Statistical analysis plan - Version 2, 13/10/2020

The effect of training on brain activity during postural control tasks in older adults

Protocol identification number

S62917

Study type

Interventional

Principle investigator

Prof. Alice Nieuwboer

Sub-investigator

Veerle de Rond, MSc

Brief summary:

Older people show deficits in dynamic weight-shifting, as we found that more time is needed to perform weight-shifts and the movements become less fluent and accurate in older versus younger adults. Deficits with weight-shifting in the mediolateral (left-right) direction has been linked to balance and falls in ageing. Balance control can be improved with training. Virtual reality (VR) based training programs for improving balance are gaining ground, as it can provide both fun and challenging balance tasks, enhancing motivation. We demonstrated earlier that older adults show an overloaded neural activation pattern compared to young adults when performing the same VR-based mediolateral weight-shifting task (wasp game). What is yet unclear, is whether improved balance capacity can be gained with training and whether such an intervention impacts the underlying neural mechanisms. Using a combination of behavioral assessments and functional Near-Infrared Spectrocopy (fNIRS), the primary aim of this study is to investigate the effects of a VR-based weight-shift training and its underlying neural imprint in older adults. Next to the wasp game, a mediolateral tracking task will be used to standarize weight-shifting speed to allow comparison of fNIRS data during stable weight-shifting performance. Furthermore, as our previous study also showed that adding an extra cognitive task in a so-called dual-task (DT) negatively affects weight-shifting performance, a secondary aim will be to test whether weight-shift training will enhance performance during such DT conditions. The results of this study may contribute to the future design of technology-based rehabilitation programs.

Primary outcome:

For the primary behavioral outcome, weight-shifting speed in the mediolateral direction will be used. Participants will shift their weight to 80% of their stability limits within the Wasp Game. As people tend to slow down when reaching the 80% limit in order to aim for the wasp, mediolateral weight-shifting speed will be determined from 90% of the 80% limit on the right side to 90% of the 80% limit on the left side and vice versa. Mediolateral weight-shifting speed will be determined and compared between the three test moments (pre, post, retention) and between the two groups (training, control) during the Wasp Game ST and DT.

Secondary outcomes:

1. Outcomes of the Wasp task

The number of wasps hit (#wasps), the anterior-posterior weight-shifting error (error from the ideal trajectory) and the anterior-posterior target error will be used within the Wasp Game. The trajectory and target error will be determined similar to the primary behavioral outcome measure. #wasps hit, trajectory and target error will be compared between the three test moments (pre, post, retention) and between the two groups (training, control).

2. Outcomes on the mediolateral tracking task

The tracking error in both the anterior-posterior and mediolateral direction as well as the maximum amplitude reached will be used as behavioral outcome measures of. The tracking error will be determined as the deviation between the target and the center of mass of the participant and the maximum amplitude reached as the maximum amplitude reached by the participant as a percentage of the maximum amplitude of the target, which will be set at 80% of individual stability limits. Outcome measures will be determined and compared between the three test moments (pre, post, retention) and between the two groups (training, control).

3. <u>Functional limits of stability</u>.

These will be determined in eight different directions (anterior, anterior-right, right, posterior-right, posterior, posterior-left, left, anterior-right) and compared between the three test moments (pre, post, retention) and between the two groups (training, control).

4. <u>fNIRS-outcomes</u>

For the neural outcome, cortical oxygenated hemoglobin (HbO2) will be measured with functional Near-Infrared Spectroscopy (fNIRS) in the prefrontal cortex (PFC), frontal eye fields (FEF), premotor cortex (PMC), supplementary motor area (SMA) and the somatosensory cortex (SSC) . HbO2 levels will be determined and compared between the three test moments (pre, post, retention) and between the two groups (training, control) during the Wasp Game ST, Wasp Game DT and the tracking task.

Tertiary outcomes:

1. <u>Clinical balance outcome</u>

The MiniBEST will be administered to assess general balance. The scale consist of 4 subscales: 1) anticipatory postural control; 2) reactive postural control; 3) sensory orientation; 4) dynamic gait. Total score (range 0-28) will be compared between the three test moments (pre, post, retention) and between the two groups (training, control).

2. <u>fNIRS-outcomes</u>

Cortical deoxygenated hemoglobin (HHb) will be measured with functional Near-Infrared Spectroscopy (fNIRS) in the same regions as HbO_2. HHb levels will be determined and compare between the three test moments (pre, post, retention) and between the two groups (training, control) during the Wasp Game ST, Wasp Game DT and the tracking task.

Main analysis:

Primary, secondary and tertiary outcomes will be compared between training and control group and pre, post and retention test using a constrained longitudinal data analysis approach using a mixed model specification. We will consider cognitive and balance skills as possible covariates, depending on between group differences and determined by a blind review of the data. Post-hoc testing will be done of significant interaction only, followed by Bonferroni corrections.

Depending on data normality, Pearson and/or Spearman correlation analysis will be performed between neural and behavioral outcomes within groups and test moments. Bonferroni corrections for multiple testing will be applied when necessary.

Secondary analysis:

A planned secondary analysis will be performed within the control group to investigate fNIRS test-retest reliability using a three-way repeated measures ANOVA (pre, post, retention). Here we will also calculate the intraclass correlation coefficient (ICC), standard error of measurement (SEM) and minimal detectable change (MDC).