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DONDERS GRADUATE SCHOOL FOR COGNITIVE NEUROSCIENCE

**Manipulating multisensory integration for reach
planning using tendon vibration**

MSC THESIS COGNITIVE NEUROSCIENCE

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1 Abstract

To plan a movement, integration of different sensory inputs is necessary to form an estimate of the current state of the body relative to the environment. Reaching movements with the hand are a very common and essential part of human interaction with the environment. Motor planning for these reaching movements relies on input from visual and proprioceptive senses. These different senses can be integrated to obtain an informative estimate of hand position in order to be able to plan a goal-directed reach. At subsequent stages of planning the two senses need to be integrated with different relative weightings allowing for optimal integration of the two estimates. The integration weighting is dependent on the respective properties of the different motor planning stages.

Here, we aim to study this integration process by manipulating the proprioceptive estimate of hand position. As the estimate of hand position can be described as a likelihood distribution around a location, we were interested in studying both manipulation of the precision and accuracy of this estimate. For the former, we developed a simultaneous agonist-antagonist vibration paradigm to test whether this can decrease precision of proprioceptive input after vibration ceases, with the muscle spindles adapting to the varying effect of vibration. We tested 6 healthy adults on their accuracy and precision in a hand positioning task during agonist-antagonist vibration. They were tested in a baseline setup without vibration, then in 4 alternate blocks of applying 100 Hz vibration or no vibration during task performance. We analysed precision of final position estimates, but also accuracy. The results suggest that precision is not decreased, and therefore that agonist-antagonist vibration does not decrease the quality of the proprioceptive input in this paradigm.

Previous research indicates that unilateral tendon vibration induces an illusory displacement of the respective joint. In a second experiment, we used this knowledge to manipulate accuracy of the proprioceptive estimate of the hand to study the role of proprioception in multisensory integration for motor planning in a reaching task, using tendon vibration either on the biceps brachii or the triceps brachii. We tested 20 healthy adults in this paradigm. Participants had to reach from a central start position through eight circularly arranged target positions in the horizontal plane. Biceps, triceps and no-vibration trials were pseudorandomly interleaved. We analysed tangential reach direction at movement initiation (40% of maximum velocity). For most target directions there was a significant effect of biceps and triceps vibration on the initial error in reach direction relative to no-vibration trials. These results support the important role of proprioception in estimating hand position and planning hand movements, where proprioception plays an especially large role when transforming planned movement vectors into executable motor commands.

2 Introduction

2.1 Background

In humans, it is crucial for planning of movements that sensory information from different sources is integrated. Integrating feedback from different sensory sources can help building a more precise and reliable estimate of the state of our body and the outside world, so that motor planning may be prepared more easily and correctly. One example of motor planning can be observed in the planning of hand movements, where multiple senses can be used to form an estimate of the arm's configuration and position relative to the location of a target object. Two vital senses in this specific process are the visual and the proprioceptive sense of the arm and hand. van Beers et al., 1999 suggested that the two senses could be integrated based on direction-dependent previous information on how reliable previous information of the respective senses were.

The integration process of these two sensory inputs has been further described by Sober and Sabes, 2003. They studied how feedback from different senses is combined to form an estimate of arm position and to plan movement. They suggest that there are two separate stages of movement planning: the computation of a movement vector in Cartesian space and the subsequent conversion of this vector into joint angular displacements. During both computations, vision and proprioception are weighted differently. To dissociate the respective contributions of proprioception and vision in the integration process, they manipulated vision by displacing the visual feedback about hand position in a reaching task. From the induced errors, the weighting of vision in the different stages of planning could be deduced. This reflects the predictions from their model and how the brain adapts weighting of sensory inputs to the goals of a task. The aim of the current study is to examine the effects of manipulating proprioceptive feedback about hand position and how this affects the estimate formed by integrating proprioception and vision. We tested two different approaches, which we will explain subsequently.

While visual feedback is received from the retina, proprioceptive feedback arises from three types of receptors. These receptors are the muscle spindles, skin receptors and joint receptors (Proske, 2015). It appears that muscle spindles play a major role in proprioception when compared to skin and joint receptors. Therefore, they are of particular relevance for the study of proprioception. The muscle spindles create motor afferents which communicate force and heaviness depending on their stretching properties (Proske and Gandevia, 2012).

Early research indicated that applying unilateral tendon vibration can create an illusion of movement (Goodwin et al., 1972). This illusion was more extensively studied by Roll and Vedel, 1982 who recorded the illusory effects for different vibration frequencies on both the biceps and triceps using microneurography, a technique in which direct neurophysiological measures are taken of peripheral nerves. They found that there is a frequency-dependent effect of vibration on the strength of the movement illusion.

In contrast to unilateral tendon vibration (tendon vibration at a single tendon) there is also the possibility to apply vibration to an agonist-antagonist tendon pair, such as the distal biceps and triceps tendons of the upper arm. In one study (Gilhodes et al., 1986) it appears that when biceps and triceps are both simulated there seems to be no or little illusory movement. If there is an illusion of movement, it appears to be in the muscle which is vibrated at a lower frequency. There has been further research on agonist-antagonist tendon vibration in the arm in more recent years, but the literature does not yet lead to a clear conclusion about the effects. While both Bock et al., 2007 and Pipereit et al., 2006 suggest that agonist-antagonist tendon leads to deteriorated proprioception, a more recent study on agonist-antagonist vibration by Gonzales and

Goble, 2014 finds there is a deterioration mainly in the period right after vibration has been turned off. Previous studies (Fuentes et al., 2012) also have shown that this sensory variability seems to be dependent on the duration of stimulation, which is an important factor for the research design of the present study.

2.2 Research Question

Based on these findings, it should be feasible to manipulate both the accuracy and precision of upper limb proprioception in multisensory integration during reach planning. Specifically, agonist-antagonist tendon vibration should decrease precision of the proprioceptive information that the brain receives, as the signal becomes less reliable in estimating true position of the hand. In the first experiment we examined whether in a hand positioning task there would indeed be higher variable error after vibration, indicating the expected decrease of proprioceptive precision.

While the first experiment focuses on decreasing precision of proprioceptive input, in the second experiment we manipulated proprioceptive accuracy. As previously explained, research conducted by Goodwin et al., 1972, but also a study by Lackner, 1988, has shown that tendon vibration can induce a perceptual shift in proprioception of a lengthening of the stimulated tendon, thus inducing a perceived displacement. This could be applied in the previously described experimental paradigm used by Sober and Sabes, 2003 in order to be able to create illusionary proprioceptive shifts. This would bear the advantage that there is no actual muscle activation (as described by Furthermore, if the results from experiment 1 indicate that agonist-antagonist tendon vibration induces a decrease in precision about proprioceptive information, this could also be used to potentially manipulate how proprioception is weighted at different stages of multisensory integration. This would allow to draw conclusions about how previous experience and present experience relatively shape the weighting process of different sensory inputs.

The research question of the second experiment would then be what the role of proprioception is in the integration of vision and proprioception for upper-limb movement planning. More specifically, in the case of single tendon vibration, we would expect the proprioceptive shift to affect motor planning by distorting the position estimates and thus creating an error in the planned reach direction and the subsequent conversion into joint angular displacements. This should be reflected by an increased directional error in the initial part of the movement, especially so along the directional axis which is most strongly influenced by biceps and triceps activation.

3 Methods

3.1 Participants

Six (3 female, 3 male, 19-25 years) and twenty (15 female, 5 male, 19-60 years, median: 24.5 years) healthy adults voluntarily participated in two experiments, respectively, in exchange for course credit or received vouchers (10€ per hour). Participants were all right-handed and recruited through an anonymous online registration portal. All signed an informed consent and there was opportunity for remarks and questions before and after the experiment. Vision of participants was normal or corrected-to-normal, and they reported to have no motor deficits or neurological disorders. The study was part of a research programme approved by the ethics committee of the Social Sciences faculty of Radboud University.

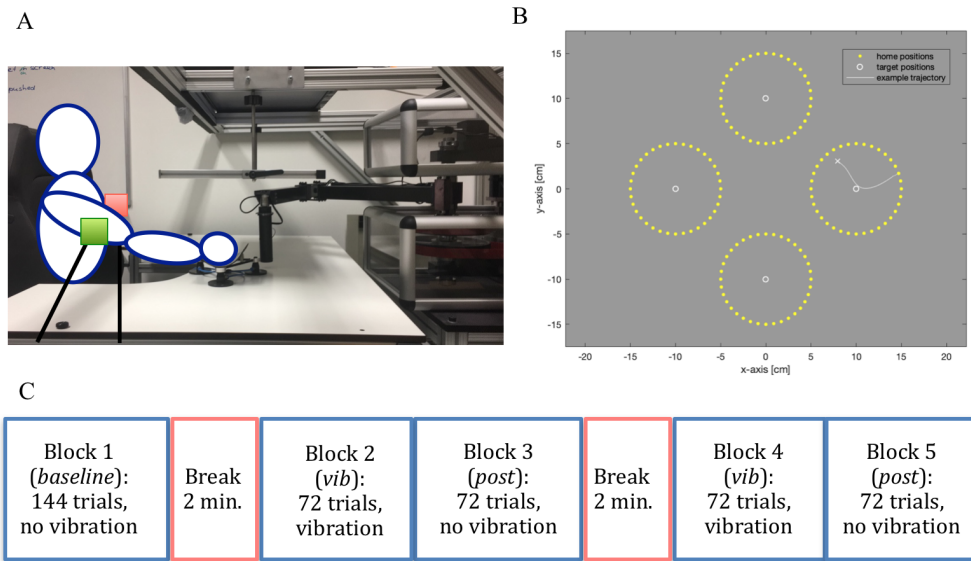


Figure 1: (A). setup of the participant during the experiment, including the vBOT (Howard et al., 2009), air sled, vibrators and the splint. The same setup was used in experiment 2. The vibrators were attached to the right upper arm. The red square represents the location of the biceps vibrator, while the green square represents the triceps vibrator. (B). All start (yellow) and target (white) locations displayed simultaneously, including an example trajectory from start to target location (white x). Participants only saw one target location at a time and no other visual feedback. (C). Experimental procedure.

3.2 Experimental Setup

The experiments were conducted using a vBOT planar robotic manipulandum (Howard et al., 2009, see figure 1(A)) with which we recorded movements of the participants' hands and passively moved them back to the start location. The measurements were taken with a frequency of 1,000 Hz. Participants' wrists were fixed using a wrist splint to reduce contributions from this joint to the movement; additionally their body movement was restrained by using seat belts.

In order to keep movements in a horizontal plane, but also to reduce friction, participants' lower arms were placed in an air sled on top of a table below the robot and display setup, at a height that allowed the participants to move their arm comfortably.

Visual stimuli were displayed on a semi-silvered mirror, which showed the reflection of an LCD display (Asus VG278H). The room was completely dark except for the light emitted by the display, and participants' view of their hand and lower arm was additionally obstructed by the mirror. Tendon vibration was applied by two vibrators, attached to the upper arm with the help of a hook-and-loop fastening band. They were industrial vibrators (NTS 120HF, Netter, Germany) and vibration was applied at a frequency of 100 Hz. They were attached at the height of the distal tendons of the biceps brachii and the triceps brachii.

3.3 Experiment 1

3.3.1 Paradigm

The task for the participants was to position their hand from a start location (yellow circles in fig. 1, not visually displayed during the experiment) towards a target location. There were four target locations ($\varnothing 0.5\text{cm}$, circle, white), all having 36 start locations placed at 10° angle intervals around their centres, at a distance of 5 cm, as can be seen in Figure 1B. Participants were passively moved by the device towards the start location, without visual feedback of hand position. This movement took 1.5 seconds, independent of movement length. When the participants arrived at the start location with their hand, the target location was displayed visually. There was no strict time constraint per trial, except if the participant took longer than 10 seconds the trial was cancelled and repeated at a later point during the experiment.

The experiment consisted of five blocks, as shown in figure 1(C). The *baseline*, the *vib(vibration)*, and *post(post-vibration)* blocks each taken together consisted of 144 trials in total, representing each combination of start position and respective target positions within each block, resulting in a total of 432 trials per participant. The order of presentation was randomised per participant.

The tendon vibration was applied throughout the vibration blocks, meaning that the vibrators were active without any breaks. They also stayed attached throughout the whole experiment to account for the effect of the physical constraints of the vibrator setup throughout testing.

3.3.2 Data Processing

The experimental data were processed and analysed using MATLAB R2017b (The Mathworks, Inc., 2017). We compared vibration and post blocks to the baseline block. The constant error and variable error of the end-points of the positioning movements per target position were calculated per participant and then across the group. Constant error was taken as a measure of the accuracy of the proprioceptive estimate, while variable error reflects the precision of the proprioceptive estimate. The constant error was defined as the Euclidean distance of estimated position relative to actual target position. We also visually inspected these variables by plotting endpoints with ellipses reflecting the 95% confidence intervals of the data per target position centered around the mean value, while the variable error was computed as the standard error of the constant error term.

3.4 Experiment 2

3.4.1 Paradigm

The second experiment consisted of a reaching task with a single start position ($\varnothing 1.4\text{cm}$, circle) and 8 target positions ($\varnothing 1.0\text{cm}$, red or green circle) oriented at 45° intervals around and at a distance of 12 cm from the start position. The setup is visualised in figure 3. The start location was presented at the beginning of the trial, or as soon as a preceding trial was finished. As soon as the participants reached the start location, the veridical position of their hand was displayed visually ($\varnothing 1.0\text{cm}$, white circle). Simultaneously, in vibration trials the vibrators were turned on and the target was displayed. Initially, the target was red, but after a random interval between 500 and 1500 ms, participants had to reach through the target as soon it turned green, accompanied by an auditory cue. When participants moved outside of the start location, the visual feedback of their hand position disappeared. As soon as they reached the target radius (circle with a radius of 12 cm centred at the start location, not visible) a fireworks animation was displayed at the visual target location as to keep participants motivated. No further feedback about veridical hand location was given until the hand returned to the start location, in order not to give the participant too much information about the accuracy of their estimate of hand position when reaching the target position.

After participants reached through the target, they were passively moved to the start location by the robotic manipulandum. The trials were pseudo-randomised for each participant with each target being repeated 12 times per vibration condition, thus resulting in 3 (vibration conditions) \times 8 (target locations) \times 12 (repetitions) = 288 trials in total per participant. In non-vibration trials, vibration remained off, while in biceps trials only the biceps tendon vibration was activated and in triceps vibration trials only the triceps tendon vibration was activated. Trials where participants moved before the go signal, or their movement was too slow (reaction times of more than 10 seconds after leaving the start location) were treated as error trials and were discarded and repeated later in the experiment. No trials were excluded. Participants did not report any strange feelings induced by the vibration or a dissociation of vision and proprioception.

3.4.2 Model

We implemented the velocity-command model from Sober and Sabes, 2003, which aims to explain how sensory inputs from vision and proprioception are combined to plan and initiate a movement. Proprioceptive and visual information is first used to compute a movement vector based on the estimated arm position at (\hat{x}_{MV}), which gives the reach direction and distance in a Cartesian reference frame. Subsequently, the movement vector needs to be converted into a motor command in joint angular space in order to drive the appropriate tendons. This is computed based on the inverse model of the current position estimate (\hat{x}_{INV}).

$$\hat{x}_{MV} = \alpha_{MV}\hat{x}_{vis} + (1 - \alpha_{MV})\hat{x}_{prop} \quad (1)$$

$$\hat{x}_{INV} = \alpha_{INV}\hat{x}_{vis} + (1 - \alpha_{INV})\hat{x}_{prop} \quad (2)$$

The estimates of hand position at both of these stages are based on a relative weighting of the position estimates given by the two sensory inputs, as described in Equation 1 and 2. Sober and Sabes, 2003 found that the estimate for the movement vector (Eq. 1) relies mostly on vision. This is reasonable, as the movement vector relates to the extrinsic space of the body. It also appears that in (Eq. 2), \hat{x}_{prop} receives a larger weight.

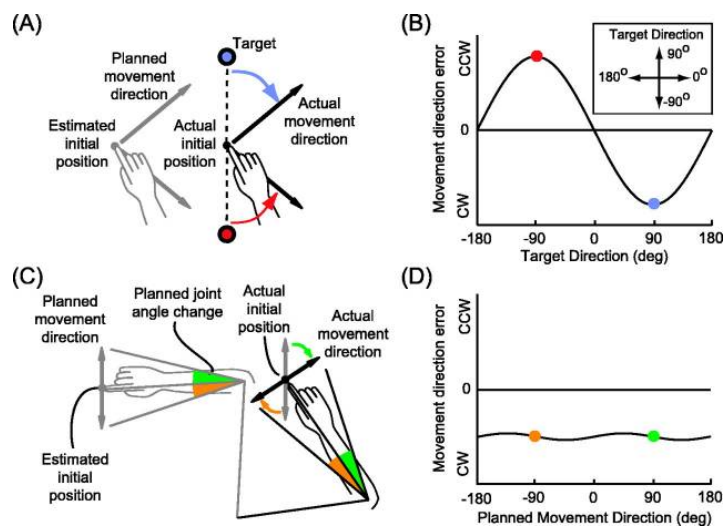


Figure 2: (from Sober and Sabes, 2003). (A) and (B) visually explain the effect of a misestimation of hand position on the two stages of motor planning for the reach movement. In the first stage of planning (A), the wrongly perceived initial position leads to an inappropriately planned movement vector. This results in a counterclockwise error for targets with a negative angle, and in clockwise errors for targets with positive angles relative to initial position, as can be seen in (B). In (C), the misestimating of the arm's joint angles consequently leads to a falsely planned change in joint angle, leading to clockwise errors across targets, as can be seen in (D). Adding the effects from the misestimation of position together, the resulting actual movement direction can be predicted, which is hinted at in (c).

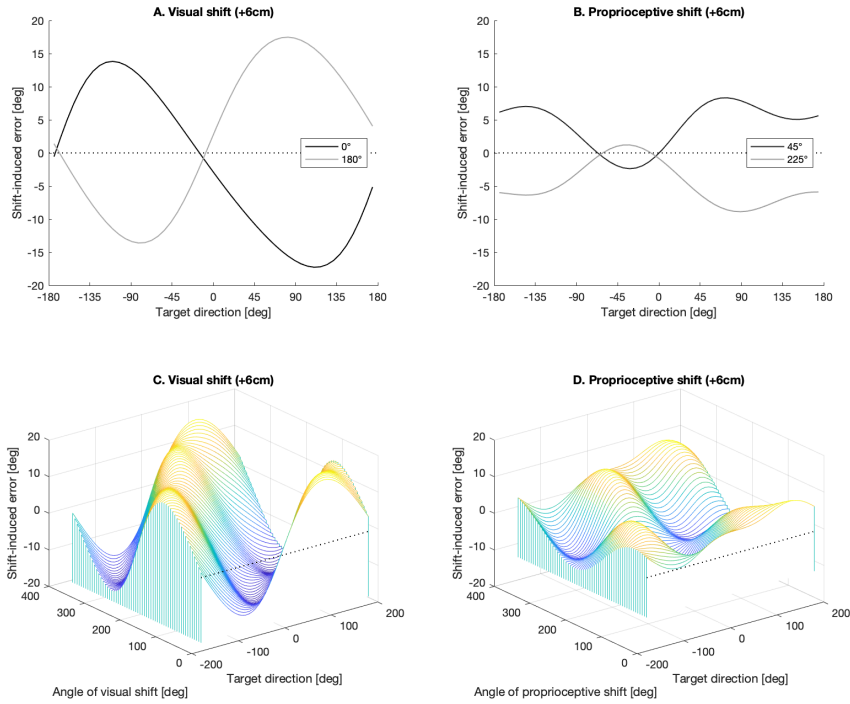


Figure 4: Predictions of the velocity-command model: Visual and proprioceptive shift-induced errors in initial target direction, with $\alpha_{MV} = 0.8$, $\alpha_{INV} = 0.3$, 6cm. (A). Visual shift-induced error pattern across possible target directions for 0° and 180° . (B). As (A), but for the proprioceptive shift, 45° and 225° . These are approximate possible shifts of the proprioceptive shifts induced by the tendon vibration in Experiment 2. (C) and (D). Errors in degrees induced by a shift in visual (C) and proprioceptive (D) estimates respectively.

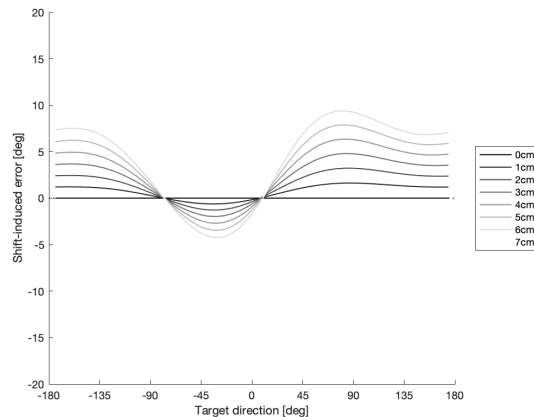


Figure 5: Proprioceptive shift-induced error with different magnitudes between 0 and 7 cm, (45°), with $\alpha_{MV} = 0.8$, $\alpha_{INV} = 0.3$.

3.4.3 Data Processing

The experimental data were processed and analysed using MATLAB R2017b (The Mathworks, Inc., 2017). The onset of the movement was defined as the first point where the tangential velocity of the reaching movement passed 40% of the maximum tangential velocity of that trial. Errors were computed as the offset in degrees of the initial reach direction from the direction of the vector between start location and target position. We performed a repeated measures ANOVA of vibration condition and target direction on individual means and medians of the initial reaching error in degrees, with Greenhouse-Geisser correction applied where the assumption of sphericity was violated. Statistical data analysis was performed in RStudio 1.2.5033 (RStudio Team, 2019) and using the R packages R.matlab (Bengtsson, 2018), tidyverse (Wickham et al., 2019), ggpubr (Kassambara, 2019a), & rstatix (Kassambara, 2019b).

4 Results

4.1 Experiment 1

In figure 6, endpoints with ellipses reflecting the 95% confidence intervals of the data per target position are plotted for one example participant. The error ellipses give a visual guidance for interpreting the precision of the proprioceptive estimate of hand position. Bigger ellipses indicate higher variability in the estimate of position, and therefore decreased precision of the estimate. Plotting vibration trials against baseline and post-vibration trials does not give an indication of less precision during vibration trials as compared to trials without vibration.

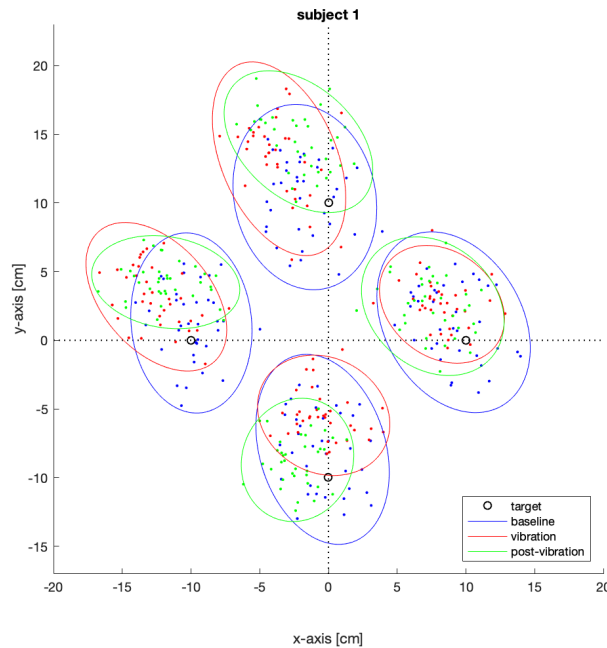


Figure 6: Actual versus estimated target positions for participant 1 for different target locations. Dots represent all individual trials for this participant. Ellipses reflect the 95% confidence interval per target location and vibration condition, centred around each mean value. The axes are displayed to highlight the skew of the data.

4.1.1 Constant and variable error of estimated final position

In order to estimate the effect of the vibration conditions on the accuracy and precision of the proprioceptive estimate, we examined the constant error (mean of Euclidean distance of estimated target position compared to the actual target position) and the variable error (standard error of the constant error). As can be seen in figure 7, the errors in estimating the target position are very variable across participants, both in accuracy and precision. Both 6 and 7 show that there are no consistent pattern of increased constant or variable error across participants. A repeated measures ANOVA of vibration condition and target location on both constant ($F(2, 10) = 0.5, p > .05$)

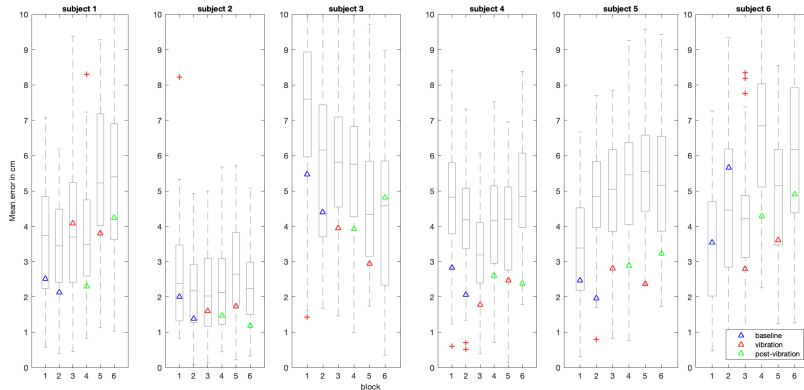


Figure 7: Boxplots: Mean constant error per participant, per block (distance in centimetres between estimated and actual target position). (Blocks 1 and 2: baseline, blocks 3 and 5: vibration, blocks 4 and 6: post-vibration), triangles: mean standard error per participant per block.

and variable error ($F(2, 10) = 0.4, p > .05$) confirmed that there was no main effect of vibration. There was also neither a main effect of target location on constant error ($F(3, 15) = 2.8, p > .05$), nor on variable error ($F(3, 15) = 2.9, p > .05$) and an interaction effect of target location and vibration condition on both constant ($F(6, 30) = 4.3, p < .01$) and variable error ($F(6, 30) = 0.5, p > .05$). Assuming that precision of the proprioceptive estimate should be deteriorated in agonist-antagonist vibration, and also after agonist-antagonist vibration has ceased, we should have observed a main effect of vibration especially on the variable error. We did not predict an effect of agonist-antagonist vibration on constant error, which is reflected in the data and in the figures of experiment 1. The error plots for all participants can be found in the supplementary materials (10).

4.2 Experiment 2

The aim of the second experiment was to examine the effect of manipulating the accuracy of the proprioceptive estimate on the formation of a movement plan in a hand reaching task. To this end, participants' proprioceptive estimate of hand position was shifted by applying vibration to their biceps and triceps tendons. Based on the induced patterns of angular error in the initial movement phase, we examined whether the induced errors support the role of proprioception in the movement planning process, which we predicted in figure 4. The strongest effect of the shift of the proprioceptive estimate should be in the axis of movement of the biceps and triceps muscles. Furthermore, as can be taken from figure 2 (D), the effect of a shift in the inverse model stage is one-directional. This is reflected in figure 4 (B), where compared to 4 (A) in the same figure the shift-induced error is much more unilateral.

In order to examine the effect of inducing an illusory proprioceptive shift using tendon vibration, we computed the per-target mean, median and standard error at the point of movement onset for each participant. The angular error was defined as the deviation in degrees of initial reach direction (reach direction at 40% of maximum speed) from the 'optimal' movement vector described by the start and target location coordinates.

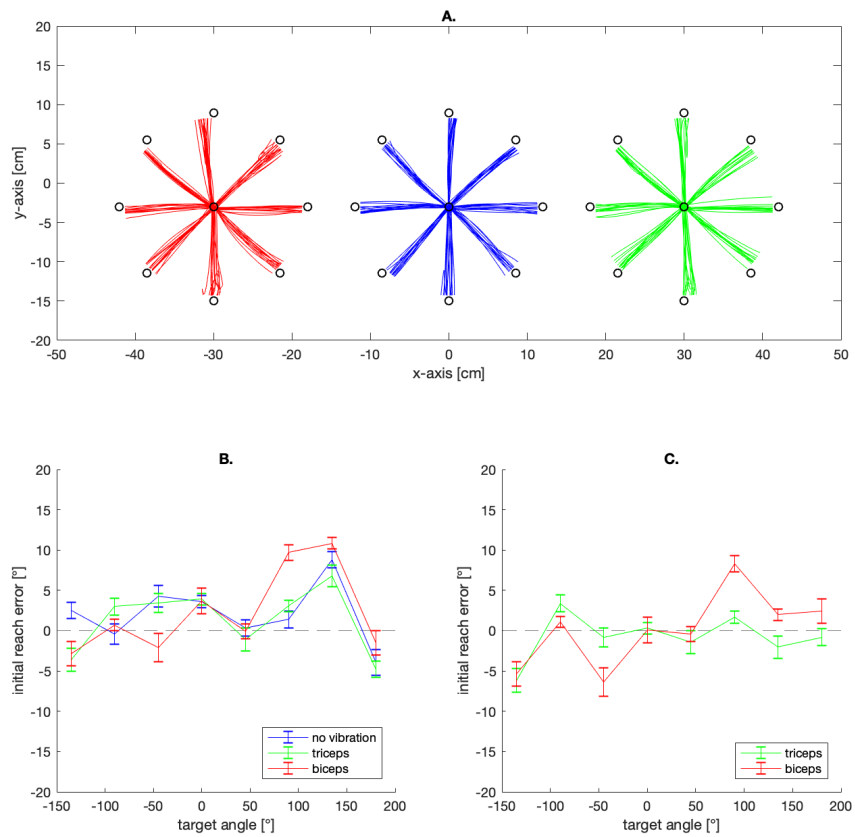


Figure 8: Exemplary data from one participant for experiment 2. (A). Trajectories of movements made from leaving the start position until the target radius is reached. Biceps vibration trials are shifted by 30cm to the left and triceps vibration trials are shifted by 30cm to the right for visual clarity. (B). Mean and standard error of initial direction of the participant per target direction and per vibration condition. (C). As in (B), with mean error of the baseline vibration subtracted per trial.

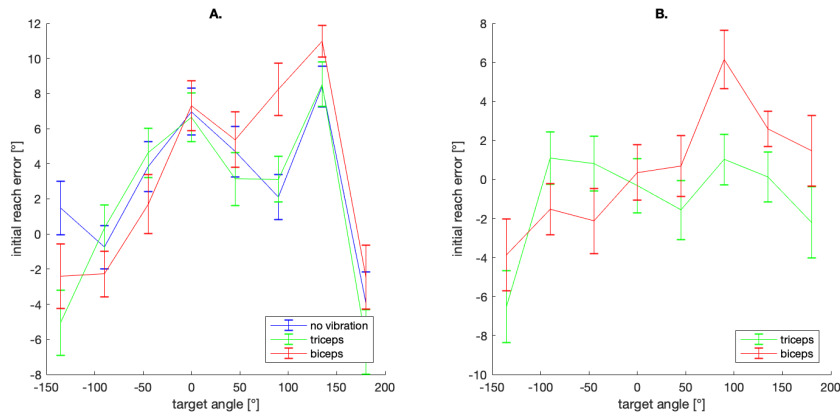


Figure 9: (A). Group mean and standard error of initial direction error in degrees across targets, different lines represent different vibration conditions. (B). As (A), with mean error of the baseline vibration subtracted per trial.

4.2.1 Mean error of initial reach direction

We examined mean and standard error of initial reach direction across targets and conditions per participant. Figure 8 shows one example participant. In 8 (A), trajectories from the different vibration conditions are displayed for different target locations. Slight offsets can be observed at the end of the trajectories. However, we are interested in the initial phase of the movement, which results directly from the phase of initial movement planning. Generally, it becomes obvious from the trajectories that the induced shifts do not create massive offsets, but rather small angular offsets towards the beginning of the movement. The plots in 8 (B) and (C) show the initial reach error for this participant across target locations and vibration conditions. In (C) the mean per target and condition is subtracted from individual trial scores. It can be observed that, indeed, the resulting error is not very large across target locations. Nevertheless, there is a peak towards the positive spectrum of the target angles, which can also be observed in the predicted model data (4 (B)). However, the peak towards the more negative spectrum of the target angles cannot be observed in the collected data from this participant (for data from all participants, see supplementary figure 11&12).

The observed patterns and direction of error were rather variable across participants, however some trend of error pattern across participants becomes clearer from the grouped error data (figure 9). As expected, at the more extreme points opposite patterns of biceps versus triceps vibration can be observed, albeit not in all participants (supplementary figure 11). Especially biceps tendon vibration shows a clear peak around 45-180° (9(A and B)). The patterns clearly indicate an induced error by the shift in proprioceptive estimate across most targets, however it remains unclear whether this pattern can be predicted by the model (4(B and D))

To find out whether the observed effects of vibration-induced proprioceptive shift were truly different between conditions, we performed a repeated measures ANOVA of target angle and vibration condition on initial reach error. We were mainly interested in the effect of vibration condition, however target angle is also a very important and possibly mediating factor due to the circular setup of the experiment. The RM-ANOVA did show the effect of both target location ($F(2, 38) = 26.3, p < .001$) and vibration condition ($F(3.47, 65.86) = 29.6, p < .001$) on mean angular error, which we could already observe in the graphics. Furthermore, a significant interaction effect between target

location and vibration condition was found ($F(14, 266) = 19.4, p < .001$), suggesting that across different target locations, vibration differently affects angular error. Due to the setup being circular, vibrating biceps versus triceps tendons will lead to opposing effects, as the biceps and triceps work in the same axis of movement, but contralaterally. Post-hoc testing (one-way ANOVA with Bonferroni correction) further revealed the main effect of vibration condition to be significant in all target locations, except for the target located at 0° . This would indicate that at 0° , the executed reach direction caused by the biceps and triceps vibration-induced shift is parallel to the desired reach direction (fig. 9). In order to account for skewed distributions we also performed the analysis on median values of initial reach error. This did not allow for different conclusions than when mean values were used.

Because there is no direct measurement of the magnitude and direction of the proprioceptive shift, fitting the data to the model predictions is currently not possible, however the observed patterns do support the significant contributions of proprioception in movement planning.

5 Discussion

The main goal of this research project was to study the role of proprioception in multi-sensory integration for reach planning, and specifically the role of proprioception relative to vision in the sensory integration for the planning of upper-limb movements. The idea was to study the effect of manipulating proprioception in order to gain insights into how movement planning is affected by such manipulation, and thus learn about the weight of proprioception in this process, relative to vision. Vision was not manipulated in the present experiments, as the effect of vision in this type of paradigm has been previously studied (Sober and Sabes, 2003, 2005; Taig et al., 2012).

5.1 Experiment 1

Based on previous literature, it appears that precision about proprioceptive input is decreased during (Bock et al., 2007; Pipereit et al., 2006) or directly after applying agonist-antagonist tendon vibration (Gonzales and Goble, 2014). This was the basis on which we decided to study the effect of agonist-antagonist tendon vibration in an active positioning task to establish an estimate of proprioceptive precision, measuring performance before, during and after vibration. However, the results indicate that there is no consistent difference in precision between vibration and no vibration. We therefore conclude that applying agonist-antagonist tendon vibration is not an effective manner of manipulating proprioceptive precision from the upper limbs. This means it was also not a useful technique to manipulate proprioception for the study of sensory integration.

A few caveats can be raised regarding the design of the first experiment. It is possible that the lack of vision already induced a great amount of variability, as the brain seems to generally rely more heavily on vision during the sensory integration process for reaching movements, which is reflected in the higher weighting of vision in the sensory integration model described by Sober and Sabes, 2003. Relying mostly on proprioception could be insufficient to compute a good estimate, especially in earlier stages of the integration process, such as the computation of the movement vector, where the brain seems to rely even more on vision. Furthermore, the amount of participants and repetitions is potentially too small to make confident statements about the lack of effect. However, based on these results, we would predict to find only a small effect of increasing variability that the current dataset might have not been able to reveal.

These findings do not necessarily contradict the findings of Gonzales and Goble, 2014 that agonist-antagonist upper-arm tendon vibration appears to degrade the proprioceptive estimate post-vibration. Where they used a passive positioning task with one degree of freedom (elbow joint), our positioning task was active and had two degrees of freedom (at the shoulder and the elbow joint). It is possible that sensory information is processed differently in these different task environments. As the literature has remained inconclusive so far, with also some research suggesting no effect of agonist-antagonist in degrading the proprioceptive estimate (Bellan et al., 2016).

5.2 Experiment 2

In the second experiment, the aim was to study how a bias in accuracy of proprioception would affect the integration of vision and proprioception for reach planning. As we did not find an increased effect of agonist-antagonist vibration on precision of proprioceptive input, we decided to instead manipulate proprioception by inducing a perceived shift using tendon vibration. The aim was to induce a illusory (but not actual) shift in the veridical hand position, as described by Lackner, 1988 and Roll and Vedel, 1982,

instead of a shift in the visual estimate of hand position, as studied by Sober and Sabes, 2003.

The results of this experiment indicate that there is indeed an effect of the perceived proprioceptive shift in hand position on the planning of reaching movements. The vibration of the distal biceps tendon consistently (except for the target position at 0°) leads to a different error in initial reach direction than the vibration of the distal triceps tendon. When comparing each vibration condition to the no-vibration condition, it seems like the biceps tendon vibration more consistently deviates from this baseline measure than triceps tendon vibration. This could be due to technical difficulties in properly stimulating the triceps tendon which is more difficult to localise than the biceps tendon, or due to physiological differences between the tendons and the processing of their information.

The measured effect of target location can be explained by the physiological context of the experimental setup. Biceps and triceps are antagonistic muscles, meaning if one of the muscles is flexed, the other muscle is extended. This means that stimulating one of the two tendons will have an approximately opposite effect as compared to stimulating its antagonist counterpart. Furthermore, the targets are oriented circularly. Therefore, stimulating one tendon versus stimulating its agonist should give opposite shifts of the proprioceptive estimate at the same target location, which can be observed in the predictions made by the model (see fig. 4). There, opposite shifts (with a 180° difference) reveal an approximately opposite pattern of initial reach direction. The opposite shifts are not exactly opposite in the model simulation due to the physiological constraints of the arm relative to the task setup, which can also differ across participants despite measures taken to ensure uniformity, such as adjusting the height of the seat and securing participants with a seat belt.

Furthermore, we found an interaction effect between target location and vibration. This is plausible, as the targets are oriented in a circular manner, and seeing that the effects of the vibration should be directionally oriented, the effect of the biceps and triceps vibration should have opposite signs at opposing orientations in the circular task setup, as biceps and triceps activity oppose each other. This is also reflected by the patterns of the initial reach errors induced by the biceps and triceps vibration respectively across target angles, as can be seen in fig. 9.

Comparing the model predictions (fig. 4) to the measured data (fig. 9), there seems to be some overlap between the peak at $45\text{-}135^\circ$ in mean initial movement error for biceps vibration, which can also be observed in the model prediction, if an approximate perceived shift of 45° in proprioception is assumed. In order to make more concrete statements about how well the data can be explained, it would be necessary to fit the model to the dataset, but more parameters would have to be known, which are currently not available, such as angle and extent of the perceived shift. This would have to be measured in a setup where the perceived proprioceptive shift of the participant is recorded, which is currently difficult to measure objectively and continuously. While it is possible to record the proprioceptive position of the hand, this extends experimental time substantially and does not guarantee accurate estimates of proprioception. In future experiments, recording proprioceptive measures of perceived shift before, during, and after the experiment could help, however, to produce an estimate of proprioception throughout the experiment. This would help with the complete implementation of the computational model, which is currently lacking a data-based estimate of the proprioceptive shift.

It should be noted, furthermore, that it is assumed in the model and based on the data from Sober and Sabes, 2003 that the introduced proprioceptive shift will generally cause a smaller initial angular error (fig. 4), as throughout the integration process, visual input is weighted more strongly overall. This also explains why the errors observed here

are of a smaller magnitude than the errors induced by visual shifts in their study, which went beyond initial angular errors of 15° , while our values reach a maximum induced error of approximately 10° .

Moreover, stimulation of the tendons might not be perfectly aligned with the assumptions we make in the model implementation about the induced shifts. As we do not have an experimental estimate of the induced misplacement of the proprioceptive estimate, we used an estimate of a shift of 6cm, as the one induced in the study by Sober and Sabes, 2003. However, this guess is not data-based and might be under-, or more probably overestimating the induced proprioceptive shift. We also guess the direction of the effect to be along the axis of movement influenced by biceps and triceps, but this is also merely an estimate without underlying experimental measurements. For this reason, it would be interesting to obtain an estimate of the proprioceptive shift in future experiments. It is important to also note that vibration on one side of the arm is still likely to somewhat affect the tendon on the opposite side (albeit minimally) and effects of continued vibration in different directions could counteract each other.

Overall, the data from the second experiment support the important role of proprioception in sensory integration for motor planning. While the effect of unilateral tendon vibration on the accuracy of the proprioceptive estimate is not as clear in triceps vibration as it is in biceps vibration, it is undeniable that generally there is an influence of manipulating proprioception on the planning of a hand movement in this paradigm. This extends the findings of Sober and Sabes, 2003 of the importance and relative weighting of visual input. Because it was not possible to fit the model to the dataset, we cannot make conclusions about the weighting of proprioception when these shifts are induced through vibration.

Investigating the actual weighting of proprioception for motor planning could give more insights into how exactly coordinate transformations of signals are performed and which steps are taken in time. This could also elucidate the role of previous expectations on how these weights are formed? and how flexible the weighting is to adjust for signal manipulations and uncertainty (low precision). Furthermore, investigating the interaction of simultaneous proprioceptive and visual shifts, and inducing a dissociation between them could help understand how exactly the system determines over time the relevance and reliability of different sensory inputs in reach control.

References

- Bellan, V., Wallwork, S. B., Stanton, T. R., Reverberi, C., Gallace, A., & Moseley, G. L. (2016). No Telescoping Effect with Dual Tendon Vibration. *Current Biology*, *11*(6), e0157351.
- Bengtsson, H. (2018). *R.matlab: Read and write MAT files and call MATLAB from within R* [R package version 3.6.2]. R package version 3.6.2. <https://CRAN.R-project.org/package=R.matlab>
- Bock, O., Pipereit, K., & Mierau, A. (2007). A method to reversibly degrade proprioceptive feedback in research on human motor control. *Journal of Neuroscience Methods*, *160*(2), 246–250.
- Fuentes, C. T., Gomi, H., & Haggard, P. (2012). Temporal features of human tendon vibration illusions. *European Journal of Neuroscience*, *36*, 3709–3717.
- Gilhodes, J. C., Roll, J. P., & Tardy-Gervet, M. F. (1986). Perceptual and motor effects of agonist-antagonist muscle vibration in man. *Experimental Brain Research*, *61*(2), 395–402.
- Gonzales, T. I., & Goble, D. J. (2014). Short-term adaptation of joint position sense occurs during and after sustained vibration of antagonistic muscle pairs. *Frontiers in Human Neuroscience*, *8*, Article ID 896.
- Goodwin, G. M., McCloskey, D. I., & Matthews, P. B. C. (1972). Proprioceptive illusions induced by muscle vibration: Contribution by muscle spindles to perception? *Science*, *175*(4028), 1382–1384.
- Howard, I. S., Ingram, J. N., & Wolpert, D. M. (2009). A modular planar robotic manipulandum with end-point torque control. *Journal of Neuroscience Methods*, *181*(2), 199–211.
- Kassambara, A. (2019a). *ggpubr: 'ggplot2' based publication ready plots* [R package version 0.2.4]. R package version 0.2.4. <https://CRAN.R-project.org/package=ggpubr>
- Kassambara, A. (2019b). *rstatix: Pipe-friendly framework for basic statistical tests* [R package version 0.3.1]. R package version 0.3.1. <https://CRAN.R-project.org/package=rstatix>
- Lackner, J. R. (1988). Some proprioceptive influences on the perceptual representation of body shape and orientation. *Brain*, *111*, 281–297.
- Pipereit, K., Bock, O., & Vercher, J.-L. (2006). The contribution of proprioceptive feedback to sensorimotor adaptation. *Experimental Brain Research*, *174*(45), 213–222.
- Proske, U. (2015). The role of muscle proprioceptors in human limb position sense: a hypothesis. *Journal of Anatomy*, *227*, 178–183.
- Proske, U., & Gandevia, S. C. (2012). The proprioceptive senses: Their roles in signaling body shape, body position and movement, and muscle force. *Physiological Reviews*, *92*(4), 1651–1697.
- Roll, J. P., & Vedel, J. P. (1982). Kinaesthetic role of muscle afferents in man, studied by tendon vibration and microneurography. *Experimental Brain Research*, *47*, 177–190.
- RStudio Team. (2019). *RStudio: Integrated development environment for R*. RStudio, Inc. Boston, MA. <http://www.rstudio.com/>
- Sober, S. J., & Sabes, P. N. (2003). Multisensory integration during motor planning. *Journal of Neuroscience*, *23*(18), 6982–6992.
- Sober, S. J., & Sabes, P. N. (2005). Flexible strategies for sensory integration during motor planning. *Nature Neuroscience*, *8*, 490–497.

- Taig, E., Küper, M., Theysohn, N., Timmann, D., & Donchin, O. (2012). Deficient Use of Visual Information in Estimating Hand Position in Cerebellar Patients. *Journal of Neuroscience*, *32*(46), 16274–16284.
- The Mathworks, Inc. (2017). *MATLAB R2017b*. Natick, Massachusetts.
- van Beers, R. J., Sittig, A. C., & Denier van der Gon, J. J. (1999). Integration of Proprioceptive and Visual Position-Information: An Experimentally Supported Model. *Journal of Neurophysiology*, *11*(6), e0157351.
- Wickham, H., Averick, M., Bryan, J., Chang, W., McGowan, L. D., François, R., Grolemund, G., Hayes, A., Henry, L., Hester, J., Kuhn, M., Pedersen, T. L., Miller, E., Bache, S. M., Müller, K., Ooms, J., Robinson, D., Seidel, D. P., Spinu, V., . . . Yutani, H. (2019). Welcome to the tidyverse. *Journal of Open Source Software*, *4*(43), 1686.

Supplementary Materials

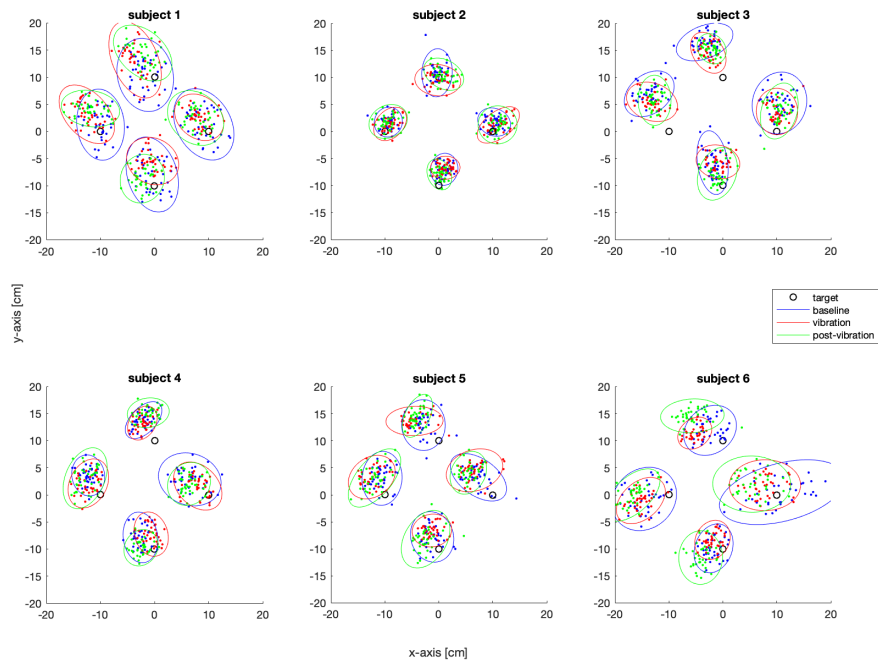


Figure 10: Actual versus estimated target positions for all participants for different targetlocations. Dots represent all individual trials for this participant. Error ellipses reflect the 95% confidence interval per target location and vibration condition, centred around each mean value.

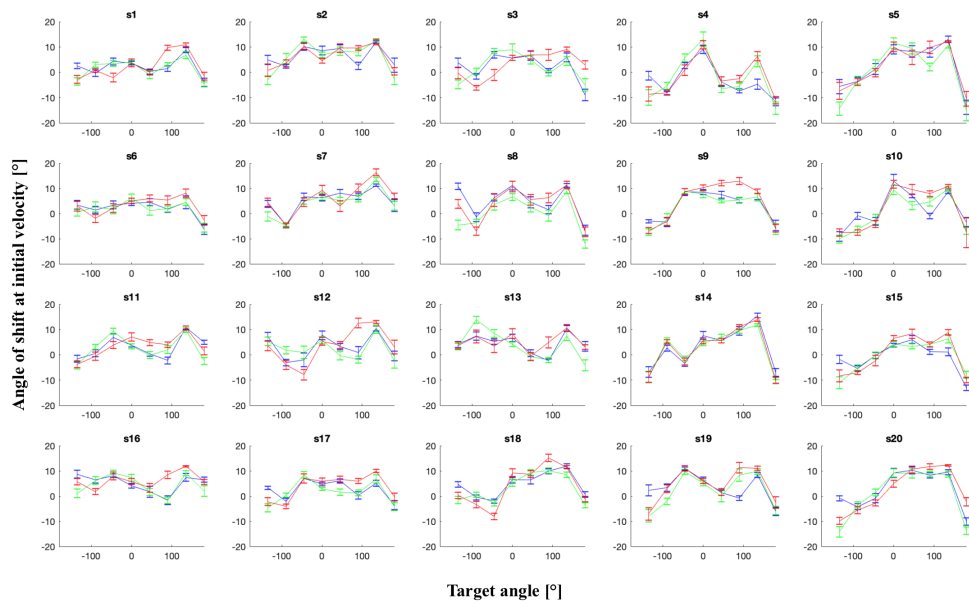


Figure 11: Mean error per target and standard error of initial reach direction per participant.

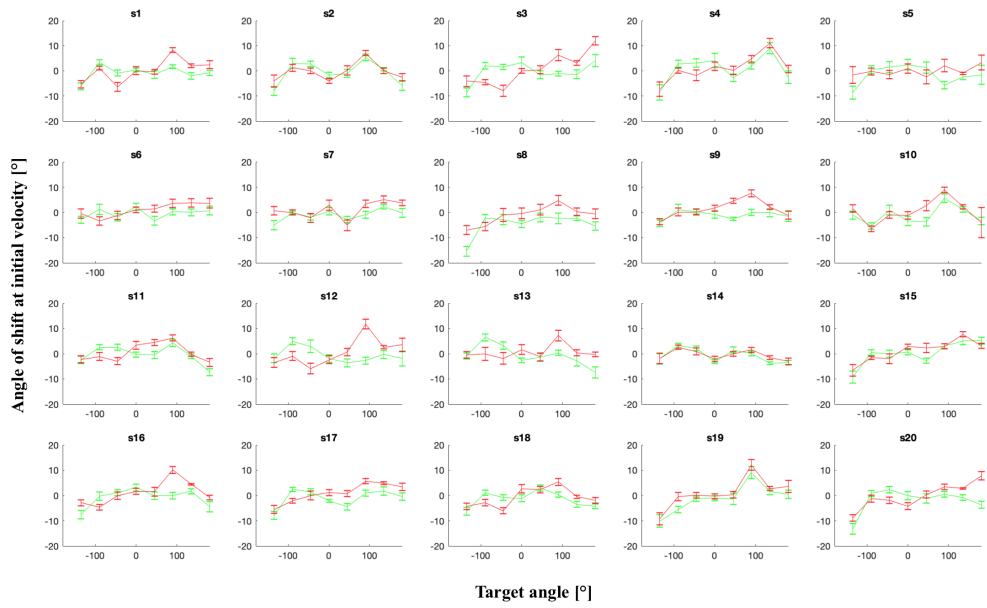


Figure 12: Mean error per target and standard error of initial reach direction per participant (subtracted).