CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

MRC | Centre for Neuropsychiatric Genetics and Genomics

PARKINSON'S UK
CHANGE ATTITUDES. FIND A CURE. JOIN US.

A GWAS of pain in Parkinson's disease

Nigel Williams (Cardiff University) and Monty Silverdale (University of Manchester)

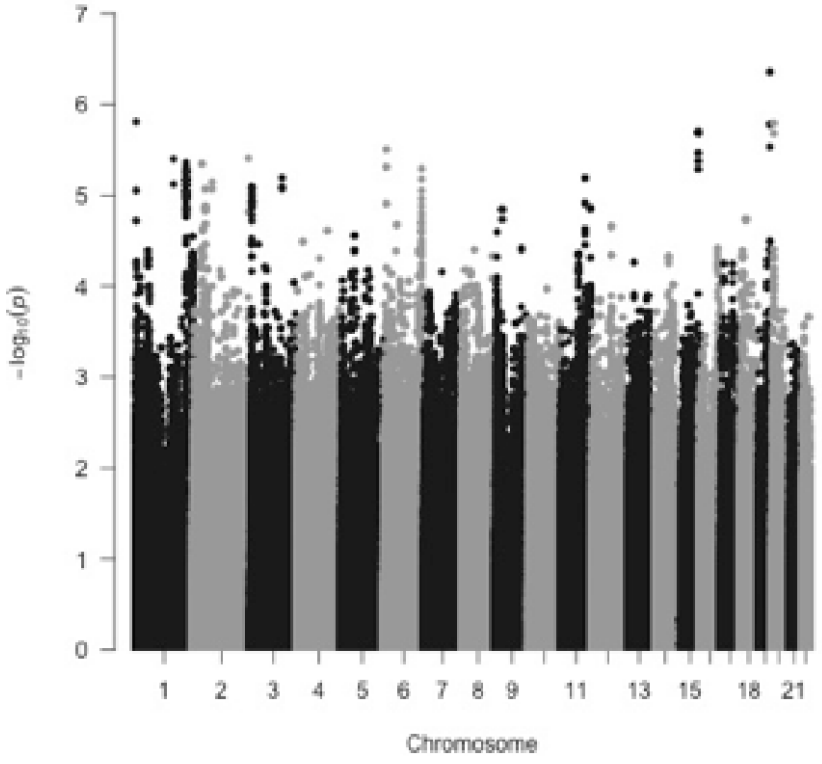
Pain in Parkinson's Disease

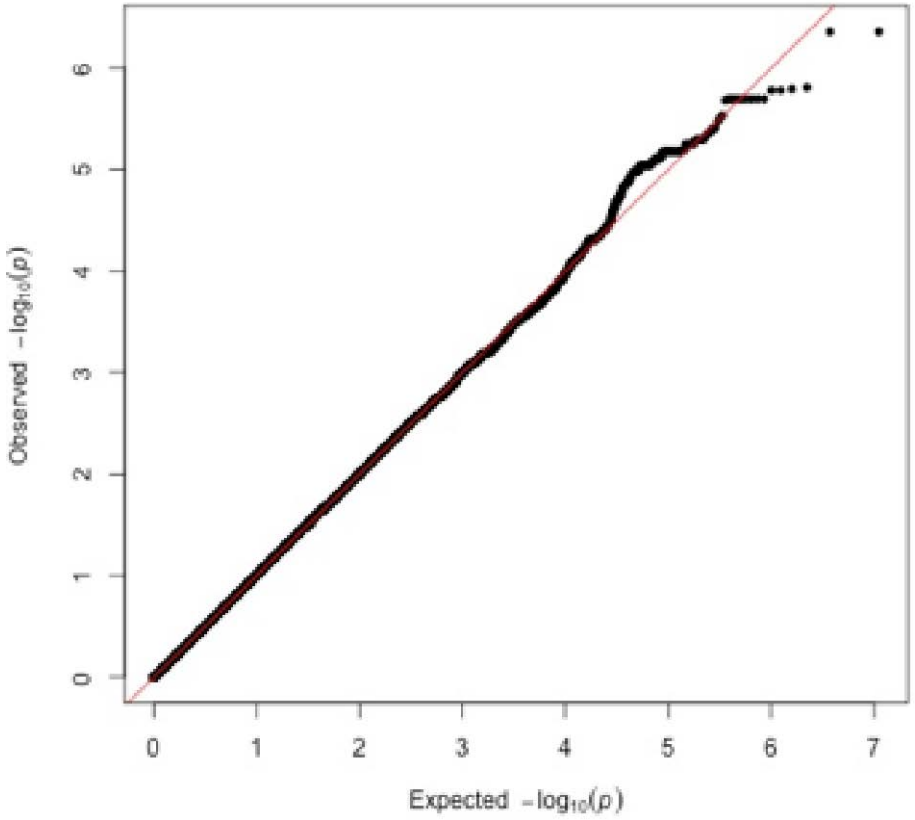
- PI: Monty Silverdale (University of Manchester)
  - CoPIs: Nigel Williams, Huw Morris, Donald Grosset
- Study was based on 1021 individuals with Parkinson's Disease from the Proband Cohort
  - McGill pain questionnaire (quantitative 1-40)
  - All samples genotyped whole genome SNP array
- 85% of patients reported pain
  - the most common subtypes of PD pain are musculoskeletal, radicular and dystonic
- Negligible correlation between
  - the severity of motor impairment and the severity of musculoskeletal or dystonic pain

GWAS: Reduced Pain vs Pain

- Rationale:
- As pain is inevitable subjective analysing the data as a quantitative trait might not be the best approach?
- Individuals who consistently score low on multiple pain scales are most likely to be those who are actually in the least pain (either due to a high pain threshold or having reduced pain).
- 2 pain scales used:
  - McGill (0-40)
  - VAS Severity (0-10) over last month
- Reduced Pain = PD patients with McGill <3 and VAS Severity <2
  - N=315
- Pain = all other PD patients
  - N=706

Pain in Parkinson's Disease GWAS (Proband Cohort Only)



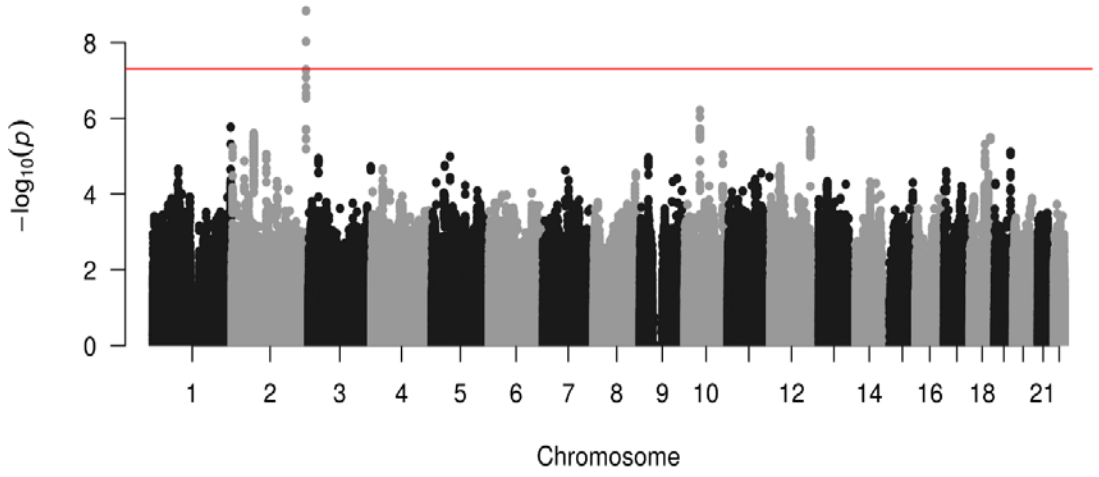


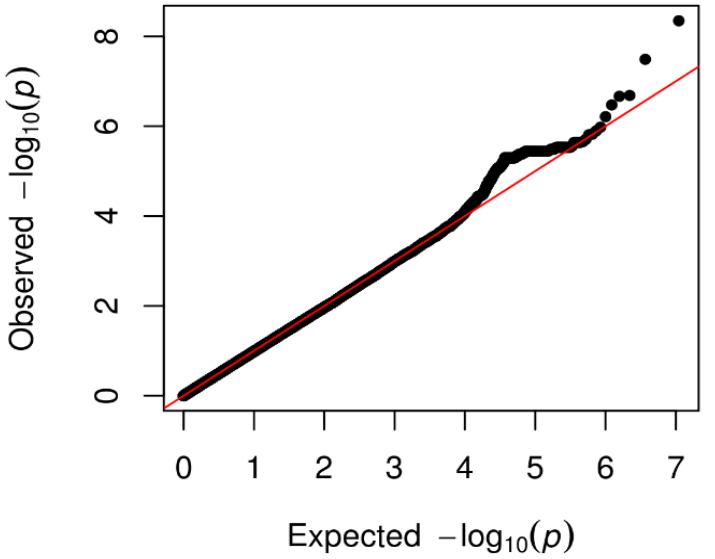
Analysis: Leon Hubbard

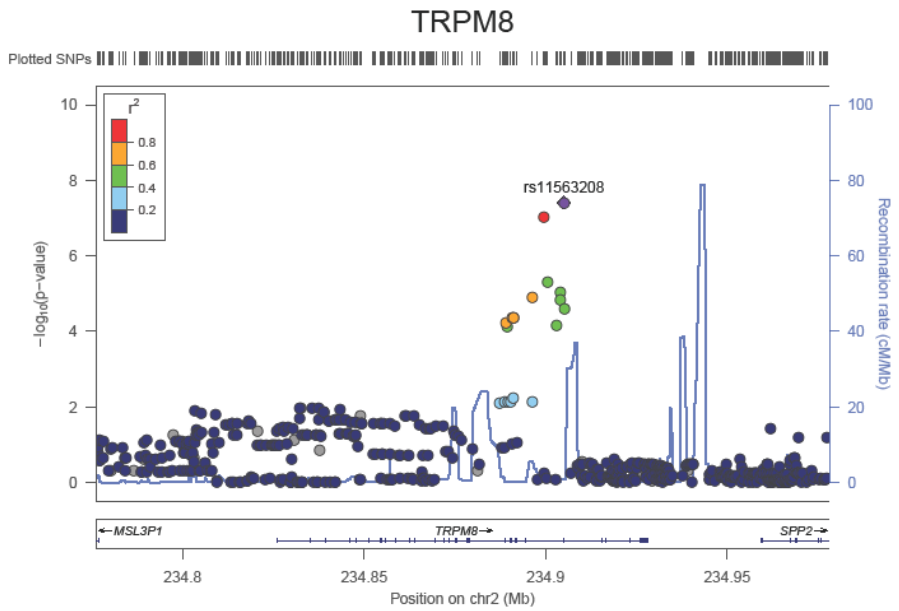
Pain in Parkinson's Disease GWAS: Association analysis Replication

- An additional 297 Parkinson patients from the Oxford Monument cohort (Caleb Weber, Richard Wade-Martins, Michelle Hu) had been assessed for Pain
  - Identical protocol
  - Genotypes were available
- Meta-analysis was then conducted at Cardiff
  - Combined sample size = 1318 (high pain =898 vs low pain =420)

Pain in Parkinson's Disease GWAS (Combined analysis of Proband and Oxford Cohorts)







Transient receptor potential melastatin 8 ion channel (TRPM8)

nature genetics

Genome-wide association analysis identifies susceptibility loci for migraine without aura

Migraine without aura is the most common form of migraine, characterized by recurrent disabling headache and associated autonomic symptoms. To identify common genetic variants associated with this migraine type, we analyzed genome-wide association data of 2,326 clinic-based German and Dutch individuals with migraine without aura and 4,580 population-matched controls. We selected SNPs from 12 loci with 2 or more SNPs associated with *P* values of $<1 \times 10^{-5}$ for replication testing in 2,508 individuals with migraine without aura and 2,652 controls. SNPs at two of these loci showed convincing replication: at 1q22 (in *MEF2D*; replication $P = 4.9 \times 10^{-4}$; combined $P = 7.06 \times 10^{-11}$) and at 3p24 (near *TGFBR2*; replication $P = 1.0 \times 10^{-4}$; combined $P = 1.17 \times 10^{-9}$). In addition, SNPs at the *PHACTR1* and *ASTN2* loci showed suggestive evidence of replication ($P = 0.01$; combined $P = 3.20 \times 10^{-8}$ and $P = 0.02$; combined $P = 3.86 \times 10^{-8}$, respectively). We also replicated associations at two previously reported migraine loci in or near *TRPM8* and *LRP1*. This study identifies the first susceptibility loci for migraine without aura, thereby expanding our knowledge of this debilitating neurological disorder.

pharmaceuticals

MDPI

Review

Development of TRPM8 Antagonists to Treat Chronic Pain and Migraine

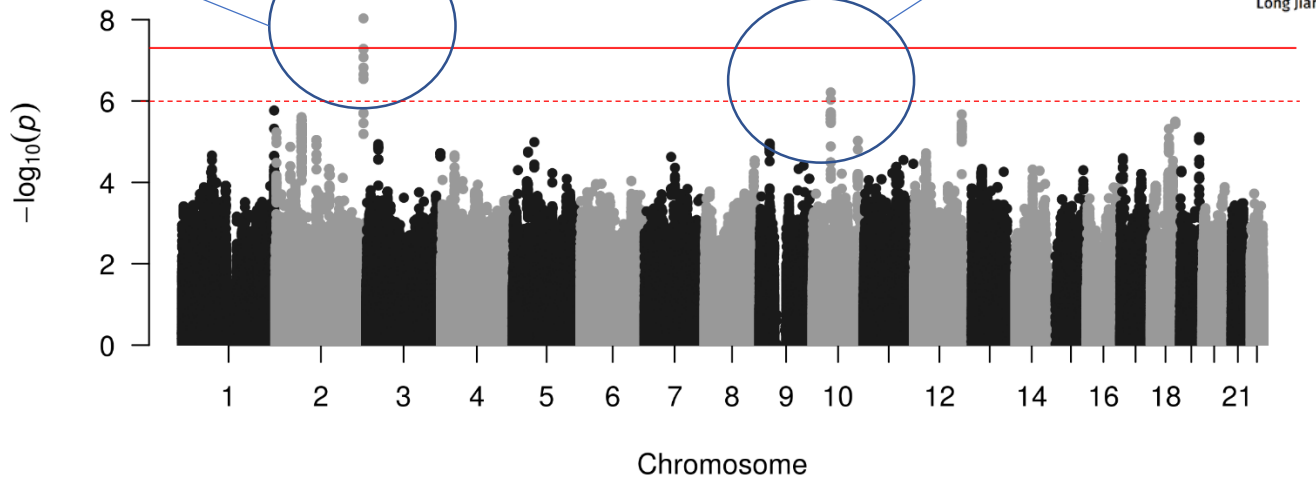
Andy D. Weyer [1] and Sonya G. Lehto [2,*]

*** the genetic variant associated with migraine/cold sensitivity is independent of the variant associated with Pain in PD

GWAS: Reduced Pain vs Pain

TRPM8

GDF10



NeuroReport. 28(8):444–450, MAY 2017
DOI: 10.1097/WNR.0000000000000785, , PMID: 28394782
Issn Print: 0959-4965
Publication Date: 2017/05/24

Share Print

Decrease of growth and differentiation factor 10 contributes to neuropathic pain through *N*-methyl-D-aspartate receptor activation

Long Jiang; Botao Tan; Sen Li; Li Wang; Liqiang Zheng; Yuan Liu; Zaiyun Long; Yamin Wu

Conclusion

- This approach has identified plausible candidates for reduced pain in PD
- Future work is required to establish the biological mechanisms
- Explore relationship with Pain in PD and Depression
- PhD studentship at Cardiff (Hannah Hendry)

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

MRC Centre for Neuropsychiatric Genetics and Genomics

PARKINSON'S UK
CHANGE ATTITUDES. FIND A CURE. JOIN US.