Wearable Technology to Characterize and Treat mTBI Subtypes: Biofeedback-Based Precision Rehabilitation (SuBTyPE)

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Statistical Analysis Plan for Wearable Technology to Characterize and Treat mTBI Subtypes: Biofeedback-Based Precision Rehabilitation (SuBTyPE)

Aim 1

The *primary outcome* for Aim 1 is the Patient Global Impression of Change (PGIC). It is an ordinal variable where participants rate their global assessment of change on a scale from 1 to 7. To test whether the group with multidimensional real-time biofeedback has larger improvements in the PGIC than the group with standard care physical therapy, we will first conduct a Mann-Whitney U test to assess group differences in PGIC scores. Additionally, we will perform subsequent analyses using ordinal logistic regression to examine group differences accounting for covariate effects (e.g., age, gender, PTSD, etc.).

Secondary outcomes (e.g., patient-reported symptoms, clinical and instrumented objective assessments) will be measured at baseline and post-rehabilitation. All secondary outcomes will be assessed for normality and we will perform a data transformation (e.g., log transformation) when appropriate. We will calculate the pre-post change in each secondary outcome for each participant. To test the difference in pre-post change between the multidimensional real-time biofeedback group and the standard care group, we will conduct a two-sample t-test or a Mann-Whitney U test for each secondary outcome. We will employ mixed effects models to assess the differences in change in secondary outcomes between the real-time biofeedback and standard care group. Two fixed effects will be included in the model: 1) group effect (real-time biofeedback vs. standard care) and 2) time effect (baseline and post-rehabilitation). The interaction between group and time (group x time) will also be included. We will include covariates in the fully adjusted model. Random intercepts will be included to account for the clustering effect within subjects over time. We will use an inverse probability weighting approach to account for participant attrition in the study cohort when appropriate.

Aim 2

In this exploratory aim, we will: 1) assess high vestibular/ocular (V/O HI) symptoms versus low vestibular/ocular (V/O LO) participants' responsiveness to rehabilitation and 2) explore the relationship between subjective and objective measures of V/O domains. Responsiveness to rehabilitation will be determined by the participants' score on the PGIC after rehabilitation. PGIC score will be dichotomized by "responder" or "non-responder". We will classify participants who score 6 or above on the PGIC as "responders" and those who score 5 or below as "non-responders". First, we will examine the distribution of PGIC scores and the proportion of responders vs. non-responders in V/O HI group and V/O LO group. Then we will conduct a logistic regression on responder vs. non-responder as the binary outcome to assess differences between V/O HI group and V/O LO group. For the next step, we will assess the PGIC as an ordinal outcome variable and test group differences in responsiveness using ordinal logistic regression. Both regression models will allow us to control for covariates (e.g., age, gender, days since injury, intervention arm) in the models. We will use the data to obtain estimates to inform future studies and power calculations. Finally, to explore the strength of associations between the Patient-reported, Clinical, and Instrumented V/O measures, we will measure the associations using Pearson correlation coefficients for continuous variables and Spearman correlation coefficients for ordinal variables.

Aim 3

Participants will be grouped using the concussion clinical profiles screening tool according to their level of severity of V/O deficits (HI or LO V/O deficits). Prior to detailed statistical modeling,

we will compute quality metrics of daily life mobility quantified from instrumented socks summarized over the duration the devices were worn by each participant (for those that wore the devices for at least 5 out of 7 days and at least 10 hours/day). Specifically, we will provide both statistical and graphical evaluation for the distributions of three quality metrics: turn angle, turn angle variability, and turn peak velocity, and then transform the values if necessary to better meet model assumptions. Then we will examine the distribution of the three quality metrics in each group. The descriptive statistics of quality metrics for each group will be reported as mean (SD). To test whether daily life mobility measures differ between V/O HI and V/O LO groups, we will test the quality metrics for group differences using a two sample t-test. In addition, we will conduct subsequent analyses to compare quality metrics between two groups accounting for covariates using the multivariate generalized linear modeling (GLM) approach. The model will be constructed for each quality metric (outcome) separately. The group estimates will be assessed with and without the co-existing covariates to explore potential confounding factors, which allows us to test for group differences while controlling for the possible effects of other covariates. In addition, for turn peak velocity variability and quantity activity measures, we will also examine the distributions using the same method and conduct two independent sample t-test between two groups for the completeness of the analysis.

To summarize the healthy military normative group, we will similarly collect data from instrumented socks worn over a 7-day period. We will examine the distribution of the quality metrics and provide descriptive statistics including means, standard deviations, median and 25^{th}, 75^{th} percentiles. Additionally, we will use histograms and Shapiro-Wilk's tests to check the normality of the data. This will provide preliminary data for our next studies exploring daily life mobility in those cleared to return to duty after mTBI.