J Neurophysiol 119: 1809–1817, 2018.
First published February 14, 2018; doi:10.1152/jn.00738.2017.

RESEARCH ARTICLE | *Control of Movement*

Reference frames in the decisions of hand choice

Romy S. Bakker, Luc P. J. Selen, and W. Pieter Medendorp
Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, The Netherlands

Submitted 11 October 2017; accepted in final form 5 February 2018

Bakker RS, Selen LP, Medendorp WP. Reference frames in the decisions of hand choice. *J Neurophysiol* 119: 1809–1817, 2018. First published February 14, 2018; doi:10.1152/jn.00738.2017.—For the brain to decide on a reaching movement, it needs to select which hand to use. A number of body-centered factors affect this decision, such as the anticipated movement costs of each arm, recent choice success, handedness, and task demands. While the position of each hand relative to the target is also known to be an important spatial factor, it is unclear which reference frames coordinate the spatial aspects in the decisions of hand choice. Here we tested the role of gaze- and head-centered reference frames in a hand selection task. With their head and gaze oriented in different directions, we measured hand choice of 19 right-handed subjects instructed to make unimanual reaching movements to targets at various directions relative to their body. Using an adaptive procedure, we determined the target angle that led to equiprobable right/left hand choices. When gaze remained fixed relative to the body this balanced target angle shifted systematically with head orientation, and when head orientation remained fixed this choice measure shifted with gaze. These results suggest that a mixture of head- and gaze-centered reference frames is involved in the spatially guided decisions of hand choice, perhaps to flexibly bind this process to the mechanisms of target selection.

NEW & NOTEWORTHY Decisions of target and hand choice are fundamental aspects of human reaching movements. While the reference frames involved in target choice have been identified, it is unclear which reference frames are involved in hand selection. We tested the role of gaze- and head-centered reference frames in a hand selection task. Findings emphasize the role of both spatial reference frames in the decisions of hand choice, in addition to known body-centered computations such anticipated movement costs and handedness.

decisions; effector selection; psychophysics; reaching; reference frames

INTRODUCTION

A long-standing problem in neuroscience is how we select appropriate responses in the continuously changing world around us. This problem is typically separated into two components: the "what-to-do" and the "how-to-act" problems (Goodale and Milner 1992; Scott 2016; Wong et al. 2015). The what-to-do problem is associated with evaluating the number of options or goals and the constraints imposed by bottom-up factors, such as sensory information and saliency (Bisley and Goldberg 2010), as well as top-down influences, such as internal desires or expectations (Andersen and Cui 2009; Haggard 2008). The how-to-act problem relates to the specification of action parameters, such as the selection of effectors (Beurze et al. 2007; Dancause and Schieber 2010; Leoné et al. 2014; Oliveira et al. 2010; Schweighofer et al. 2015), the movement trajectory, and the muscular contractions that generate this trajectory (Ting et al. 2012; Todorov 2004). The specification of action parameters is often supposed to be based on the costs of the movements (Soechting and Flanders 1992), including the costs associated with contraction of the muscles that actually generate the action (Cos et al. 2011; Schweighofer et al. 2015). In this article, we focus on the how-to-act problem in the context of deciding which hand to use to reach a goal.

In a dynamic environment with varying configurations of the actor and targets, the relationship between the choice of action and its outcome is not fixed. To describe this relationship, the notion of a spatial reference frame is indispensable (Crawford et al. 2004, 2011). For example, Scherberger and colleagues (2003) tested the reference frames involved in target selection for reaching and saccadic eye movements. Monkeys had to saccade or reach to one of two stimuli presented in close succession to the left and right of a fixation position. The authors probed target preferences by manipulating the relative timing of the two stimuli: e.g., rightward reaching movements are favored when the rightward stimulus is presented earlier. By varying gaze, head, and trunk position, they found that these target preferences are embedded in a mixture of gaze- and head-centered reference frames, and not a body-centered frame, for both saccade and reach targets (Scherberger et al. 2003; see also Horstmann and Hoffmann 2005 for analogous findings in humans).

If target and hand selection were part of an integrated computation for movement planning (Beurze et al. 2007; Cisek 2007; McGuire and Sabes 2009) one could also predict a role of gaze- and head-centered reference frames in hand selection, but this has not been tested. Recent work on hand selection has only considered body-fixed, muscle-based factors, such as handedness (Bryden et al. 2000; Gabbard et al. 2003) and biomechanical movement cost, which depends on the distance and direction of the target relative to the hand (Dancause and Schieber 2010; Oliveira et al. 2010; Schweighofer et al. 2015). In the present study, we keep these biomechanical factors constant and test the role of gaze- and head-centered reference frames in hand selection for reaching movements.

We measured hand choices of human subjects instructed to perform unimanual reaching movements toward targets pre-

Address for reprint requests and other correspondence: W. P. Medendorp, Donders Inst. for Brain, Cognition and Behaviour, Radboud Univ. Nijmegen, Montessorilaan 3, 6525 HR Nijmegen, The Netherlands (e-mail: p.medendorp@donders.ru.nl).

sented at various directions relative to their body midline. Using an adaptive procedure, we determined the target direction for which subjects selected both hands equally often. This balanced target angle (BTA) was taken as a quantitative measure of hand preference. By systematically varying gaze direction and head orientation, we determined the frame of reference used for this decision of hand choice.

METHODS

Participants. Nineteen subjects (11 women, 8 men; aged 19–40 yr), with normal or corrected-to-normal vision and no known motor deficits participated in the experiment. All subjects gave their written informed consent before the experiment. The Edinburg Handedness Inventory (Oldfield 1971) showed that all subjects were right-handed (mean laterality quotient: 89, SD: 15). The study was approved by the ethics committee of the Faculty of Social Sciences of Radboud University Nijmegen. One subject was excluded because of failure to follow task instructions.

Setup. Subjects were seated, viewing a touch screen positioned in the horizontal plane at the level of their thoracic diaphragm. Their trunk was restrained by a five-point seat belt, and their head was kept in a fixed orientation around the yaw axis by an ear-fixed mold. A horizontal bar with five lights (red LEDs, luminance 1 cd/m^2) was positioned 60 cm away from the subject, below eye level (Fig. 1*A*), and at 13 cm above the far edge of the touchscreen. The central LED was aligned to the subject's midsagittal plane. The other LEDs had directions of −18°, −9°, +9°, and +18° relative to the cyclopean eye when the head is facing straight ahead (Fig. 1*B*) and served to direct gaze in the desired direction. In addition, these LEDs served as landmarks to orient the head. Subjects wore a head-mounted laser that projected a faint dot that could be aligned with one of these LEDS to guide the head into the desired orientation. Once the head had adopted the correct orientation we fixed it in this orientation with the ear-fixed mold. It should be noted that, because changing head orientation after every single trial would practically be infeasible, we maintained the same head orientation for a block of trials. The targets for the reaching movement were presented on the touch screen in the lower visual field. Subjects' hands never obscured the fixation LEDs. Because of the LEDs and the back light of the touch screen, the experimental room was dimly lit.

The resolution of the 27-in. touch screen (ProLite Iiyama; Iiyama, Tokyo, Japan) was full HD (1,920 × 1,080 pixels). The two starting positions (green circles, diameter 3.5 cm) for the left and right index fingers were presented on the screen at a distance of ~30 cm from the subject's sternum and 9 cm on either side of the body midline. Reach targets were presented as yellow circles of 3.5-cm diameter on an imaginary semicircle with a radius of 25 cm and its midpoint between the starting positions. Target directions ranged from −60° to 60°, with 0° representing the forward direction from this midpoint (Fig. 1*A*). The onset of the target was determined with a photo diode and used for off-line calculation of reach reaction times.

Binocular eye position was recorded at 500 Hz with an eye tracker (EyeLink 1000; SR Research). Before the experiment began, the eye tracker was calibrated in the horizontal dimension involving a three-point calibration procedure with the LEDs at −9°, 0°, and 9°. Since the body was stationary during the experiment, head-on-body orientation equals head-in-space orientation and is referred to as head orientation for short. The orientation of the eyes within the head, as measured by the tracker, in combination with the orientation of the head relative to the body, defined the orientation of the eyes on body/space [i.e., gaze (G) = eye-in-head (E) + head-on-body (H)]. Rightward orientations were taken as positive. The experiment was controlled with custom-written software in Python.

Experimental paradigm. The experiment was designed to test the effect of gaze direction and head orientation on the decisions of hand choice in reaching to visual targets that were presented at various directions (but at the same distance) relative to the midpoint of the hands' starting positions. Before a block of trials, the subject's head was oriented in one of the five possible directions (H; Fig. 1*B*). At the beginning of a trial, gaze was directed to an LED on the horizontal bar above the touch screen. Subsequently, subjects had to place the tips of their index fingers on the respective starting positions, which were green circles that turned to yellow once achieved. Next, after a delay of 1 s, while the subject's fingers were still on their starting locations, the reach target was presented, which subjects had to reach as fast and accurately as possible with either their left or right hand. The target disappeared from the screen as soon as it was touched, which instructed the subject to bring the hand back to the starting position, and the next trial started. If the first reach did not end on the target, subjects had to correct their movement until the target was touched.

Target directions were determined according to an adaptive psi procedure (Kontsevich and Tyler 1999). On the basis of the chosen hand in the current trial, the adaptive Psi procedure computes the direction of the target to be presented in the next trial, based on maximizing the expected information gain, i.e., based on entropy. Although this adaptive procedure results in a variable number of trials probed for a particular target direction, it quickly converges to the target angle that balances left and right hand responses. We refer to the angle for which left and right hand responses are equally probable as the balanced target angle. The procedure also provides a good estimate of the transition range from left to right hand responses (i.e., the slope of the psychometric curve).

In 10% of the trials, two targets were presented simultaneously, forcing subjects to reach with both hands. These catch trials were introduced to deter subjects from making the hand choice before target onset and were not part of the adaptive psychometric procedure. In another 10% of the trials, targets were presented at the peripheral end of the target range (>40° relative to the head) to ensure that subjects kept paying attention to the task. The hand choices in these trials were included in the computation of the next target direction.

Because of the constraints of the oculomotor range, we did not test trials in which eye-in-head orientation (E = G − H) was beyond ±18°, which led to a balanced, but incomplete, 5 × 5 block design

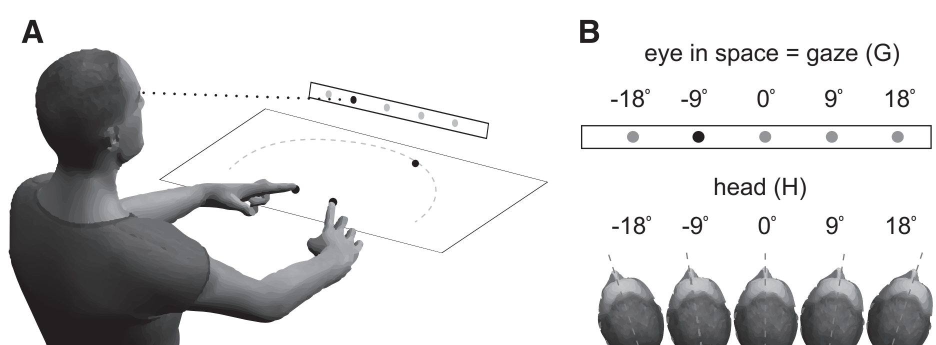

Fig. 1. Experimental setup. *A*: with gaze (dotted line) and head in specific orientations, subjects had to make a unimanual reach from a start position (1 for each hand; circles indicate where the index fingers are placed) to a target in front of them (potential targets appear on an imaginary circle, illustrated by dashed gray line). *B*: gaze directions (*top*) were enforced by a fixation LED and varied from −18° to 18° in steps of 9°. The head (*bottom*) was restrained with an ear-fixed mold and adopted an orientation between −18° and 18° (in 9° steps) relative to the body/space.

with a total of 19 unique combinations of gaze direction and head orientation (see Fig. 1*B*). The five different head orientations were tested in separate blocks, with two orientations tested on one day and three on the other day. Blocks were counterbalanced across subjects, with the exception that the 0° head orientation was always tested on the first day (either as the first or second block of trials). Furthermore, the −18° and +18° head orientations were always examined on the second day, which involved fewer trials than the other conditions because of the constraint on the eye-in-head orientation. For a particular head orientation, there were three to five possible gaze directions (Fig. 1*B*). Gaze directions were selected pseudorandomly. Each condition involved a separate psi procedure for updating target directions based on the associated hand choices.

Data analysis. Off-line data analyses were performed in MATLAB 2015b (MathWorks). To check whether subjects maintained gaze fixation we analyzed the eye position signal derived from the EyeLink data. The downward gaze to the LEDs combined with viewing the screen in the horizontal plane severely complicated the eye tracking. To this end, we required that eye position was recorded in at least two-thirds of the fixation epochs, i.e., the interval between target onset and movement onset. In only 5% of those epochs were the eye position differences >2.5° (fixation constraint), suggesting that overall subjects maintained fixation.

Choice data were based on the touch screen measurements. Reaction time was defined as the time between target onset and movement onset. Movement time was defined as the time between movement onset and the time the target was reached. Trials with movement times >600 ms were excluded since these often involved corrective movements. Because of a coding error, movement time data (not reaction time data) and data of one condition (head orientation 18° combined with gaze direction 18°) were lost in two subjects.

We used a linear mixed model to test whether reaction time and movement time depended on head orientation and gaze direction. In this model, head orientation, gaze direction, and head × gaze direction were fixed variables and reaction time and movement time were dependent variables.

We determined hand choice as the hand that departed first from the touch screen, i.e., lost contact with its starting position after the target was presented. Hand choice preferences were quantified as the proportion of choosing the right hand for each target direction. We summarized the psychometric data from a single combination of gaze direction and head orientation by fitting a cumulative Gaussian distribution using a maximum likelihood approach (Wichmann and Hill 2001).

$$P(x) = \lambda + (1 - 2\lambda)\frac{1}{\sigma\sqrt{2\pi}}\int_{-\infty}^{x} e^{-(y-\mu)^2/2\sigma^2}dy$$

in which x represents the target direction from the midway point between the start positions (see above). The mean of the curve, μ, represents the BTA, i.e., the angle at which the right and left hands were chosen equally often. A negative BTA indicates a shift toward selecting the right hand more often than the left hand. Parameter σ is the standard deviation of the Gaussian and reflects the variation in choice behavior. Parameter λ represents the lapse rate, accounting for deviant arm choices caused by subject lapses or mistakes, e.g., unduly reaching with the left hand to a far right target. Its value was restricted to small values (see Fig. 5).

We determined independent psychometric functions for each of the 19 combinations of head orientation and gaze direction, with each psychometric curve characterized by its own μ, σ, and λ, amounting to 19 × 3 parameters to describe the whole data set of one subject.

Because we independently varied gaze direction and head orientation, and hence also eye-in-head direction, we can determine how the BTA depends on these reference frames. We used a linear mixed model to test the effects of gaze and head on the BTA, with gaze direction, head orientation and gaze × head as fixed factors and BTA as dependent variable. Figure 2 illustrates idealized two-dimensional response matrices, showing exemplar BTAs for the various combina-

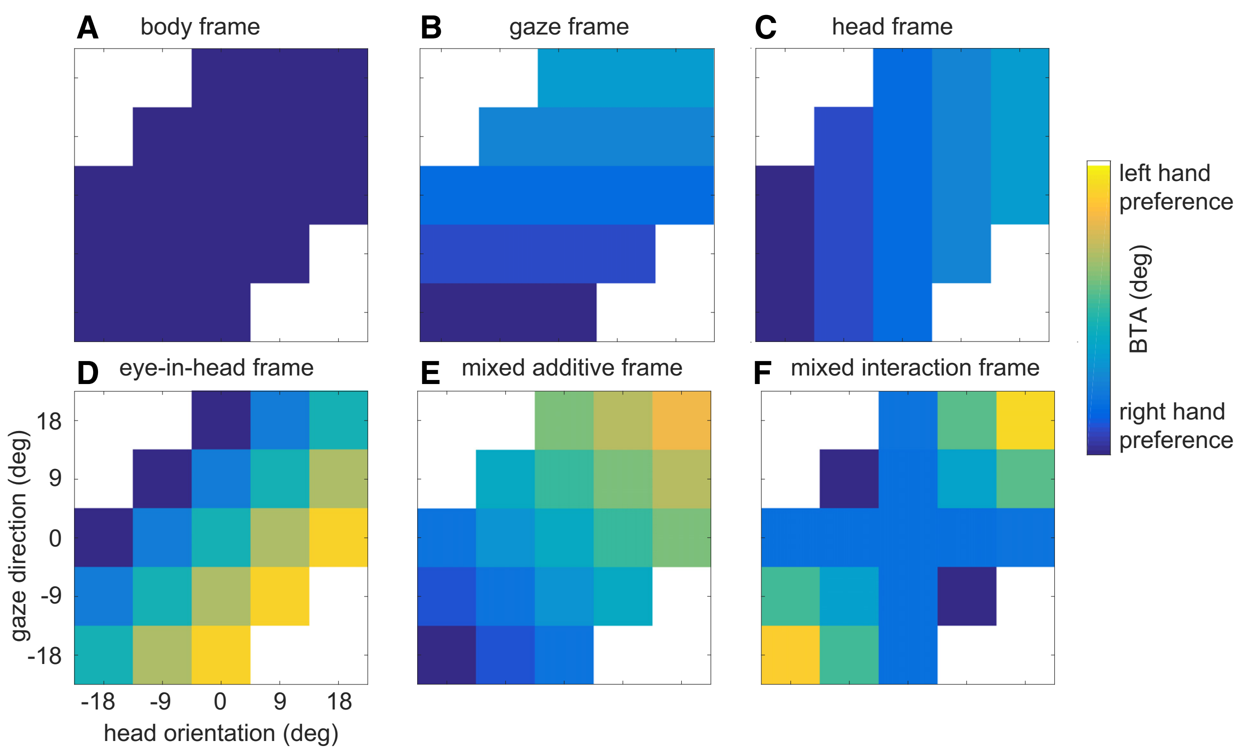

Fig. 2. Hypotheses for spatial reference frames: predictions for changes in BTA values as a function of gaze direction and head orientation. Spatial reference frames for body (*A*), gaze (*B*), head (*C*), eye-in-head (*D*), mixed additive (*E*), and mixed interaction (*F*) are shown. Color scheme from negative BTA values, i.e., left hand preference (yellow) to positive BTA values, i.e., right hand preference (blue).

tions of gaze direction and head orientation. The figure serves to illustrate various hypotheses about spatial reference frames involved in guiding hand choices, as derived from a psychometric model of the BTA with different constraints on gaze direction and head orientation. For example, in Fig. 2*A*, there is no influence of gaze or head, consistent with a body-based reference frame (BTA = a_0). This model predicts a constant value for the BTA, irrespective of gaze direction and head orientation, as demonstrated by the constant color coding. In Fig. 2, *B–D*, we illustrate the dependence of the BTA on gaze direction only (BTA = $a_0 + a_G$G), head orientation only (BTA = $a_0 + a_H$H), and eye-in-head orientation only [BTA = a_0 + a_E(G − H)], respectively.

Figure 2*E* illustrates the expected BTA pattern under the hypothesis of a mixed, additive reference frame, with an independent influence of gaze direction and head orientation (BTA = $a_0 + a_G$G + a_HH). Finally, Fig. 2*F* depicts the interacting reference frames hypothesis, with the assumption that gaze and head interact in the modulation of the choice bias [BTA = $a_0 + a_G$G + a_HH + a_{GH}(G × H)].

We fit all six models to the response data from the individual subjects. In all of these models, we assumed that the steepness of the psychometric curves ($1/\sigma^2$) is constant across the different conditions, which was statistically validated with a linear mixed model (see RESULTS). For model comparison, it should be realized that the body frame model has three free parameters: a_0, σ, and lapse rate; the gaze, head, and eye-in head frame models have four free parameters (a_0, $a_G/a_H/a_E$, σ, and lapse rate); the mixed additive frame model has five free parameters (a_0, a_G, a_H, σ, and lapse rate), and the mixed interaction frame model has six free parameters (a_0, a_G, a_H, a_{GH}, σ, and lapse rate). To account for the different numbers of free parameters, we compared these models using the Akaike information criterion (AIC; Burnham and Anderson 2002), AIC = $-2\log L + 2k$, in which L represents the total likelihood of the data given the model and k is the number of free parameters.

RESULTS

We studied the effect of gaze direction and head orientation on hand choice in a unimanual reaching task. Subjects were free to use either hand to reach for a target while gaze and head orientation were systematically manipulated relative to the body. Hand choices were psychometrically evaluated based on different hypotheses about the underlying reference frame(s) in which hand selection could take place.

Hand choices are modulated by gaze direction and head orientation. Figure 3 shows the choice data in each of the 19 unique conditions of one representative subject in a panel for each of the five different gaze directions. Each panel shows the proportion of right hand choices (circles), separately for the different head orientations, and the fitted psychometric curves as a function of target direction; the size of the circles indicates the number of trials in a given bin of target directions. As shown, the ipsilateral hand was typically selected to reach for peripheral targets, i.e., the left hand reached to targets at directions less than −50°, the right hand was chosen for targets at directions greater than +50°.

We fitted a cumulative Gaussian function to the choice data of each condition. These fits provide an estimate of the condition-specific BTA. A negative BTA indicates that the right hand is selected more often than the left hand, whereas a positive BTA indicates the reverse. While the subject in Fig. 3 shows a general preference for selecting the right hand, this preference depends on both gaze direction and head orientation. For example, in Fig. 3*A*, when gaze is at +18°, the BTA tends to become more positive when the head is oriented more to the right (from 0° to 9° to 18°). A similar modulation can be seen in Fig. 3, *B–E*, showing the choice for the other gaze directions. The BTA becomes more positive, which means that the left hand is used increasingly more, when head orientation is varied from leftward to rightward directions. Next to a head orientation effect, the panels of Fig. 3 also show that the BTA increases with gaze direction. For example, across Fig. 3, *A–E*, the yellow curve, which is associated with a head orientation of 18°, suggests a BTA of ~18° when gaze is at 18° (Fig. 3*A*), ~10° when gaze is at 9° (Fig. 3*B*), and ~5° when gaze is at 0° (Fig. 3*C*). The BTA is more positive when gaze is directed to more rightward directions, which means that the left hand is used increasingly more when gaze is directed from leftward to rightward directions.

Hand choice is embedded in a mixed, additive reference frame. Figure 4*A* illustrates the gaze direction- and head orientation-dependent BTA averaged across subjects, in the same format as Fig. 2. Data mimic the single-subject observations in Fig. 3. The overall negative BTA indicates a preference for selecting the right hand, but the color gradient shows that this selection preference diminishes, and sometimes even reverses to the left hand, with increasing gaze direction and head orientation (i.e., more rightward gaze or head results in more left hand use). In support, for each gaze direction the BTA shows a significant increase with head orientation [$F(4,321)$ = 9.90, $P < 0.001$] and for each head orientation the BTA increases significantly with gaze direction [$F(4,321)$ = 6.16, $P < 0.001$]. Note that these systematic dependencies were not found in relation to the slope (= width) of the psychometric curves [head orientation: $F(4,321) = 0.95$, $P = 0.44$], gaze direction [$F(4,321) = 0.40$, $P = 0.81$], or interaction gaze × head [$F(10,321) = 0.85$, $P = 0.58$], which is a prerequisite for distinguishing between the candidate models.

In terms of the proposed hypotheses, the pattern in Fig. 4*A* seems to match most closely with Fig. 2*E*, which illustrates the hypothesis that hand choice is performed in a mixed, additive spatial reference frame. The response patterns shift with the changes in both head orientation and gaze direction, indicating that both reference frames are involved in guiding hand choice. To verify this observation, we used the AIC to select the best model of the six fitted candidate models. A lower AIC value indicates a better-fitting model, including the penalty for increasing the number of parameters in the model (see METHODS).

As shown by Fig. 4*B*, the mixed additive reference frame model outperforms the other models (BTA = $a_0 + a_G$G + a_HH). The model describing an interaction effect of gaze and head was the second-best model, but the addition of an interaction term (which is an additional degree of freedom) did not make this model statistically better than the mixed additive reference model. The AIC values for the other, simpler, models were orders of magnitude higher, indicating they fall short in providing an adequate account of the data.

Figure 4, *C* and *D*, illustrate the quality of the mixed additive reference frame model as a description of the data. As shown, the model is qualitatively in good agreement with the measured BTAs. The within-subject correlation coefficient between the model predictions for the BTA and the BTAs from the psychometric fits varied between 0.18 and 0.81 and was significant in 15 of 18 participants.

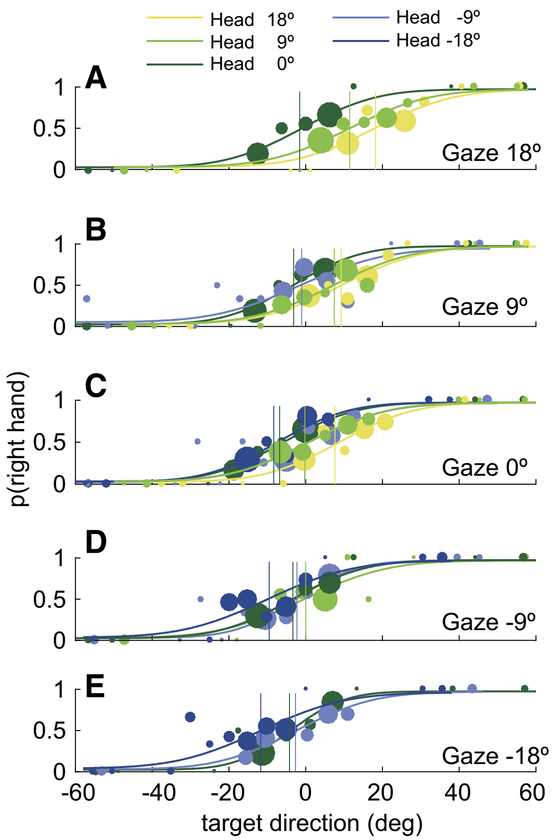

Fig. 3. Psychometric choice data and fitted curves of a representative subject. *A–E* are organized by gaze direction; colors refer to different head orientations. Circle size indicates the number of trials for a particular target direction. Thin vertical lines indicate the BTA for each head direction.

Figure 5 illustrates the parameter values of the mixed additive reference frame model, fit to single-subject data and the data averaged across subjects. Parameter a_0, describing the general choice bias, was on average −8.1° (SD = 0.9°), indicating an overall preference for using the right hand, consistent with the right-handedness of our subjects. Parameters a_G and a_H had similar magnitudes [mean a_G 0.19 (SD = 0.04), mean a_H 0.19 (SD 0.04)], suggesting that both gaze and head reference frames have comparable effects on hand selection. σ was on average 21° (SD = 3.5) and lapse rate around 0.07 (SD 0.04).

Reach reaction time and duration do not depend on gaze and head orientation. It is possible that the manipulations of head orientation and gaze direction affect the time by which the competition between the hands is resolved, which would behaviorally be reflected in changes of reaction time. A linear mixed model analysis, however, revealed no significant difference among reaction times for reaches made with different orientations of the head and/or directions of gaze [all $P > 0.2$, average reaction time: 405 ms (SD = 85 ms)]. The same analysis also did not reveal an effect on movement time [$P > 0.6$, mean movement duration 309 ms (SD = 72 ms)]. This suggests that gaze direction and head orientation do not influence the complexity of the decision process of hand choice per se. Their choice-biasing effects rather reflect the spatial reference frames that are involved in these computations.

DISCUSSION

Recent studies have considered hand selection as a competitive process (Bakker et al. 2017; Oliveira et al. 2010; Schweighofer et al. 2015; Stoloff et al. 2011), in which relative costs, rewards, task demands, and handedness are modulating factors (Schweighofer et al. 2015). Here we systematically tested the spatial reference frames that are involved in these computations by manipulating gaze direction, head orientation, and target direction. We used a psychometric approach, adopted from Oliveira et al. (2010), asking participants to reach with a freely chosen hand to a visual target that appeared at a variable direction relative to the body.

We determined the target angle that led to equiprobable right/left hand choices, referred to as the balanced target angle (BTA). Our results show that subjects generally chose the hand ipsilateral to targets in the periphery and showed a general preference for selecting the dominant right hand for targets around the BTA. While Oliveira and colleagues (Oliveira et al. 2010) did not manipulate gaze and head orientation, we examined how the BTA varied with gaze and head orientation. Findings show that both gaze direction and head orientation had a significant effect on the BTA. The BTA shifts with both gaze and head, as if subjects are more likely to use the contralateral hand when gaze and head are oriented to more eccentric directions. A single model, constraining the BTA by a linear dependence on both gaze and head orientation, provided a good fit (i.e., mean $R = 0.61$) to all psychometric data simultaneously. Interestingly, this linear combination does not bear out as an eye-in-head (gaze minus head) effect: both gaze and head direction affect the hand choice bias in the same way. Also, the addition of an interaction term between gaze and head did not allow for a statistically better account of the data. We conclude that a linear mixture of head- and gaze-centered reference frames is involved in guiding the decisions of hand choice.

It is important to emphasize that effects unrelated to gaze- and head-centered reference frames, such as handedness and biomechanical costs (Bakker et al. 2017; Schweighofer et al. 2015; Soechting and Flanders 1992), known to affect hand choice, are associated with a body-centered reference frame. If hand selection involves a purely body-centered computation, e.g., of biomechanical movement cost, then we must conclude on the basis of our data that head and gaze reference frames affect these cost computations, although physically movement costs are invariant to changes in head orientation and gaze direction.

One could consider multiple ways in which gaze- and head-centered reference frames affect body-centered cost calculations. For example, it could be argued that the transformation of the target location from retinal into body-centered coordinates, which involves gaze and head reference frames (Crawford et al. 2011), is erroneous and has resulted in the choice biases that we have observed. The alternative is that peripheral targets are misperceived and this misperception depends on gaze (Lewald and Ehrenstein 2000) but the reference frame transformation is correct. The visual positional uncertainty increases as a function of eccentricity because visual detail depends on the region of the retina that receives visual information (Carrasco et al. 1998). While this could also affect the choice bias, we consider this explanation less likely

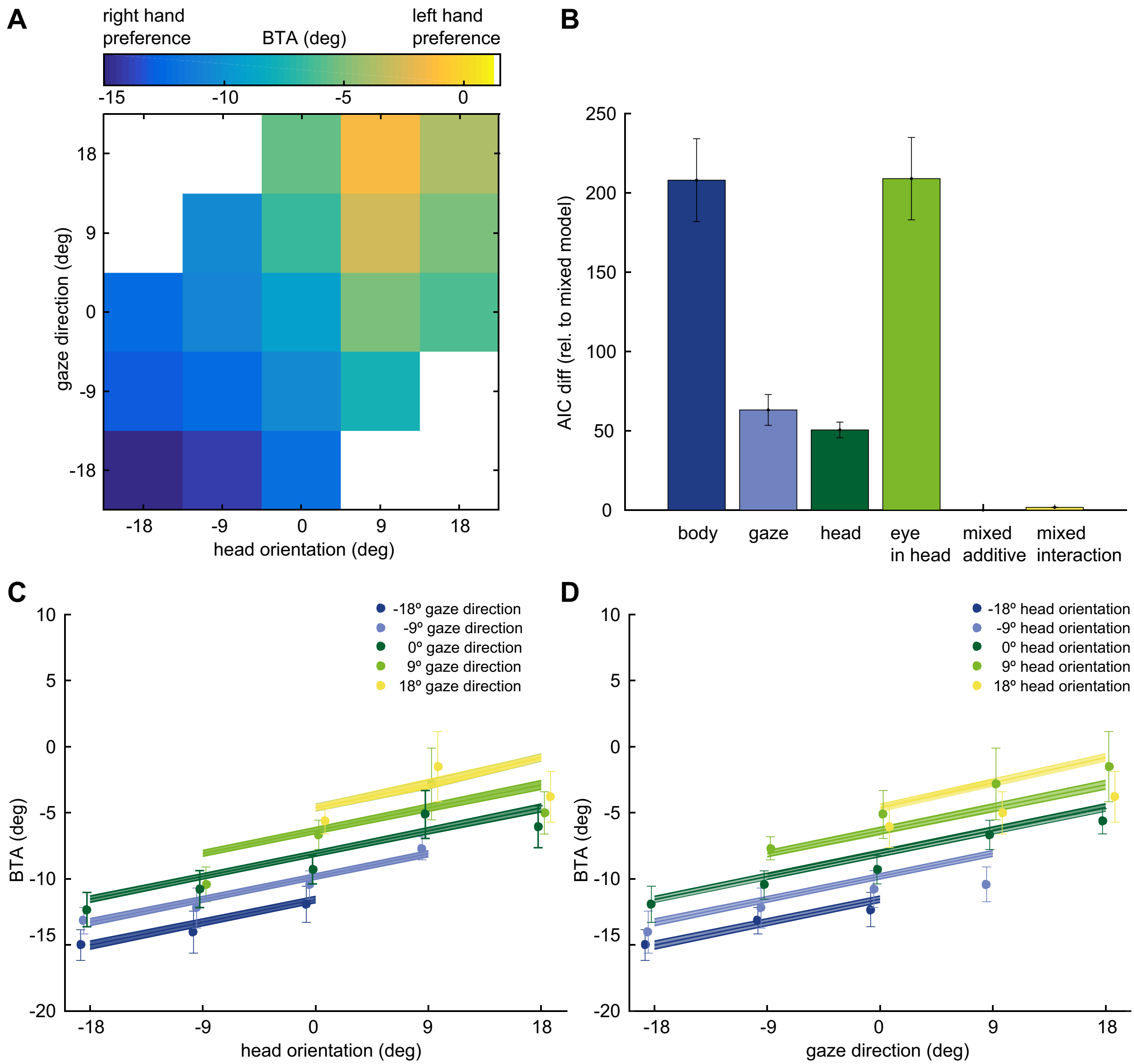

Fig. 4. Effects of gaze direction and head orientation on the BTA. *A*: BTA values, averaged across subjects, mimic the mixed additive frame illustrated in Fig. 2*E*. Yellow, left hand preference (negative BTA value); blue, right hand preference (positive BTA value). *B*: model comparison by means of AIC relative to the mixed additive reference frame model. *C* and *D*: fit of mixed additive reference model to the BTA data as function of head orientation (*C*) and gaze direction (*D*). Mean BTAs (dots) are plotted as a reference.

because our results show that hand selection is also biased by changes in head orientation, even when gaze is kept constant. Finally, it has been argued that the perception of the body midline shifts with changes in the direction of gaze and head (Jeannerod and Biguer 1987; Werner et al. 1953). If hand selection is performed in body coordinates, it is not unreasonable to expect changes in the choice bias when this body midline percept is manipulated.

We are not aware of other behavioral studies that have investigated the effects of gaze and head orientation on the decision of hand choice in humans. A recent study in monkeys (Dancause and Schieber 2010) examined hand choices made by monkeys under different head orientations. Hand preference produced the strongest bias on hand choice, but the authors also reported a modulation by head orientation; monkeys were more likely to choose the hand ipsilateral to the head direction. The latter appears inconsistent with the present results, but it can be argued that the difference in gaze has contributed to their observed bias. The present data set, which is richer in terms of gaze and head manipulations, allows us to exactly point that out. As shown in Fig. 4, gaze and head effects sum up in the bias of hand choice, so any contralateral or ipsilateral bias on hand choice follows from the combination of the two reference frames.

In the present study, we constrained the processes related to target selection (i.e., the what-to-do process) by presenting subjects with single targets and examining their hand choice. In natural conditions, however, not only do reaching movements require a solution to the how-to-act process but also the what-to-act process needs to be resolved. Along these lines,

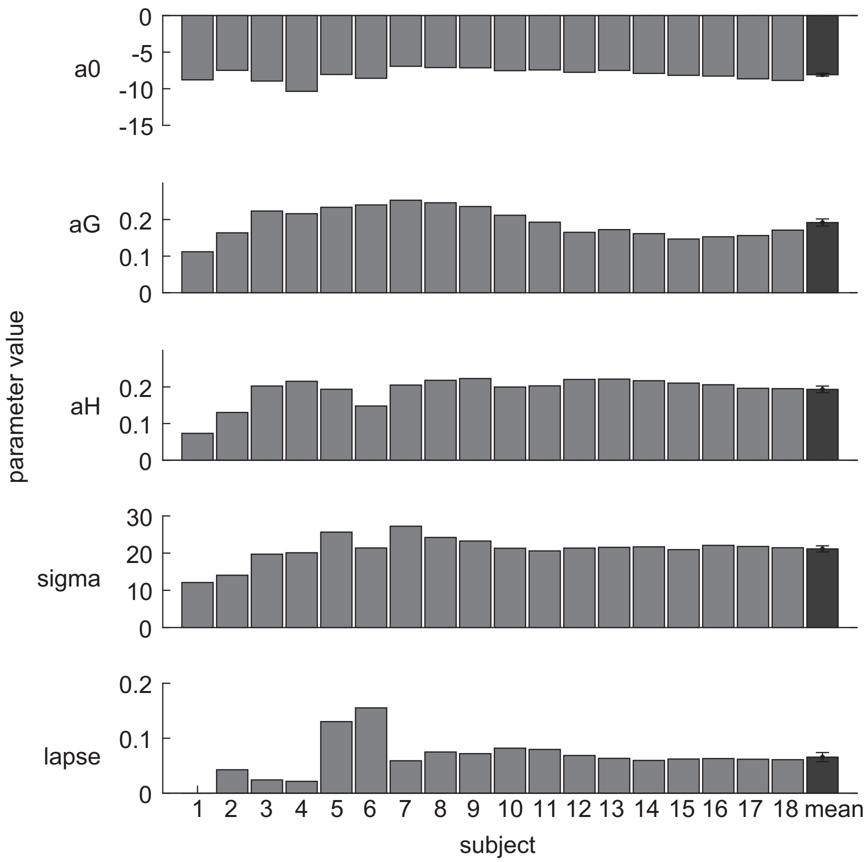

Fig. 5. Best fit parameters of the mixed additive reference frame model (BTA = $a_0 + a_G G + a_H H$) plotted for each subject (gray) and the overall mean accompanied by SE bars (black).

earlier studies have demonstrated a target preference in relation to the hand that is used (Fisk and Goodale 1985; Horstmann and Hoffmann 2005; Scherberger et al. 2003). Scherberger et al. (2003) studied the reference frames of target selection of reaching movements. They varied gaze direction, head orientation, as well as trunk orientation and found that target selection of reaching movements depended on a mixed head- and gaze-centered reference frame. They also reported similar findings for saccadic eye movements, which were later replicated by Horstmann and Hoffmann (2005), who also found them to hold for coordinated, i.e., simultaneous, movements of eyes and hand (see also Rincon-Gonzalez et al. 2016; Wardak et al. 2002 for other studies on saccadic target selection).

Thus the what-to-do and the how-to-act decision processes demonstrate similar choice characteristics in that both share a mixed head- and gaze-centered reference frame in their computations. This can be taken to suggest that both processes are part of an integrated computation, consistent with current models of action selection (Cisek and Kalaska 2010; Gold and Shadlen 2007). Signatures of these reference frames can even be detected at the level of movement execution, in movement errors and other kinematic variables (Beurze et al. 2006; Crawford et al. 2011; Henriques and Crawford 2002; McGuire and Sabes 2009; Sainburg et al. 2003).

From a neural perspective, movement selection has been suggested to involve the selective (dis)inhibition of cortical sensorimotor populations governed by rhythmic neural activity in various frequency bands (Hamel-Thibault et al. 2018; Tzagarakis et al. 2015; Van Der Werf et al. 2010). Our results predict that crucial rhythms for hand selection show selectivity in both gaze- and head-centered reference frames, which would be a test for future work. Using the same hand selection paradigm in EEG, but with only central head and gaze, Hamel-Thibault et al. (2018) revealed that hand selection strongly depended upon the instantaneous phase of delta band oscillation at target onset, as if selection occurs through interactions between these competing neuronal ensembles. This effect was maximal over parietofrontal motor regions, suggesting that the competition of hand selection is resolved directly within the sensorimotor system. In support, using transcranial magnetic stimulation, Oliveira et al. (2010) reported causal evidence that the posterior parietal cortex is involved in decisions of hand choice. Our results are consistent with the variety of reference frames that have been reported for these cortical regions (Beurze et al. 2010; Bremner and Andersen 2014; Pesaran et al. 2006) as well as their contralateral hand bias (Beurze et al. 2007; Haar et al. 2017).

Interestingly, in area 5, neurons become only activated after the hand of the reach is specified (Cui and Andersen 2011), thereby showing a flexible, task-dependent reference in the representation of target information (Bremner and Andersen 2014). Similar results have also been found in humans (Bernier et al. 2012), as though effector selection is a prerequisite for a movement plan, or multiple movement plans, to be specified. While these results suggest that the process of effector selection occurs in a more serial manner than target selection, our findings suggest that a mixture of reference frames is involved in both mechanisms, perhaps to dynamically facilitate the integration of the outcome of both processes.

GRANTS

This work was supported by the Netherlands Organization for Scientific Research (NWO-VICI: 453-11-001 to W. P. Medendorp).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

R.S.B., L.P.S., and W.P.M. conceived and designed research; R.S.B. performed experiments; R.S.B. and L.P.S. analyzed data; R.S.B., L.P.S., and W.P.M. interpreted results of experiments; R.S.B. prepared figures; R.S.B. and W.P.M. drafted manuscript; R.S.B., L.P.S., and W.P.M. edited and revised manuscript; R.S.B., L.P.S., and W.P.M. approved final version of manuscript.

REFERENCES

Andersen RA, Cui H. Intention, action planning, and decision making in parietal-frontal circuits. *Neuron* 63: 568–583, 2009. doi:10.1016/j.neuron.2009.08.028.

Bakker RS, Weijer RH, van Beers RJ, Selen LP, Medendorp WP. Decisions in motion: passive body acceleration modulates hand choice. *J Neurophysiol* 117: 2250–2261, 2017. doi:10.1152/jn.00022.2017.

Bernier PM, Cieslak M, Grafton ST. Effector selection precedes reach planning in the dorsal parietofrontal cortex. *J Neurophysiol* 108: 57–68, 2012. doi:10.1152/jn.00011.2012.

Beurze SM, de Lange FP, Toni I, Medendorp WP. Integration of target and effector information in the human brain during reach planning. *J Neurophysiol* 97: 188–199, 2007. doi:10.1152/jn.00456.2006.

Beurze SM, Toni I, Pisella L, Medendorp WP. Reference frames for reach planning in human parietofrontal cortex. *J Neurophysiol* 104: 1736–1745, 2010. doi:10.1152/jn.01044.2009.

Beurze SM, Van Pelt S, Medendorp WP. Behavioral reference frames for planning human reaching movements. *J Neurophysiol* 96: 352–362, 2006. doi:10.1152/jn.01362.2005.

Bisley JW, Goldberg ME. Attention, intention, and priority in the parietal lobe. *Annu Rev Neurosci* 33: 1–21, 2010. doi:10.1146/annurev-neuro-060909-152823.

Bremner LR, Andersen RA. Temporal analysis of reference frames in parietal cortex area 5d during reach planning. *J Neurosci* 34: 5273–5284, 2014. doi:10.1523/JNEUROSCI.2068-13.2014.

Bryden PJ, Pryde KM, Roy EA. A performance measure of the degree of hand preference. *Brain Cogn* 44: 402–414, 2000. doi:10.1006/brcg.1999.1201.

Burnham KP, Anderson DR. *Model Selection and Multimodel Inference: A Practical-Theoretical Approach*. New York: Springer, 2002.

Carrasco M, McLean TL, Katz SM, Frieder KS. Feature asymmetries in visual search: effects of display duration, target eccentricity, orientation and spatial frequency. *Vision Res* 38: 347–374, 1998. doi:10.1016/S0042-6989(97)00152-1.

Cisek P. Cortical mechanisms of action selection: the affordance competition hypothesis. *Philos Trans R Soc Lond B Biol Sci* 362: 1585–1599, 2007. doi:10.1098/rstb.2007.2054.

Cisek P, Kalaska JF. Neural mechanisms for interacting with a world full of action choices. *Annu Rev Neurosci* 33: 269–298, 2010. doi:10.1146/annurev.neuro.051508.135409.

Cos I, Bélanger N, Cisek P. The influence of predicted arm biomechanics on decision making. *J Neurophysiol* 105: 3022–3033, 2011. doi:10.1152/jn.00975.2010.

Crawford JD, Henriques DY, Medendorp WP. Three-dimensional transformations for goal-directed action. *Annu Rev Neurosci* 34: 309–331, 2011. doi:10.1146/annurev-neuro-061010-113749.

Crawford JD, Medendorp WP, Marotta JJ. Spatial transformations for eye-hand coordination. *J Neurophysiol* 92: 10–19, 2004. doi:10.1152/jn.00117.2004.

Cui H, Andersen RA. Different representations of potential and selected motor plans by distinct parietal areas. *J Neurosci* 31: 18130–18136, 2011. doi:10.1523/JNEUROSCI.6247-10.2011.

Dancause N, Schieber MH. The impact of head direction on lateralized choices of target and hand. *Exp Brain Res* 201: 821–835, 2010. doi:10.1007/s00221-009-2097-6.

Fisk JD, Goodale MA. The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. *Exp Brain Res* 60: 159–178, 1985. doi:10.1007/BF00237028.

Gabbard C, Tapia M, Helbig CR. Task complexity and limb selection in reaching. *Int J Neurosci* 113: 143–152, 2003. doi:10.1080/00207450390161994.

Gold JI, Shadlen MN. The neural basis of decision making. *Annu Rev Neurosci* 30: 535–574, 2007. doi:10.1146/annurev.neuro.29.051605.113038.

Goodale MA, Milner AD. Separate visual pathways for perception and action. *Trends Neurosci* 15: 20–25, 1992. doi:10.1016/0166-2236(92)90344-8.

Haar S, Dinstein I, Shelef I, Donchin O. Effector-invariant movement encoding in the human motor system. *J Neurosci* 37: 9054–9063, 2017. doi:10.1523/JNEUROSCI.1663-17.2017.

Haggard P. Human volition: towards a neuroscience of will. *Nat Rev Neurosci* 9: 934–946, 2008. doi:10.1038/nrn2497.

Hamel-Thibault A, Thénault F, Whittingstall K, Bernier P. Delta-band oscillations in motor regions predict hand selection for reaching. *Cereb Cortex* 28: 574–584, 2018.

Henriques DY, Crawford JD. Role of eye, head, and shoulder geometry in the planning of accurate arm movements. *J Neurophysiol* 87: 1677–1685, 2002. doi:10.1152/jn.00509.2001.

Horstmann A, Hoffmann KP. Target selection in eye-hand coordination: do we reach to where we look or do we look to where we reach? *Exp Brain Res* 167: 187–195, 2005. doi:10.1007/s00221-005-0038-6.

Jeannerod M, Biguer B. The directional coding of reaching movements. a visuomotor conception of spatial neglect. In: *Neurophysiological and Neuropsychological Aspects of Spatial Neglect*, edited by Jeannerod M. Amsterdam: Elsevier Science, 1987, p. 87–113. doi:10.1016/S0166-4115(08)61710-0

Kontsevich LL, Tyler CW. Bayesian adaptive estimation of psychometric slope and threshold. *Vision Res* 39: 2729–2737, 1999. doi:10.1016/S0042-6989(98)00285-5.

Leoné FT, Heed T, Toni I, Medendorp WP. Understanding effector selectivity in human posterior parietal cortex by combining information patterns and activation measures. *J Neurosci* 34: 7102–7112, 2014. doi:10.1523/JNEUROSCI.5242-13.2014.

Lewald J, Ehrenstein WH. Visual and proprioceptive shifts in perceived egocentric direction induced by eye-position. *Vision Res* 40: 539–547, 2000. doi:10.1016/S0042-6989(99)00197-2.

McGuire LM, Sabes PN. Sensory transformations and the use of multiple reference frames for reach planning. *Nat Neurosci* 12: 1056–1061, 2009. doi:10.1038/nn.2357.

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9: 97–113, 1971. doi:10.1016/0028-3932(71)90067-4.

Oliveira FT, Diedrichsen J, Verstynen T, Duque J, Ivry RB. Transcranial magnetic stimulation of posterior parietal cortex affects decisions of hand choice. *Proc Natl Acad Sci USA* 107: 17751–17756, 2010. doi:10.1073/pnas.1006223107.

Pesaran B, Nelson MJ, Andersen RA. Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning. *Neuron* 51: 125–134, 2006. doi:10.1016/j.neuron.2006.05.025.

Rincon-Gonzalez L, Selen LP, Halfwerk K, Koppen M, Corneil BD, Medendorp WP. Decisions in motion: vestibular contributions to saccadic target selection. *J Neurophysiol* 116: 977–985, 2016. doi:10.1152/jn.01071.2015.

Sainburg RL, Lateiner JE, Latash ML, Bagesteiro LB. Effects of altering initial position on movement direction and extent. *J Neurophysiol* 89: 401–415, 2003. doi:10.1152/jn.00243.2002.

Scherberger H, Goodale MA, Andersen RA. Target selection for reaching and saccades share a similar behavioral reference frame in the macaque. *J Neurophysiol* 89: 1456–1466, 2003. doi:10.1152/jn.00883.2002.

Schweighofer N, Xiao Y, Kim S, Yoshioka T, Gordon J, Osu R. Effort, success, and nonuse determine arm choice. *J Neurophysiol* 114: 551–559, 2015. doi:10.1152/jn.00593.2014.

Scott SH. A functional taxonomy of bottom-up sensory feedback processing for motor actions. *Trends Neurosci* 39: 512–526, 2016. doi:10.1016/j.tins.2016.06.001.

Soechting JF, Flanders M. Moving in three-dimensional space: frames of reference, vectors, and coordinate systems. *Annu Rev Neurosci* 15: 167–191, 1992. doi:10.1146/annurev.ne.15.030192.001123.

Stoloff RH, Taylor JA, Xu J, Ridderikhoff A, Ivry RB. Effect of reinforcement history on hand choice in an unconstrained reaching task. *Front Neurosci* 5: 41, 2011. doi:10.3389/fnins.2011.00041.

Ting LH, Chvatal SA, Safavynia SA, McKay JL. Review and perspective: neuromechanical considerations for predicting muscle activation patterns for movement. *Int J Numer Methods Biomed Eng* 28: 1003–1014, 2012. doi:10.1002/cnm.2485.

Todorov E. Optimality principles in sensorimotor control. *Nat Neurosci* 7: 907–915, 2004. doi:10.1038/nn1309.

Tzagarakis C, West S, Pellizzer G. Brain oscillatory activity during motor preparation: effect of directional uncertainty on beta, but not alpha, frequency band. *Front Neurosci* 9: 246, 2015. doi:10.3389/fnins.2015.00246.

Van Der Werf J, Jensen O, Fries P, Medendorp WP. Neuronal synchronization in human posterior parietal cortex during reach planning. *J Neurosci* 30: 1402–1412, 2010. doi:10.1523/JNEUROSCI.3448-09.2010.

Wardak C, Olivier E, Duhamel JR. Saccadic target selection deficits after lateral intraparietal area inactivation in monkeys. *J Neurosci* 22: 9877–9884, 2002.

Werner H, Wapner S, Bruell JH. Experiments on sensory-tonic field theory of perception. VI. Effect of position of head, eyes, and of object on position of the apparent median plane. *J Exp Psychol* 46: 293–299, 1953. doi:10.1037/h0055733.

Wichmann FA, Hill NJ. The psychometric function: I. Fitting, sampling, and goodness of fit. *Percept Psychophys* 63: 1293–1313, 2001. doi:10.3758/BF03194544.

Wong AL, Haith AM, Krakauer JW. Motor planning. *Neuroscientist* 21: 385–398, 2015. doi:10.1177/1073858414541484.