Neurobiological risk factors for future low back pain after an acute episode: the *UPWaRD* prospective cohort study

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BACKGROUND:

- A limitation of current prognostic models is that biological, psychological and symptom-related risk factors are often studied in isolation, leaving predictive models that lack integration between psychological and symptom-related factors and underlying biology
- The Understanding persistent Pain Where it ResiDes (***UPWaRD***) study aimed to determine whether neurobiological, psychological, symptom-related and demographic risk factors could predict six-month pain and disability.

METHODS:

- 120 participants.
- Six-month follow-up.
- 15 candidate predictors across the following domains: somatosensory and anterior cingulate cortex excitability, corticomotor excitability, markers of neuroplastic potential, psychological status, demographics and symptom-related
- Sensory evoked potentials derived using electroencephalography. Corticomotor excitability derived using transcranial magnetic stimulation.
- Lasso penalized regression variable selection
- Internal validation using ten-fold cross-validation

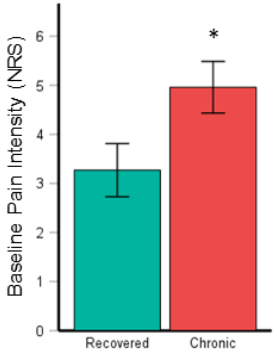

Fig1. Average baseline pain intensity ratings are higher during acute LBP for participants with ongoing LBP at six-months (P<0.001). *Statistical significance. NRS indicates numerical rating scale.

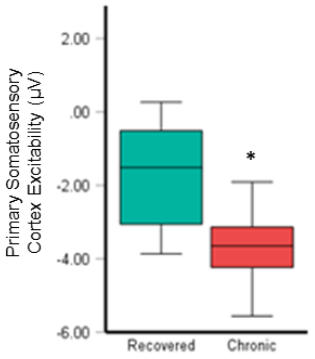

Fig2. Primary somatosensory cortex excitability is lower during acute LBP for participants with ongoing LBP at six-months (P<0.001). *Statistical significance.

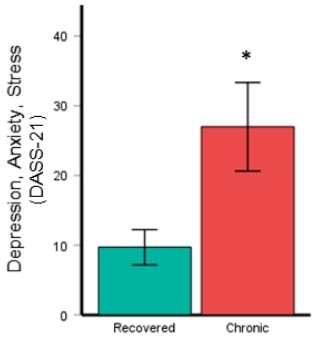

Fig3. Participants with ongoing LBP at six-months have higher depression, anxiety and stress during acute LBP (P<0.01). *Statistical significance. DASS-21 indicates 21-item depression, anxiety, stress subscale.

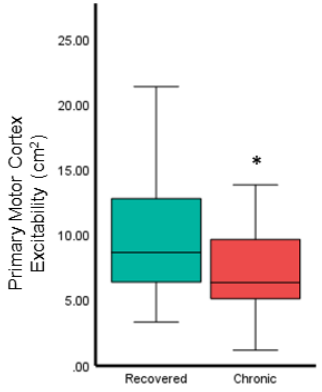

Fig4. Primary motor cortex excitability is lower during acute LBP for those with ongoing LBP at six-months (P=0.01). *Statistical significance.

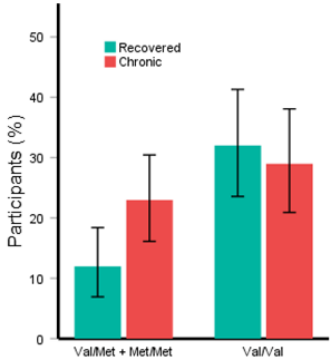

Fig5. More participants with ongoing LBP at six-months were found to carry the minor allele at BDNF rs6265 (P=0.09).

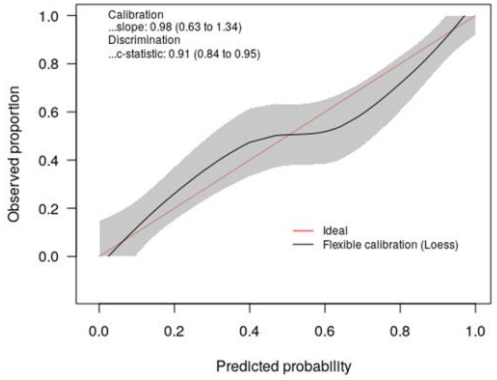

Fig6. Calibration curve for the internally validated multivariable logistic model, that predicts development of chronic LBP. Calibration slope = 0.98 [0.63 to 1.34].

RESULTS:

- 54% of participants complained of LBP at six-month follow up and were considered to have persistent or recurrent LBP
- Lower primary sensory cortex excitability, lower corticomotor excitability, higher baseline pain intensity, higher depression, anxiety and stress, MET allele carriers of the BDNF genotype and a previous history of LBP predicted the development of chronic LBP with very high discriminatory performance (c-statistic 0.91 [0.84 to 0.95])
- Brier Score = 0.12 (SD = 0.03)

DISCUSSION AND CONCLUSIONS:

- This study identified novel risk factors for the development of future LBP that could predict an individual's pain intensity and level of disability at six-month follow-up, and accurately discriminate between those who did, and did not, have LBP at this time-point.
- Future research that externally validates these findings may lead to the development of a prognostic model with clinical applicability for identifying patients at high risk of developing chronic LBP.

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