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Gait: a biomarker for pain and function in chronic low back pain

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OBJECTIVES/GOALS: Chronic low back pain (cLBP) is associated with gait impairments. Gait may serve as an important biomarker for improvement following therapy interventions; however, gait has not been sufficiently studied in relationship to pain and function in cLBP. METHODS/STUDY POPULATION: Adults with cLBP completed a two-minute-walk-test around a 37.5 m oval track while wearing an inertial measurement unit (IMUâ€"Lifeware LLC, Pittsburgh, PA) over the L5 spinous process. Step time average, step time variability, step length, and symmetry (harmonic ratio) were calculated based on linear trunk accelerations, and gait speed was calculated based on distance walked. Participants completed the PEG tool (Pain, Enjoyment, General activity; scores closer to 10 indicate worse pain) to quantify pain intensity/interference and the PROMIS Physical Function SF-6b tool (mean t-scores=50 +/- 10; higher scores indicate better function) to quantify physical function. Pearson correlation coefficient (r) was used to determine strength of associations between gait and pain/physical function. RESULTS/ANTICIPATED RESULTS: Eleven adults (8 female, age 40 +/- 17, pain duration≥3 months) with cLPB participated in this study after completing an informed consent process approved by the University of Pittsburgh Institutional Review Board. Participants with a history of cancer, spinal cord compression, discitis, or activity restrictions prohibiting them from protocol completion were excluded. The mean PEG scores and PROMIS Physical Function t-scores were 2.8 +/- 1.8 and 47.8 +/- 8.2 respectively. There was a moderate-strong correlation between step time average and PEG (r=0.67, p=0.02), and a moderate-strong correlation between gait speed and PROMIS Physical Function (r=0.62, p=0.04). There were no other significant associations. DISCUSSION/SIGNIFICANCE: Gait speed and step time may be important movement biomarkers to consider when evaluating patients with cLBP. Generalizability of results are limited by the small study cohort and this cohort's relatively low pain burden and high level of physical function.

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Generalizable Machine Learning Methods for Subtyping Individuals on National Health Databases: Case Studies Using Data from HRS, N3C, and All of Us

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OBJECTIVES/GOALS: While disease subtypes are critical for precision medicine, most projects use unipartite clustering methods such as k-means which are not fully automated, do not provide statistical significance, and are difficult to interpret. These gaps were addressed through bipartite networks and tested for generalizability on three national databases. METHODS/STUDY POPULATION: Data. All participants with self-reported stroke from the 2010 Health and Retirement Study (HRS), with cases (n=798) having one or more 8 depressive symptoms measured by the Centers for the Epidemiological Study–Depression 8 scale, and controls (n=389) with none of those symptoms. The replication data set consisted of independent identically-defined participants (cases=725, controls=190) from 1998 HRS. Method. (1) Bipartite network analysis and modularity maximization to automatically identify patient-symptom biclusters with significance. (2) Rand Index to measure the replicability of symptom co-occurrences in the replication data. (3) ExplodeLayout to visualize and interpret the subtypes. (4) R libraries to generalize the methods, upload them to CRAN, and then tested on the N3C and All of Us platforms. RESULTS/ANTICIPATED RESULTS: The analysis identified 4 depressive symptom subtypes (https://postimg.cc/Ny8YwXJW) which had significant modularity (Q=0.26, z=3.03, P DISCUSSION/SIGNIFICANCE: We developed generalizable methods to automatically identify biclusters, measure the clustering significance, and visualize the results for interpretation. These methods were successfully tested on three national level data bases. Such generalizable methods should accelerate the analysis of subtypes, and the design of targeted interventions.

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Genetic Variation in the SLC22A1-3 Genes Influence the Risk of Congenital Anomalies

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OBJECTIVES/GOALS: Congenital anomalies (CA) are common, but the cause is often unknown. The interplay between known environmental teratogens, such as medication use in pregnancy, and genetic predisposition impacts CA risk, but such interactions are poorly understood. We test the hypothesis that pharmacogenomic (PGx) variation impacts CA risk. METHODS/STUDY POPULATION: We performed a drug absorption, distribution, metabolism, and excretion (ADME) gene-wide association study (GWAS), which tests for a possible association between ADME gene single nucleotide polymorphisms and individuals with CAs. This analysis was performed in BioVU and utilized billing codes to identify 5,845 cases, individuals with at least one CA, and 50,059 controls of genetically European ancestry. Using Plink software we analyzed 5,398 SNPs in 292 ADME genes across cases and controls. Results from this analysis drove us to further investigate the association between CA risk and SLC22A1-3. Next, we performed PrediXcan analyses to estimate the association between genetically predicted gene expression (GPGE) of SLC22A1-3 genes across all available tissues in the GTEx resource and CA risk. RESULTS/ANTICIPATED RESULTS: The ADME GWAS identified multiple variants on chromosome 6 in the region of SCL22A1-3 that were associated with the risk for CAs. The most significant variants were rs2048327, rs2292334, rs3088442, rs1810126, rs376563, and rs7758229, p DISCUSSION/SIGNIFICANCE: The combination of the known crucial pharmacological roles of OCT1-3 and the results of our ADME GWAS / PrediXcan analyses demonstrates that PGx burden, specifically variation in the SLC22A1-3 genes, influences the risk of developing CAs. This new understanding has the potential to personalize care for pregnant individuals to reduce the risk of CAs.

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