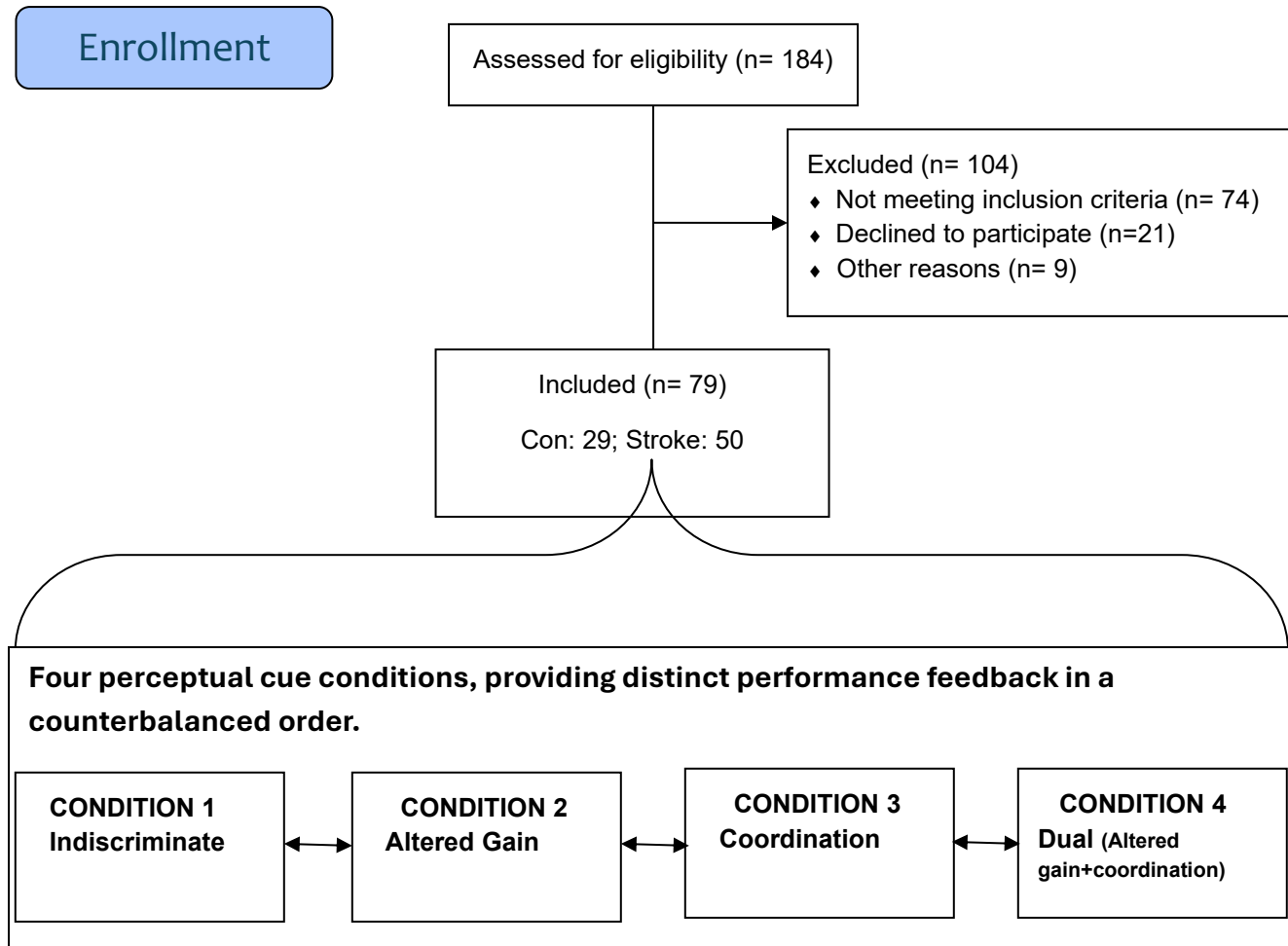


Perceptual-motor Interaction to Improve Bimanual Coordination After Stroke

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CONSORT Flow Diagram



Study protocol:

Specific Aim: Determine the immediate effects of perceptual cues on bimanual coordination in stroke survivors. This aim was to determine the immediate effect of perceptual cues providing feedback about (a) between-limb coordination and (b) differential weighting of the two arms on spatial and temporal measures of bimanual coordination during a common goal bimanual reaching task.

Hypotheses: (a) Feedback on the relative timing between arms (i.e., between limb coordination), provided in the form of a horizontal tilt of the virtual brick, will shorten the time lag and increase CCr over practice. (b) A greater weighting coefficient applied to the weaker arm along with feedback of relative timing between arms (i.e., both cues) may transiently impair temporal and spatial bimanual coordination measures but will improve over practice.

Rationale: Perceptual cueing has a strong effect on motor performance. The requirement to minimize the tilt of the brick will reduce redundancy by constraining the two arms to move simultaneously, thus improving the coordination between arms. In addition to the tilt, when each arm is differentially weighted, a greater movement of the paretic arm is required to move the virtual brick to the target window. However, this requires the paretic arm to move farther and faster than the non-paretic arm to ensure that the brick is moved horizontally to the target. These differential demands on each arm may impair temporal and spatial coordination measures early after the introduction of differential arm-weighting cues. However, as evident from our preliminary data, patients will improve their spatial and temporal coordination with more trials.

Participants: A total of 184 potential participants were screened and seventy nine participants were included in the study. These consisted of fifty individuals with chronic (> 6 months since stroke) hemiparesis following unilateral cortical or subcortical stroke and twenty-nine age-matched controls. An equal number of patients with left- and right-sided brain damage were recruited. The inclusion criteria were as follows: (a) ability to reach

along a diagonal direction at least 80% of their arm length while fully supported on a frictionless surface and trunk constrained. Our previous experience suggested that this performance criterion will recruit a relatively large spectrum of severity from mild to moderate impairments (Fugl-Meyer (FM) scores 32-66). Although this excluded patients with more severe impairments, such as those with complete paralysis, it is now known that different stroke severities require distinct treatment approaches. In addition, patients with severe motor impairments may not be able to engage their arms in bimanual or unimanual activities, thus limiting the testing of coordination. Patients with very mild impairments (FM 60-66) will be included because they may have higher-order coordination deficits due to lesions in brain regions crucial for planning and coordinating bimanual actions. (b) Minimal scale score > 26, (c) score of 4 or above on the auditory verbal comprehension part of the Western Aphasia Battery to ensure intact comprehension and following commands, and (d) no evidence of hemispatial neglect tested by a line bisection test. (e) No contraindications to TMS or MRI. Attempts were made to include as many men and women as possible. The exclusion criteria were as follows: bilateral stroke, complete paralysis, basal ganglia/cerebellar stroke, pain or stiffness in the upper extremity that would interfere with the task, or inability to follow task instructions.

Procedure: Participants were instructed to “move” a common virtual brick with both arms to a target window without tilting the brick within a target MT of 1.2 seconds. Participants completed four 60-trial blocks in pseudorandom order. Each block consisted of a distinct task condition depending on the nature of the perceptual cues provided. The conditions were:

Condition 1: Indiscriminate: Participants transported a common virtual brick fixed in a no-tilt position to the target position in a pseudorandom order. The movement of the brick in the X and Y axis is an unweighted average of the two arm movements, that is, each arm contributes to 50% of the virtual bar movement (50-50 weighting). Thus, the feedback cue was indiscriminate (i.e., just the movement of the brick without any additional information about the relative time lag or differential weighting).

Condition 2: Altered gain: This was similar Condition 1 (virtual brick fixed in no-tilt), but the arm weighting will be such that the gain of the paretic arm was reduced. With this manipulation, a farther movement of the paretic arm was required to maintain its contribution. Thus, the only perceptual cue provided here was related to the differential weighting of the paretic arm.

Condition 3: Coordination: For Condition 3, the weighting coefficients of the two arms were equal (i.e. 50-50); and the virtual brick tilted in the direction of the lagging arm proportional to the relative time lag between the arms. Thus, the only perceptual cue provided was the relative time lag between the arms. *Operational definition of relative time lag:* Relative time lag is different from the absolute time lag. The relative time lag is the time lag between the relative timings of each arm within its trajectory. To illustrate, if the left and right arms contribute to 70 and 30% of the brick movement, respectively, the relative time lag at mid-movement will be zero if the left and right arms have covered half of their respective trajectories. Therefore, the relative time lag is influenced by the temporal and spatial components of the movement of each arm. Concurrent and post-response feedback regarding the tilt and path of the virtual brick was provided after each trial.

Condition 4: Dual cues: In addition to the “tilt” feedback about the relative time lag (like in Condition 3), each arm was differentially weighted, that is, the paretic arm had a lower gain (or higher weighting coefficient) than the nonparetic arm (like Condition 2). Specifically, based on our preliminary studies, the lower gain the paretic arm contributed to ~60-70% of the virtual brick movement, whereas the nonparetic arm contributed to ~30-40% of the virtual brick movement. Thus, in this condition, participants received both perceptual conditions (relative time lag and differential weighting) simultaneously.

Dependent measures Coordination between the two arms was quantified by cross-correlation between the tangential velocities of the two arms. Spatial coordination was characterized by the peak cross-correlation coefficient (CCr) between the tangential velocity profiles of the two arms. CCr values closer to 1 indicated better spatial coordination. Temporal coordination was quantified as the time lag at which the peak

cross-correlation coefficient was obtained via cross-correlation analysis. A shorter time lag (closer to zero) indicated stronger temporal bimanual synchrony. A positive lag indicated that the paretic arm (non-dominant in the control) lagged behind the non-paretic arm (dominant in controls).

Statistical plan: The study design included between-subject variables (stroke and control groups) and two within-subject variables (perceptual cue conditions: 1-4; and two time points: start of practice (SOP) and end of practice (EOP). Z-score (Fisher's z)-transformed cross-correlation coefficients (CCrs) were used for analyses. Box-cox transformation was used for the time-lag data. Transformed measures of spatial and temporal coordination measures were analyzed using a separate 2 GROUP (stroke, controls) \times 4 PERCEPTUAL CUE CONDITIONS (veridical, coordination, altered gain, and combined coordination+ altered gain feedback) \times TIME (SOP, EOP) with repeated measures on the last two factors. The focus of this study was to compare the effects of different perceptual cues on individuals with stroke and age-matched neurotypical controls. Sex was used as the covariate.

Expected results and interpretation: We expected to observe a significant group main effect and a significant interaction between feedback and arm weighting. When the brick is fixed, we expect that there will be no difference in the arm weighting conditions; when the brick is free to tilt, we expect that 50-50 arm weighting will result in better temporal and spatial coordination compared to 70-30 arm weighting. Similarly, we expected poorer coordination for parallel conditions compared to the mirror condition. 70-30 arm weighting will lead to a greater contribution of the paretic arm than the 50-50 weighting.

Pitfalls and contingencies: It is likely that the tilt cue conveys spatial rather than temporal information. In such cases, we reiterate our instructions assisted by example templates of how the tilt is determined. We ensured that the participants' understanding was clear.