pain related-worry there appears to be little agreement on what is core to measure
- Social processes are important, but we neglect the social components e.g. we know things are different but we do not understand the mechanisms why e.g., gender.
- Need to move away from mechanisms in groups towards mechanisms in the individual
- We study patients in clinics – but what about the ‘resilient’ ones who don’t make it to clinic?
- Language and concepts are important – potentially stigmatizing?

Workshop 2 – Nociplastic pain

Questions for discussion:

Q1. In what ways is the term nociplastic pain helpful in clinical and research settings?

Q2. What tools do we have to assess nociplastic pain in clinical and research settings?

Q3. What are the best ways of communicating the nociplastic pain beyond the pain community e.g., wider audience MDT, researchers, public, student, policy-holder – what resources are available? Who are champions for the term etc?

Key take-home messages and priorities:

- Feeling that the term ‘nociplastic’ is helpful overall but there are some drawbacks
- Umbrella term or holding bucket, may be further sub-divided in classes of nociplastic pain
- Clinical usefulness? Mixed response, in some contexts it was felt helpful
- Nociplastic pain likely a spectrum not dichotomous
- At a mechanistic level in the lab, the concept of nociplastic pain may be less helpful as an umbrella term for already more clearly defined mechanisms.
- What drives nociplastic pain is unclear? More research is needed to fill the gaps
- Plasticity is a consequence of something, vulnerability?
- Reversibility suggested by `plasticity’
- Is all (nociplastic) pain maladaptive?
- Nociplastic pain is not a mutually exclusive category, an individual might have both nociceptive and nociplastic pain

Workshop 3 – 'Omics' in pain

Questions for discussion:

Q1. What are the relevant tissues in different pain populations indication? How can we harmonize the sample, collection and storage to enable reproducible research through omics? How can we ensure continued future access to the samples?

Q2. How can we perform deep phenotyping of pain subjects and control to identify and characterise pain subtypes?

Q3. What are the useful omics data types in pain research? What are the challenges to generate high quality Omics data?

Q4. What are the challenges and opportunities to use Omics data a) for patient stratification, b) to find biomarkers c) to find novel therapeutic targets?

Q5. How relevant is rodent omics in pain research? What are the difference and similarities between pain mechanisms between species?

Key take-home messages and priorities:

Q1. What are the relevant tissues and samples for Omics?

- Saliva: 5-10% samples not enough DNA, easy to extract, COVID: challenge
- Blood: easy and cheap to analyse
- Inflammatory T cells: constantly changing –difficult to maintain
- Biopsy: very challenging in humans, circadian rhythm effects
- Synovial fluid: cell-sorting issues
- Post-mortem tissue: e.g. human DGR – very challenging to get good quality samples

Q2: How can we properly perform deep phenomics in pain subjects?

- QST- reliable
- Omics data for real separation between groups
- Isolated cells vs ex-vivo
    - Injury response-artificial setting
- Power: 6 animals per group, in humans: power calculation needed, hypothesis-driven

Q4: What are the challenges to generate high quality Omics data?

- Availability of datasets for Mendelian randomisation is limited
- Data analysis: different tools produce different results
    - Training sets
    - Challenging especially for newer technologies
- Conservation pathways between humans and animals

- Life-course differences
- Sex and hormonal differences
- Deep phenotyping to develop better animal models
- Depression-state: should it be adjusted for in animal models of pain?
- Human manipulation issues

Workshop 4 – Peripheral mechanisms of chronic pain

Questions for discussion:

Q1. Do peripheral pain mechanisms explain widespread pain?

Q2. The importance of neuroimmune interactions in chronic pain is becoming ever more apparent: what are the best methods for studying neuroimmune interactions?

Q3. Do human induced pluripotent stem cell derived sensory neurones provide a good translational system for studying (chronic) pain?

Q4. What are the most appropriate behavioural methods for studying chronic pain in rodent models?

Q5. How can we best employ -omics methods to study the peripheral aspects of chronic pain?

Q6. Which animal models are most relevant for studying chronic pain?

Key take-home messages and priorities:

Q1. Do peripheral pain mechanisms explain widespread pain?

- The peripheral input seems to be important in widespread pain in disease states.
- Appears that you need to look holistically at peripheral and central mechanisms, rather than either/or.
- Discussed the time-course of peripheral and central mechanisms, and their relative importance during transition from acute to chronic pain.
- Is the abolishment of peripheral input sufficient to relieve widespread pain.

Q2. What are the best methods for studying neuroimmune interactions?

- Translational differences between rodents and humans.
- Discussed the differences in investigating tissue resident cells vs circulating cells.
- Discussed the need to clearly describe protocols in full to allow for better consistency in the field.
- Discussed which approaches are best for studying neuroimmune interactions; IHC, FACs, scRNAseq or proteomics?

Q3. Do human IPSC derived sensory neurons provide a good translational system for studying (chronic) pain?

- Which is better: primary rodent culture or huIPSCs?
- Important to be clear and transparent about the protocols used for the generation of huIPSC cultures.
- Diversity of sensory neuron subtypes is lost.

Q4. What are the most appropriate behavioural methods for studying chronic pain?

- Important to think about measuring behaviours that are normal for the species.
- Difficult to identify behaviours that are native to species and whether they are related to neuronal sensitivity.

Q5. How can we best employ -omics methods to study the peripheral aspects of chronic pain?

- Should look at specific locally affected tissues if possible.
- Discussed the use of proteomics as technologies improve.
- Important to bear in mind the statistical power of these studies.

Q6. Which animal models are most relevant for studying chronic pain?

- Think about species outside of the usual rat/mouse models.
- Important to consider the differences in physiology between humans and rodents; maybe studies should focus on back-translation for target generation.

Workshop 5 – Comorbidities for chronic pain

Questions for discussion:

Q1. Which comorbidities are relevant in the context of chronic pain, and why are they relevant to explore?

Q2. How should we capture information on comorbidities in future studies (clinical or preclinical)?

Q3. How would you like to investigate comorbidities in the context of chronic pain

Key take home messages and priorities:

Q1. Which comorbidities are relevant in the context of chronic pain?

- There are different types of comorbidities; i) independent of each other but ‘co-occuring’, ii) shared risk factors, iii) interrelated / causing each other, and perhaps last iv) ‘latrogenic’ comorbidities, that may be induced by for instance treatment.
- How do we define comorbidity? Does it have to be clinically diagnosed in order to count, or do we risk missing something important if requiring diagnosis? This may be particularly relevant as some patient-groups have

much more focus on treating their primary condition, than having a potentially less troublesome comorbidity diagnosed/treated…?

- Preclinical study as relevant as clinical, and may supplement each other well. Patients are more complex and may have several conditions on top of each other, which is difficult (and un-ethical) to model preclinically, - but preclinical model may show a more clean and controlled picture of the impact on each individual aspect and the causal relationships.

Q1. Why are they relevant?

- Impact on quality of life
- Impact on the ability to use some types of medication?
- To understand overlapping diagnosis and mechanisms
- Different relevance for research vs clinical practice

Q2. How should we capture information on comorbidities in future studies?

- We should capture!
- Perhaps initially use broad questionnaires (clinical) or assays (preclinical) that capture change in diagnosis, comorbidities, symptoms, and covariates, which may then give indications if there are relevant comorbidities, that deserve further attention in follow-up studies
- Realistic amounts of data so as not to overwhelm the patient or preclinical subject

Q3. How would you like to investigate comorbidities in the future?

- Look at timeline of the development of comorbidities and can pharmacology improve this?
- Preclinical studies to focus on more than just sensory measures
- ‘Real World’ studies
- Primary care databases could be good at encompassing the entire picture of symptoms affecting the patient
- Discussion with regulators, as some may see inclusion of these aspects in studies as too exploratory.

Conference Feedback:

> The feedback form showed that the delegates appreciated the diverse representation we created in terms of location, career stage and jobs.

> Those attendees whose objective for attending the conference was networking believe that the conference was successful in creating a positive environment that encouraged effective communication and new connections.

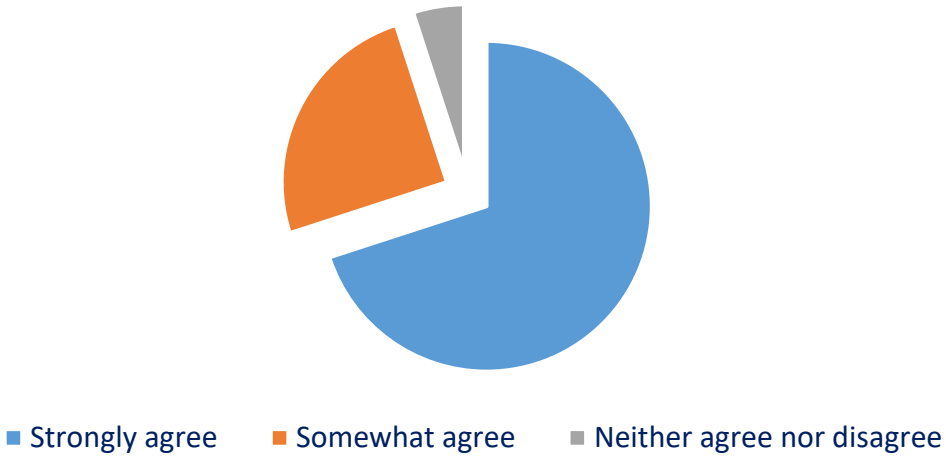
> The delegates were overall content with the poster sessions, and the presenters especially appreciated the separation of the sessions, allowing them to explore the research of others.

> The Plenary Lecture has been very well received, and we will aim to replicate the results in future conferences.

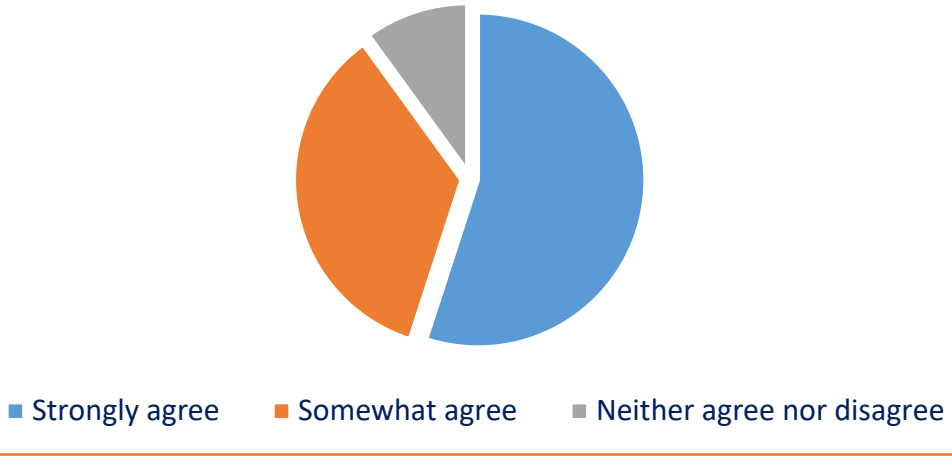
> The attendees were happy with the choice of venue, and we credit this positive feedback to a central location and its accessibility in terms of transport.

> We received positive feedback regarding overall communication with the administrative team and support before and during the conference, and we will aim to adhere to this high standard of support in the future.

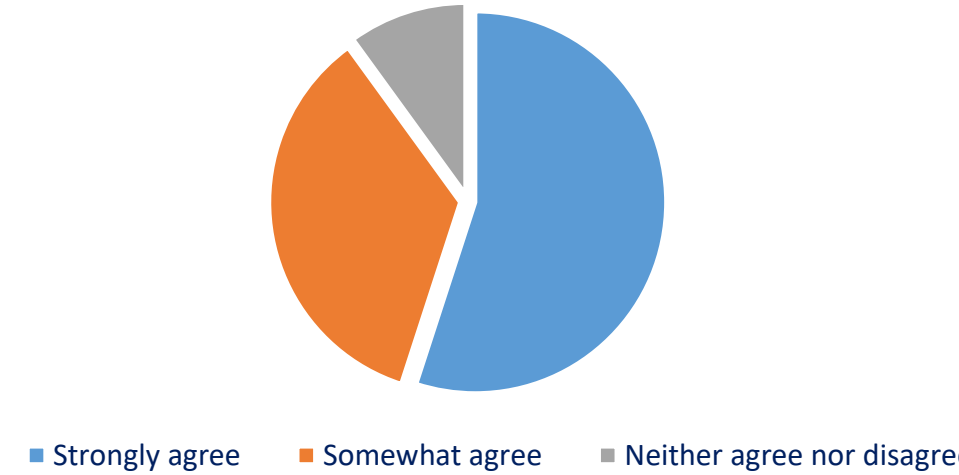
I have deepened my knowledge of chronic pain and arthritis



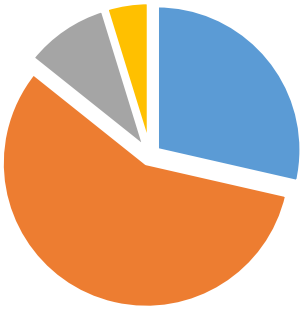
The conference was beneficial for my professional or personal development



I have made new professional connections at the conference



Workshop content and discussion



Somewhat satisfied
Very satisfied
Neutral
Somewhat dissatisfied

Choice of Venue

Very satisfied
Somewhat satisfied

Elevator Pitches

Very Satisfied
Somewhat Satisfied
Neutral

Poster Sessions

Somewhat satisfied
Very satisfied