276

Effect of Practice Schedule on Motor Learning of Protective Stepping Responses in Persons with Parkinson's Disease and Age-matched Controls.

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OBJECTIVES/GOALS: Persons with Parkinson's disease (PwPD) have set-shifting impairments that may limit motor learning of protective responses to prevent falls. This study compares the effect of blocked versus random practice schedules on acquisition and retention of protective stepping stability in PwPD & age-matched controls. METHODS/STUDY POPULATION: Twenty PwPD & 20 age-matched controls will be randomly assigned to random or blocked practice groups to experience slip and trip-like perturbations which induce stepping responses. Blocked practice is repeating a task (e.g., slip) several times before the next task, while random practice is randomly practicing two or more tasks (e.g., slips & trips). Each subject will wear a safety harness to prevent falls, each fitted with a load cell that indicates when a fall would have occurred. We will assess the anterior-posterior and mediolateral margin of stability at 1st protective step, step length, and in-task fall incidence before, 10 minutes, and two days after practice. We will also compare outcomes between participants in the blocked vs. random practice schedule using two ANOVA. RESULTS/ANTICIPATED RESULTS: To date, we have recruited three control subjects. We anticipate that blocked practice will be superior to random practice for protective stepping acquisition and retention PwPD. Existing literature on motor learning of voluntary tasks indicates that PwPD have difficulty acquiring and retaining motor skills via random practice due to the higher cognitive processing required than blocked practice. Furthermore, since the basal ganglia's set-shifting role is crucial for random practice, it is expected that random practice will limit protective steps acquisition and retention in PwPD. In healthy control, while blocked practice is better for acquisition, random practice will be superior for retention. DISCUSSION/SIGNIFICANCE: The study's findings will provide knowledge that may foster the development of robust balance rehabilitation protocols to improve postural responses in PwPD and reduce delayed and ineffective stepping responses that results in falls among PwPD.

278

Eight Pharmacokinetic-related Genetic Variants Were Not Associated with Bleeding from Direct Oral Anticoagulants in Non-valvular Atrial Fibrillation Patients

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OBJECTIVES/GOALS: Assess the association of PK-related single nucleotide variants (SNVs) with the risk of bleeding from DOACs in non-valvular AF patients. METHODS/STUDY POPULATION: A retrospective cohort study was carried out with 2,364 Caucasians with non-valvular AF and treated with rivaroxaban or apixaban. Patients were genotyped as part of the genomic biobank at the University of Michigan Health System. The primary endpoint was a composite of major and clinically relevant non-major (CRNM) bleeding. Cox proportional hazards regression with time-varying analysis assessed the association of 8 SNVs in 5 PK genes (ABCB1, ABCG2, CYP3A4, CYP3A5, CYP2J2) with the risk of bleeding from DOACs in unadjusted and covariate-adjusted models. Six tests were performed as 3 of the SNVs are in the same haplotype. P-values below the Bonferroni-corrected level of 8.33e-3 were considered statistically significant. RESULTS/ANTICIPATED RESULTS: A total of 412 (17.4%) major and CRNM bleeding events occurred over 2.27 ± 2.03 years of follow-up. None of the PK SNVs were significantly associated with bleeding risk on DOACs in both unadjusted and covariate-adjusted Cox regression models. DISCUSSION/SIGNIFICANCE: The effects of these eight genetic variants on exposure to DOACs may not be strong enough to translate into differences in clinical outcomes. Especially if the genetic inheritance underlying the risk of bleeding from DOACs is polygenic, reinforcing the need for further genomic studies on this subject.

279

Electronic Health Record Data and Topological Data Analysis to Predict Clinical Outcomes Post Myocardial Infarction*

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OBJECTIVES/GOALS: The aim of this study is to analyze electronic health record (EHR) data using Mapper PLUS (MP), a new mathematical model, to classify acute myocardial infarction (MI) patients by risk of major adverse events (AE). We tested MP's ability to define patient subgroups with distinctive risk for death, heart failure or recurrent MI after revascularization. METHODS/STUDY POPULATION: An EHR retrospective analysis of 797 MI patients and 29 variables (i.e., laboratory tests, imaging, vitals, and clinical traits) collected at the time of hospitalization was conducted. All patients received percutaneous coronary intervention and standard pharmacotherapy. MP analysis produced a multi-dimensional nodal graph of the patients based on similarities found within variables. Two algorithms, Walk Likelihood and Walk Likelihood Community Finder were applied to the graph which formed joint clusters according to spatial distance within nodes. The final output was three clusters for risk level evaluation. Risk level (low vs. high) was relative to the average risk of AEs for the entire cohort one year post MI. RESULTS/ANTICIPATED RESULTS: Of three patient subgroups, one (n= 318) had a >1 fold change for the probability of survival without AE when compared to the overall cohort and thus was defined as the low-risk group. The second group (n=304) had DISCUSSION/SIGNIFICANCE: MP stratifies patients into three groups according to predictive variables which relate to the risk for AE following an acute MI treatment. This is a new topological method for patient classification based on minimal input strictly from pre-collected EHR data. More cohort studies are needed to validate MP to classify patients for precision medicine.

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