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The Nervous System Uses Nonspecific Motor Learning in Response to Random Perturbations of Varying Nature

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Wei K, Wert D, Körding K. The nervous system uses nonspecific motor learning in response to random perturbations of varying nature. *J Neurophysiol* 104: 3053–3063, 2010. First published September 22, 2010; doi:10.1152/jn.01025.2009. We constantly make small errors during movement and use them to adapt our future movements. Movement experiments often probe this error-driven learning by perturbing movements and analyzing the after-effects. Past studies have applied perturbations of varying nature such as visual disturbances, position- or velocity-dependent forces and modified inertia properties of the limb. However, little is known about how the specific nature of a perturbation influences subsequent movements. For a single perturbation trial, the nature of a perturbation may be highly uncertain to the nervous system, given that it receives only noisy information. One hypothesis is that the nervous system can use this rough estimate to partially correct for the perturbation on the next trial. Alternatively, the nervous system could ignore uncertain information about the nature of the perturbation and resort to a nonspecific adaptation. To study how the brain estimates and responds to incomplete sensory information, we test these two hypotheses using a trial-by-trial adaptation experiment. On each trial, the nature of the perturbation was chosen from six distinct types, including a visuomotor rotation and different force fields. We observed that corrective forces aiming to oppose the perturbation in the following trial were independent of the nature of the perturbation. Our results suggest that the nervous system uses a nonspecific strategy when it has high uncertainty about the nature of perturbations during trial-by-trial learning.

INTRODUCTION

Most motor adaptation studies have used a blocked design where the same type of perturbation is applied to human movements repetitively. Over a sequence of trials, subjects gradually learn to correct for visual perturbations (Dionne and Henriques 2008; Redding et al. 2005), velocity-dependent force fields (Shadmehr and Mussa-Ivaldi 1994), position-dependent force fields (Tong et al. 2002), acceleration-dependent force fields (Hwang et al. 2006), and more complicated force fields (Thoroughman and Taylor 2005). The nature of these perturbations (referring to what aspects of the movement are affected by the perturbation) varies across studies. The general finding is that humans can eventually learn to generate a response that roughly mirrors the perturbation and enables them to move as if they were not perturbed.

The learning in such experiments that repetitively use the same perturbation is usually modeled as incremental learning.

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An implicit assumption of these models is that the nervous system expects a related perturbation during the next movement. For blocked-design experiments, this assumption is valid; however, we need to recognize that perturbations experienced during daily life usually change frequently and that even the nature of perturbation may vary over time. Imagine you reach for a cup but fall short; this movement error can be a result of displacement of the cup or an incidental shove on your arm by someone. Perturbations of varying nature, either visual or dynamic, can influence your movements randomly, and you will make adaptation in subsequent movements. How does the brain deal with such perturbations when they vary over time?

The trial-by-trial adaptation paradigm, which usually varies the perturbation amplitude from trial to trial, is suitable to study this problem (Baddeley et al. 2003; Fine and Thoroughman 2007; Scheidt et al. 2001; Wei and Körding 2009). The nature of perturbations has not been systematically varied in this paradigm and little is known about how the nervous system copes with diverse perturbations in such a setting. Here we examine the extent to which the nervous system can estimate the nature of perturbations on a trial-by-trial basis for learning.

This work centers around two working hypotheses. Our first hypothesis derives from state space models, which usually assume learning to be proportional to experienced perturbations (Baddeley et al. 2003; Donchin et al. 2003; Fine and Thoroughman 2007). These models predict that adaptation is weak on a trial-by-trial basis, and the after-effect mirrors the preceding perturbation as a function of its nature. Our second hypothesis derives from recent theoretical advances that emphasize that a perturbation is often ambiguous and its estimation is a statistical inference problem (Berniker and Körding 2008). This statistical account suggests that, in a trial-by-trial paradigm, the nervous system may have uncertainty about the nature of perturbations and would have to fall back on a nonspecific adaptation strategy.

Here we test how subjects adapt to perturbations of different nature, visuomotor rotations or various force fields, in a trial-by-trial paradigm. Our results support the second hypothesis that the nervous system uses a nonspecific adaptation strategy when it is uncertain about perturbations of varying nature.

METHODS

This study includes two experiments that share identical protocol and experimental setups and similar data analysis. The primary difference between the two experiments is how trial-by-trial learning is evaluated: in *experiment 1*, catch trials without perturbations were randomly interspersed with perturbation trials; in *experiment 2*, catch

trials are implemented with an error-clamping force channel (Scheidt et al. 2000; Sing et al. 2009) to probe the learning. We will first present methods of *experiment 1* in detail and then introduce *experiment 2* and its differences.

Experimental procedure (experiment 1)

Eight naïve subjects participated in *experiment 1* after providing informed consent. All subjects were right-handed with normal or corrected-to-normal vision. All procedures were approved by the institutional review board of Northwestern University.

The subjects were seated in front of a table and held the handle of a two-dimensional (2-D) robotic linkage with their right hand (Fig. 1A; see elsewhere for detailed description, Shadmehr and Mussa-Ivaldi 1994). The hand could be moved freely, with low friction, but was restricted to move in the horizontal (transverse) plane of the robot. The seat height was adjusted for each subject to keep the right arm at shoulder level. The right upper arm was also supported by a customized harness hung from the ceiling to minimize the effect of fatigue and to keep posture constant. The movement of the hand was measured by the manipulandum at 250 Hz, but vision of the actual hand was obscured as the movement was performed underneath a projection screen that was positioned horizontally at the neck level. Visual feedback of the hand position was given as a projected cursor with a display frequency of 75 Hz. Each subject performed a total of 1,008 reaching movements, resulting in ~1 h of participation.

The starting position of the reaching movement was represented as a white cross at the middle of the workspace, aligned with the midline of the seated subject. Each trial started when the subject placed the cursor at the starting position. After the hand remained stationary at that position for 1 s, the trial started. A target, represented as a yellow circle of 0.6 cm diameter, was displayed 10 cm ahead of the starting position while the cross representing the starting position disappeared. Subjects were instructed to execute an accurate forward movement to

the target at that moment. Once the cursor had moved 10 cm in the y direction, the target changed color: green if hit, red if not. The starting position was displayed again to signal the subject to return the hand and start a new trial. On the way returning to the starting position, the cursor display was turned off until the hand was within 2 cm of the starting position. This omission of visual feedback reduced visual calibration, which usually decreases the learning effect for the visuomotor rotation condition. Subjects were paid 4 cents for each successful hit in addition to the \$10 they received for participating in the experiment. Subjects were encouraged to make fast movements, and a text warning “too slow” would appear if they failed to finish the movement in 350 ms. They were also instructed that movements that were made too slowly would not be rewarded, regardless of whether or not the target was reached. The small amplitude of the reaching movement and the emphasis on short movement duration minimized any feedback corrections within a reaching movement. Because the focus of this study is on how subjects adapt to a previously experienced perturbation, this serves to minimize any response to ongoing perturbations.

One half of the movements were affected by one of six possible perturbations that were randomly selected, whereas the rest of the trials were catch trials without perturbations (Fig. 1B). In the visuomotor rotation condition, the cursor location was displayed as if the visual scene was rotated 15° around the starting position, either clockwise or counterclockwise. The remaining five types of perturbations were forces applied by the handle of the manipulandum orthogonal to the line connecting the start and the target position. These forces were defined by the hand position (Fig. 1B): linear (ramp condition), piecewise linear (triangle condition), or sine waves of varying frequencies (half sine, full sine, and double sine conditions). The maximal force was 4 N in the ramp condition and 8 N in the other four conditions. Each type of perturbations was presented 42 times, either in the left or right direction with equal chances, for a total of

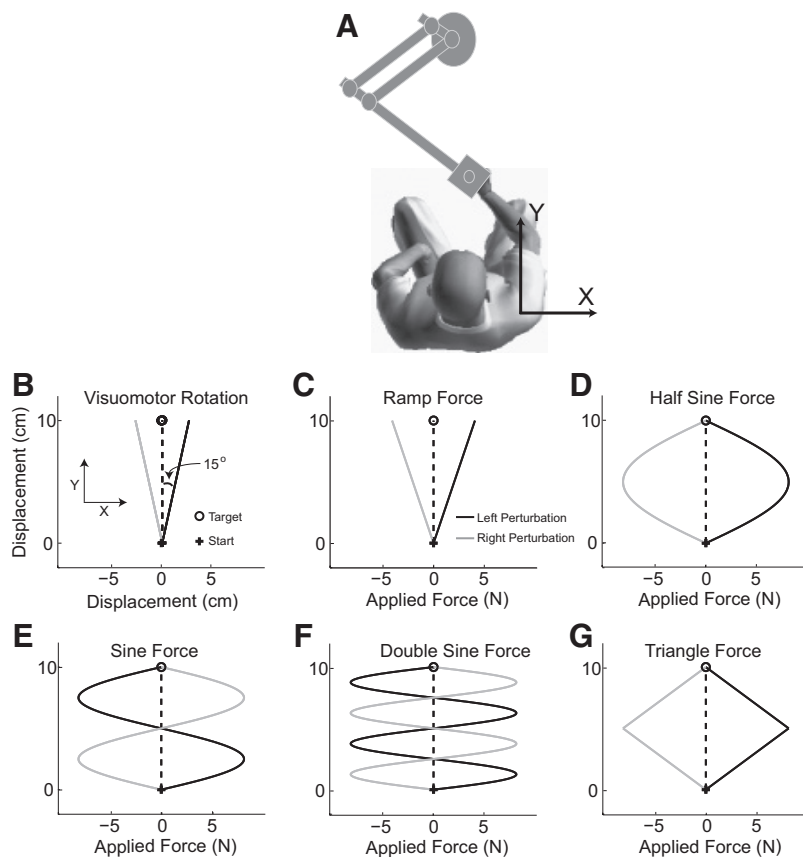


FIG. 1. A: sketch of the manipulandum and the experimental setup. B–G: 6 different perturbations are shown in both left and right directions. The target is 10 cm away in depth direction (Y direction) and all the perturbations are applied in the lateral direction (left and right, X direction). Note for the visuomotor rotation (shown in B), the X axis is for displacement and it is different from other panels where the X axis is for applied perturbation force.

504 perturbation trials. Five hundred four catch trials (no perturbation) were interspersed with perturbation trials. The probability of a perturbation trial following another perturbation trial was lower than chance and set to 30% through a resampling procedure. In this way, the immediate adaptive effects for opposing the perturbations can be assessed in catch trials while avoiding subjects' anticipation of catch trials.

Experimental procedure (experiment 2)

Seven subjects were recruited in *experiment 2*. *Experiment 2* shared identical procedures as in *experiment 1* with only one difference: catch trials were presented with strong error-clamping force instead of zero force as in *experiment 1*. This lateral force behaves like a channel that clamps the lateral deviation of the hand movement by a restoring force defined as

$$F = K \times x + D \times v_x$$

where x stands for lateral deviation of the forward movement and v_x for its velocity, K is a spring constant that specifies the position-dependent restoring force (set at $-6,000$ N/m), and D is a damping constant that specifies the velocity-dependent restoring force (set at -250 Ns/m). The parameter setting of this force channel is identical to the one used in a previous study (Sing et al. 2009). The sampling frequency increased to 2,000 Hz to meet the high demands of producing realistic force channel. The error-clamping force channel effectively limited lateral deviation from a straight line to ~ 1 mm. It has been proposed that the force invoked by the force channel following a force perturbation is indicative of the learning-related predictive changes (Sing et al. 2009). We thus analyze the force profile in catch trials to quantify the trial-by-trial learning.

Data analysis

The position and velocity data in both directions were measured. In *experiment 1*, the earliest and latest parts of the reach ($y < 0.5$ and > 8 cm) were excluded from the analysis. Because of the low friction and low inertia of the hand-held manipulandum, the hand randomly drifted at the starting position (visually marked as a 0.6 cm disc in diameter) before the movement was initiated. To minimize this effect, we excluded the first 0.5 cm movements. The reason for excluding the last 2 cm of the movement is that our study focuses on the adaptation to perturbations that exhibits itself as a predictive control, whereas the last segment of a reaching movement is dominated by feedback control (see a similar treatment, Scheidt et al. 2001). The other reason for this exclusion is that some subjects stopped movement somewhat short of the target distance, and our original code did not well control for that. In *experiment 2*, we excluded only 3 mm of the initial movement trajectory because the force channel constrained the initial drift and 8 mm of the trajectory end because of improved movement-termination judgment in the data acquisition program. Nevertheless, we argue that the exclusion of partial movement trajectory does not affect our study of trial-by-trial learning. Trials where the subject did not complete the full reaching movement in the y -direction were excluded ($< 5\%$ of trials in both experiments). Position and velocity data that were directly available from data acquisition were filtered using a fourth-order Butterworth low-pass filter (cut-off frequency 12 Hz) before resampling to obtain spatial trajectories characterized by 200 points that are evenly spread in the y -direction. The velocity data were differentiated to obtain the acceleration profile. In *experiment 2*, the force measured by force channels was not filtered.

Under normal circumstances without perturbation, the hand reaching does not produce a perfectly straight path but shows some asymmetry, which can be viewed as a bias existing universally across all trials. Averaging all catch trials that did not follow perturbation trials yielded a good approximation of the bias in the natural (asymmetrical) path of the subject's reaching movement. This average was

subtracted from each trial, effectively eliminating the asymmetry. The perturbation trials and the catch trials following perturbations were grouped and averaged according to conditions. To compare between these trajectories, linear correlation was performed in a pairwise fashion among conditions. Because we are only interested in how much they are correlated and not in what direction they are correlated, only absolute values of the correlation coefficients are reported.

To study the force developed in catch trials to cope with perturbations, we analyzed acceleration trajectories which share the same form as force trajectories subjects produce at the hand (*experiment 1*) and force profiles invoked by the force channel (*experiment 2*). We performed most of our analyses on these data because they directly reflect the corresponding strategies (forces) subjects developed to compensate for perturbations. Using the fact that these trajectories are rather symmetrical for perturbations in the two opposite directions (Fig. 2), we mirrored the trajectory in the left of the workspace to the right and only analyzed the average trajectory of these two trajectories. Mathematically this was achieved by subtracting the acceleration/force in the left workspace from the acceleration/force in the right workspace. This averaging captures the form of trajectory and also reduces the number of condition comparisons and we simply call these averages the acceleration trajectory (*experiment 1*) and the force trajectory (*experiment 2*) throughout the paper. Principal component analysis was performed on these trajectories from different conditions to evaluate their similarities and differences.

To quantify how much the shape of the corrective response can be accounted by the just experienced perturbation, we decomposed the acceleration/force trajectory in the catch trial into two components: one is a scaled version of the acceleration/force trajectory in the preceding perturbation trial and the other is a generic (common) trajectory across conditions

$$X_{\text{catch},i} = \alpha X_{\text{perturbation},i} + X_{\text{generic}}$$

$X_{\text{catch},i}$ is the acceleration/force trajectory in the catch trial for the i th condition, and $X_{\text{perturbation},i}$ is the acceleration/force trajectory from the corresponding perturbation. These two trajectories are available

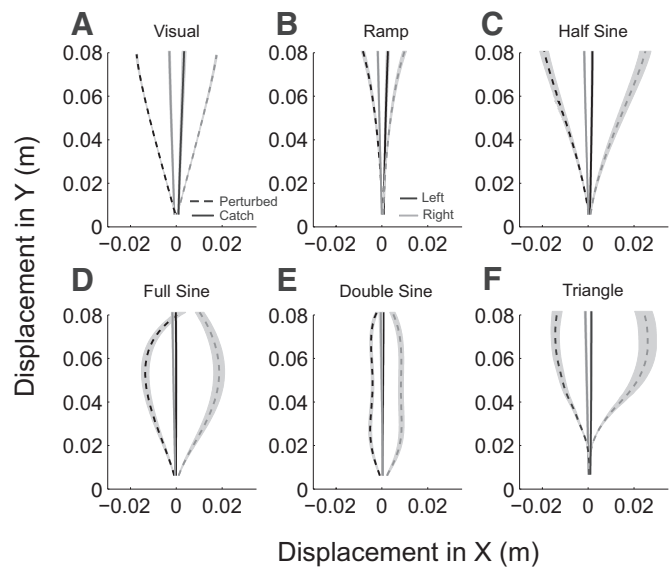


FIG. 2. Average of the hand trajectories from perturbation trials and subsequent catch trials are shown for different perturbation conditions separately. The perturbation trials are shown as dash lines and the catch trials as solid lines. Trials with left perturbations are shown in black and right in gray. The gray shades stand for the SE across subjects. Note in the 1st panel that shows the visual perturbation condition, the perturbation trajectories are the displayed visual feedback instead of the actual hand trajectories. Data are only from *experiment 1*; *experiment 2* produced similar data for perturbation trials, but its catch trials have constrained the lateral deviation within 1 mm (data not shown).

from the data. The other two variables can be fitted from the data: X_{generic} is the common acceleration/force trajectory that is shared by different perturbation conditions; α is a weighting variable characterizing how much influence the perturbation trial has on the compensatory response. We used an expectation-maximization (EM) algorithm to fit each subject's data separately. Visuomotor rotation was not included in this analysis because acceleration trajectories in this condition are fairly small around zero in *experiment 1* (see Fig. 3A), and the EM algorithm does not converge on these small values, whereas there is no force perturbation in *experiment 2*. Thus α is a 5 (conditions) \times 1 vector, and X_{generic} is a time series vector that has the same length as that of the acceleration/force trajectory. We are particularly interested in the absolute amplitude of α : the larger it is, the more the corrective response is related to the specific perturbation.

To understand what error information the nervous system uses to adapt, we calculated the error measures proposed in recent studies on

adaptation in reaching movements. These measures include the absolute distance of the movement end position to the target (endpoint error), the maximal lateral deviation of the hand away from the straight path connecting the starting position and the target, the lateral deviation of the hand from the straight path at the time of maximal speed, the integral of lateral deviations over the course of movement, and the directional error from the straight line at the time of maximal speed (Baddeley et al. 2003; Cheng and Sabes 2007; Donchin et al. 2003; Fine and Thoroughman 2006, 2007; Krakauer et al. 1999; Lai et al. 2003; Osu et al. 2003; Scheidt et al. 2001). We subsequently regressed these measures in the perturbation trials to the first principal component of acceleration/force trajectories in following catch trials. These linear regressions were performed for each type of error measures separately and also for every possible combination of two error measures, in search of the best correlation between error measures and adaptation. We expect that relevant error measures will lead to significant correlations.

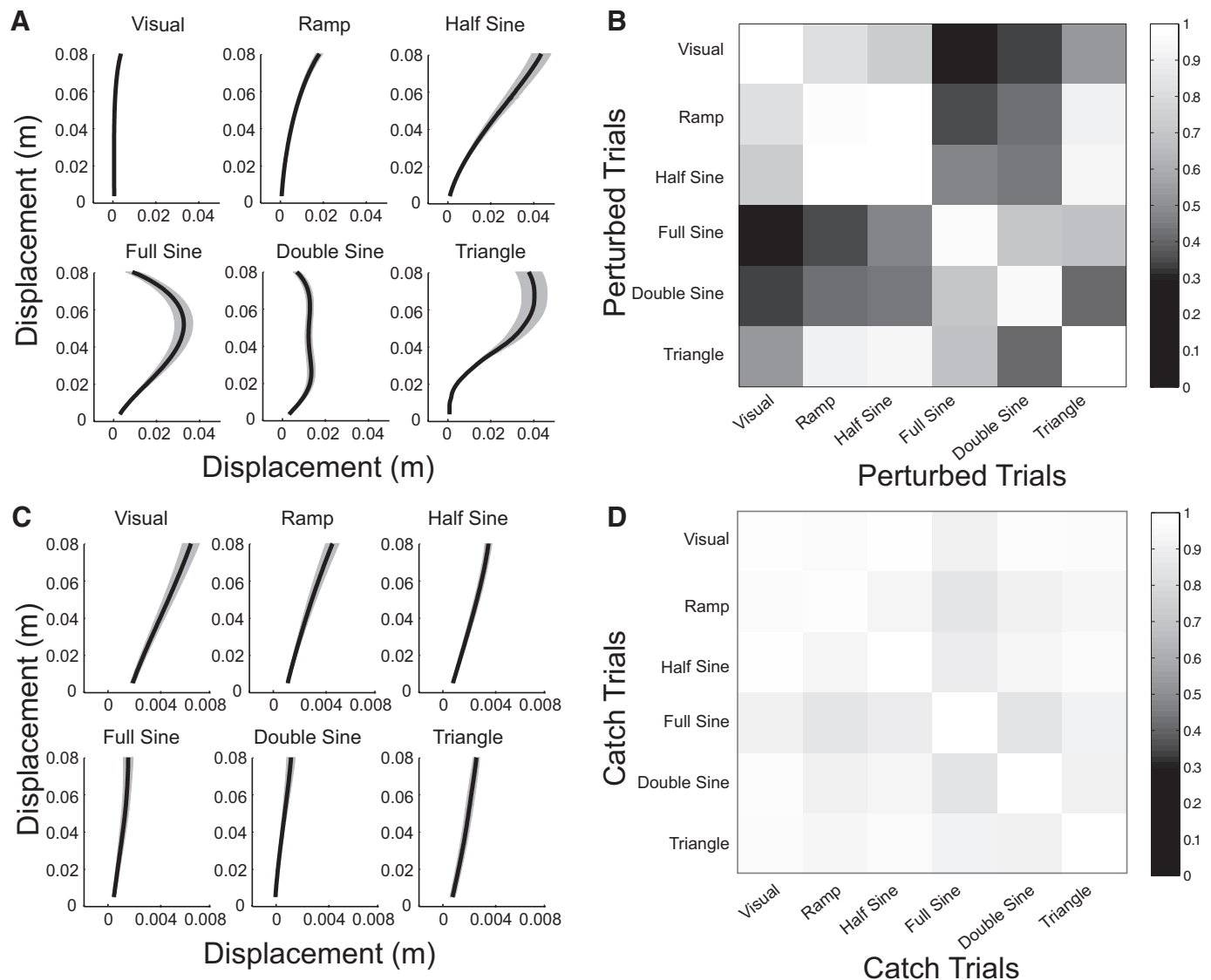


FIG. 3. A and C: the visual trajectories (in the lateral direction) in perturbation trials (A) and catch trials (C) are plotted for different perturbation conditions separately. The black lines are the subject average, and the gray shadowed areas (often tiny) indicate the SE across subjects. B and D: correlation coefficients from cross-correlation analysis of visual trajectories resulted from perturbed trials (B) and catch trials (D) are plotted as a matrix of gray shades. The correlation varies widely across pairwise comparisons for perturbed trials, but on average, they are low, indicating distinct perturbation effects. On the other hand, the correlation coefficients for catch trials are much higher, indicating similar 1-trial learning across conditions. Data are from *experiment 1*; *experiment 2* does not permit analyses of trajectories because it constrained the lateral movements in catch trials by applying strong force channels.

The force measured by using the error-clamp force channel has been proposed as a direct readout of feedforward control signal (Sing et al. 2009). However, a range of studies suggested that goal-directed movement involves two separate control strategies: the early part of the movement relies on feedforward control commands that are particularly relevant for trial-by-trial learning studied here; the later part of the movement relies on feedback-based endpoint control to stabilize at the final goal (Dizio and Lackner 1995; Ghez et al. 2007; Sainburg and Wang 2002; Scheidt and Ghez 2007; Tseng et al. 2007). Based on these early studies, we postulate that the force measured in catch trial carries the signature of feedforward learning in the early segment of the movement that progressively declines toward the movement end. To capture this change, we give weights to the force in catch trials (*experiment 2*) by multiplying with a ramp that linearly changes from 1 to 0 over the course of the movement. Assuming one control scheme transitions into another, the force after this treatment should resemble the acceleration trajectory measured in *experiment 1*.

RESULTS

In our experiment, we measured the after-effects of various perturbations (see Fig. 2) on the subsequent catch trials (no perturbation). The imposed perturbations lead to a sizable effect during the movement on that trial (Fig. 2, dashed). Subjects seem to adapt to the perturbations and exhibit after-effects in the opposite direction on the following trials when no perturbation is applied as in *experiment 1* (Fig. 2, solid). This kind of adaptation effect was expected and has been described in many previous trial-by-trial (Fine and Thoroughman 2006; Scheidt et al. 2001) and block-learning studies (cf. Kawato 1999). In *experiment 2*, the kinematic after-effect in catch trials is absent because the force channel constrained most of trials within a 1 mm wide straight line (data not shown).

For both experiments, the reach trajectories are fundamentally distinct in perturbation trials. The visuomotor rotation leads to a linearly displaced cursor (Fig. 2A, only data from *experiment 1* is shown). Because the movements are relatively

fast, and the presentation of perturbations is random, the visually displaced cursor can only be taken into account during the later part of the reach (not included in the analysis). The ramp perturbation leads to movements that curve away from a straight line, but its effect is very gradual (Fig. 2B). The half sine perturbation leads to trajectories that are perturbed in a roughly linear way (Fig. 2C). The full sine perturbation makes trajectories roughly cosine shaped and toward the end of the movement perturbs the hand back to the target (Fig. 2D). The double sine perturbation roughly translates the trajectory sideways (Fig. 2E). Last, the triangle perturbation results in a quarter sine wave trajectory (Fig. 2F). All these perturbation effects are distinct and produce a range of trajectory shapes, endpoint errors, and errors at the time of maximal velocity. As such, the six perturbations seem to produce a broad range of error information that the nervous system can incorporate in the adaptation process.

Because the perturbation effects are largely symmetrical, we collapsed the movement trajectories averaging the after-effect of the leftward perturbation with the negative after-effect of the rightward perturbation (see METHODS). As such, we reduced the number of conditions and can quantitatively test the difference/similarity of visual errors between perturbation conditions (Fig. 3). Indeed the visual errors in perturbed trials look quite distinct (Fig. 3A): pairwise linear correlation analyses yielded correlation coefficients between 0.27 and 0.98, with an average of 0.60 ± 0.06 (Fig. 3B). This is in sharp contrast to the trajectory errors observed in the catch trials. These movement trajectory appear rather straight (as if subjects aimed for different targets) and stereotypical, and the average correlation coefficient is high at 0.92 ± 0.01 (Fig. 3, C and D). This coarse analysis thus suggests that visual errors resulting from different perturbations are quite distinct, but trial-by-trial adaptation is rather insensitive to these distinct perturbations.

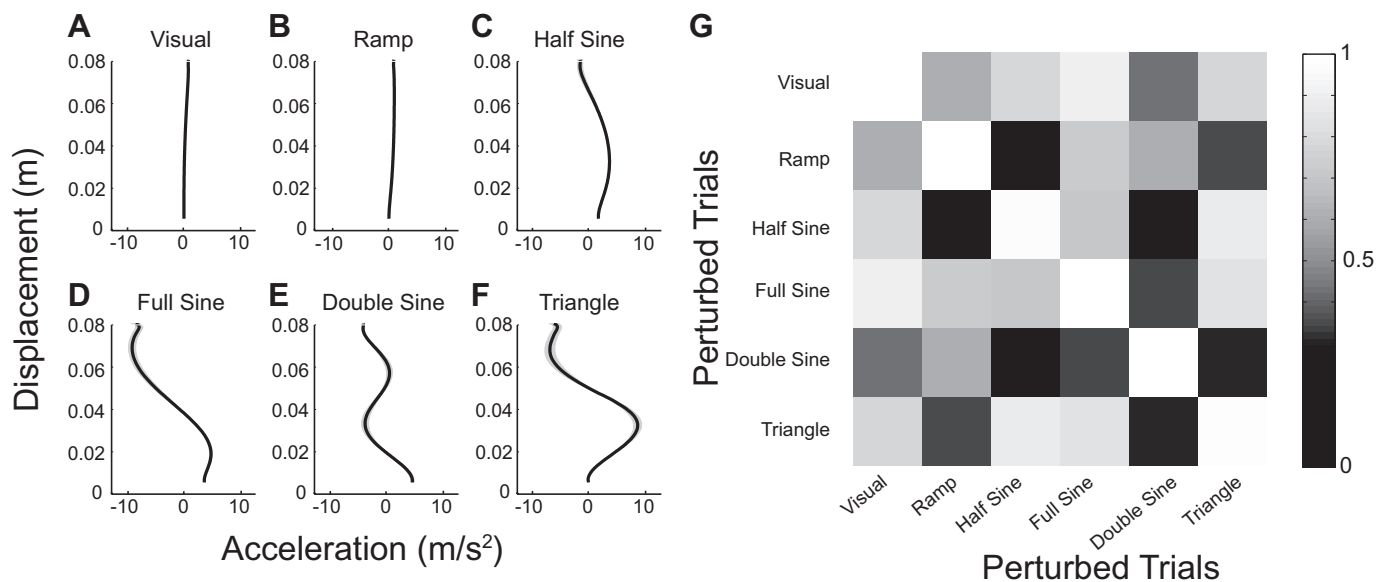


FIG. 4. A–F: the acceleration trajectories (in the lateral direction) in perturbation trials are plotted for different perturbation conditions separately. The black lines are the subject average, and the gray shades (not very visible) stand for the SE across subjects. G: correlation coefficients from cross-correlation analysis of acceleration trajectories resulted from different perturbations are plotted as a matrix of gray shades. The correlation varies widely across these pairwise comparisons, but on average, they are low, indicating distinct perturbation effects. Data are from *experiment 1*; *experiment 2* used identical perturbations and thus produced similar data.

To confirm that the forces experienced by subjects were distinct, we analyzed acceleration trajectories from perturbation trials (Fig. 4, only data from *experiment 1* is shown). These trajectories seem to be different in both amplitude and shape (Fig. 4, A–F). The visuomotor rotation does not induce much lateral acceleration of the hand in the initial portion of these fast reaching movements. The later, feedback-based corrections appear at the very end of these movements and are not included in our analysis. The ramp force perturbation does not show much effect either, because the disturbing forces are small during most of the analyzed movement. All other force perturbations induce very characteristic acceleration profiles. We performed linear correlation between the trajectories from different conditions in a pairwise fashion (Fig. 4G). Correlation coefficients (R) vary from 0.11 to 0.93; on average, the correlations are relatively small (0.58 ± 0.07), indicating the forces experienced on the hand are distinct across perturbations. The smallest correlations were found between the ramp and half sine, the half sine and double sine, and the double sine and triangle (R values of 0.27, 0.11, and 0.28, respectively).

To address how the perturbations affect the corresponding corrective responses, we examined the hand's acceleration/force profiles in catch trials. In *experiment 1*, we found that these acceleration trajectories look remarkably similar in shape across conditions (Fig. 5A).

Recall that, during catch trials, the robot produced no forces, so the similar acceleration profiles indicate subjects produced similar forces under all conditions. This is especially apparent when the acceleration trajectories from all conditions are scaled by their own range and plotted together (Fig. 5B). This suggests that the nervous system may make nonspecific response to distinct but randomly presented perturbations. It should be noted that “initial” accelerations shown in the figure are not zero because these are accelerations measured at 0.5 cm into the movement. Apparently, subjects adapted to the perturbations and decisively moved in the opposite direction of the previous perturbation.

To test the similarity between catch trials from different conditions, we performed correlation analysis on these acceleration trajectories in the same way as we did for the perturbation trials. The correlation coefficient's average value across comparisons was 0.73 ± 0.03 . These correlation coefficients are significantly higher than those found across perturbation trials (compare with data from Fig. 4G; 1-sided paired t -test, $P < 0.05$), indicating the corrective responses are less different from the perturbation trials. In *experiment 2*, forces in the catch trial, measured by the force channel, are not as smooth as the acceleration trajectories (Fig. 5C, black traces). By assigning linearly decreasing weights to force trajectories (Fig. 5C, red traces; see METHODS) in accordance to findings from recent

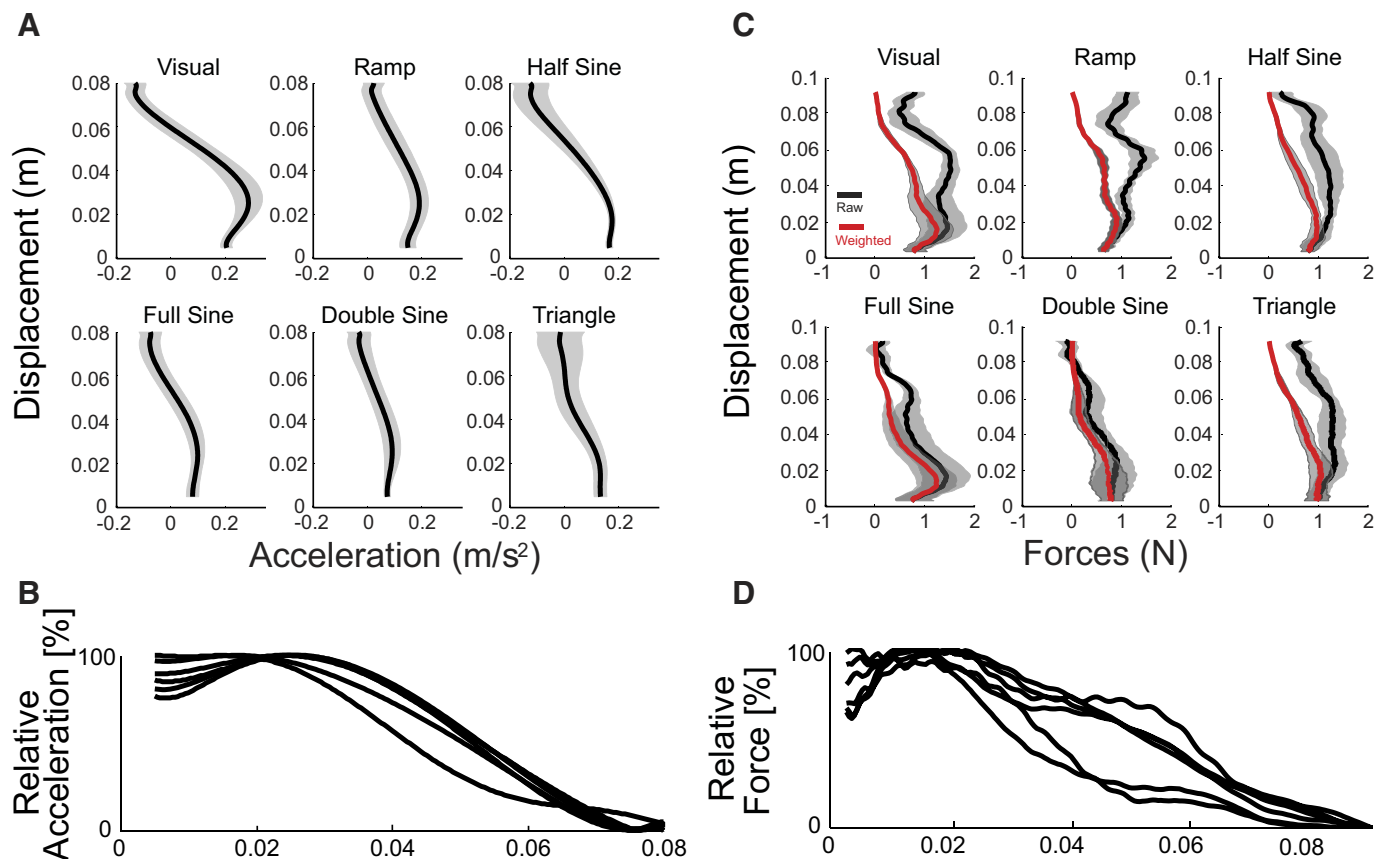


FIG. 5. *A*: the acceleration trajectories (in the lateral direction) in catch trials from *experiment 1* are plotted for different perturbation conditions separately. The black lines are the subject average, and the gray shades stand for the SE across subjects. *B*: the same acceleration trajectories as shown in *A* are scaled according to their own range and stacked together. Each line is from a single condition. *C*: the force trajectories (in the lateral direction) in catch trials from *experiment 2* are plotted for different perturbation conditions separately. The black lines are the subject average, and the gray shades stand for the SE across subjects. The red lines denote the forces that are calculated by multiplying the raw force with decreasing gains. *D*: the force trajectories as shown in *C* are scaled according to their own range and stacked together. Each line is from a single condition.

studies (Dizio and Lackner 1995; Ghez et al. 2007; Sainburg and Wang 2002; Scheidt and Ghez 2007; Tseng et al. 2007), the resultant forces seem to closely resemble those acceleration trajectories in *experiment 1*; more importantly, they also seem similar across different perturbation conditions. This similarity is apparent if they are scaled to their ranges and plotted together (Fig. 5D). Taken together, acceleration trajectories and force trajectories measured in catch trials suggest that first-trial adaptations to different perturbations are remarkably similar.

If a catch trial mirrors its preceding perturbation, it should be more correlated with the preceding perturbation than catch trials following other perturbations. We thus calculated pairwise correlations between perturbation trials and catch trials and displayed the correlation coefficients in a matrix. This correlation was calculated on acceleration trajectory for *experiment 1* and on force trajectory for *experiment 2* (shown in Fig. 6, A and B, respectively). Note the correlation between the perturbation trial and the catch cannot be calculated for visuomotor rotation condition in *experiment 2* because there is no force trajectory for this perturbation (Fig. 6B). If responses to perturbations are specific, the highest correlation coefficient for each row (1 type of perturbation trials vs. all 6 types of catch trials) should fall on the diagonal line of the correlation matrix. However, this is in general not the case, even when we count the second largest correlation for each row. Instead, in *experiment 1*, we found that catch trials after a visuomotor rotation correlated highest with almost all perturbation trials (Fig. 6A). Catch trials following half sine force perturbation correlated the second highest, with four of six perturbations. Similarly, in *experiment 2*, the highest or the second highest correlation usually falls off the diagonal line of the correlation matrix (Fig. 6B). We tested further whether these off-diagonal correlations are significantly different from diagonal correlation values. The acceleration trajectories from individual subjects were submitted to bootstrapping, and correlation analysis was subsequently performed. This bootstrapping could not be conducted for *experiment 2* because the force trajectory for perturbation trials was the same across subjects. The average 95% CI of correlations in *experiment 1* (Fig. 6A) was 0.051, whereas

the average difference between the largest correlation and the diagonal correlation was as large as 0.093 (excluding the visuomotor rotation condition because it has the highest correlation value on the diagonal line). Therefore this sanity check confirmed that the pairwise correlation was indeed off-diagonal. Taken together, these results further show that the compensations shown in the catch trials are not specific to the perturbations.

Despite finding that corrective responses are remarkably similar across different perturbations, they might still resemble (or mirror) the previous perturbations but to a very small extent. If mirroring of preceding perturbations is evidenced, it will support that people indeed learned the form of the perturbation in one trial. We thus decomposed the acceleration/force trajectories in catch trials into two components: a generic trajectory for all conditions and a weighted version of the specific acceleration/force trajectories in the preceding perturbation trials (see METHODS). The weight (α) is an indicator of what percentage of the variance in the trajectory shape can be explained by the just experienced perturbation (Fig. 6C). This weight is not significantly different from zero for all conditions except the ramp condition for acceleration trajectory and the triangle condition for the force trajectory ($P < 0.01$ and $P < 0.001$, paired *t*-test), further showing the small or negligible contribution of specific force perturbations on the corrective responses.

The weight (α) is small and close to zero; however, we might ask how negative the weight could be in reality so that we would have had a significant chance (5%) of missing it. This value sets the maximal strength of the specific adaptation that can be expected from our data. The ramp condition, whose α has the largest deviation from zero, has <5% probability of having an α that is more negative than -0.15 (bound obtained from Gaussian statistics). Similarly for each of other conditions, α is no more negative than -0.04 . Previous studies have found that the size of first-trial error correction is of the order of 0.4 (Krakauer et al. 1999; van Beers 2009). Hence, the perturbation-specific component of the adaptation for trial-by-trial perturbations thus seems to be smaller in comparison to the total error correction by an order of magnitude.

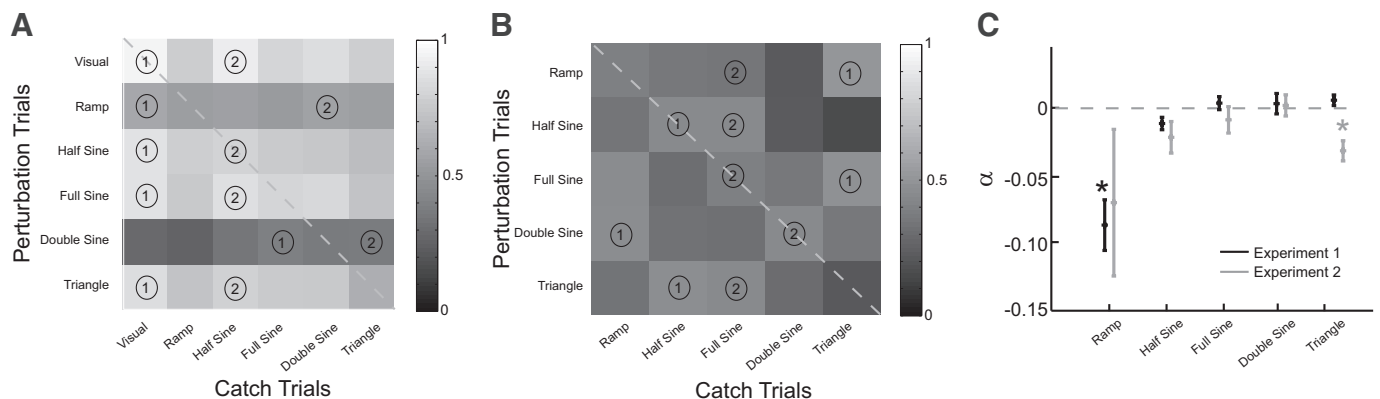


FIG. 6. A and B: correlation coefficients of pairwise correlation between perturbation trials and catch trials are displayed as gray shades for *experiment 1* and *experiment 2*, respectively. The correlation analysis is performed on acceleration trajectories for *experiment 1* and force trajectories for *experiment 2*. If the catch trial is specific to its preceding perturbation trial, the largest correlation should be found for their pairwise correlation, which lies on the diagonal that is displayed as a gray dash line. The largest correlation and the 2nd largest correlation on each row are shown, most of which are not on the diagonal line. This suggests there is no close correspondence between the perturbation and its corresponding catch trial. C: the influence (α) of the perturbation trial onto corrective responses in the catch trial is plotted as a function of conditions. None of the conditions has influence significantly different from 0 except the ramp condition for *experiment 1* and the triangle condition for *experiment 2*. This indicates that, for most perturbations, the 1st-trial adaptation is not specific.

To quantify the dimensionality of different perturbations and their corresponding compensations, we applied principal component analysis (PCA) to acceleration trajectories in *experiment 1*. Subsequently, we can study how different perturbation trials and their subsequent catch trials are by comparing their principal components. This comparison was not performed for *experiment 2* because perturbation forces were deterministic, and we cannot calculate PCA components on perturbation trials. The PCA was performed on acceleration trajectories for each condition separately (data as shown in Figs. 4 and 5). For perturbation trials, the first and second components explained 81.0 ± 2.6 and $14.7 \pm 2.1\%$ of the total variance across conditions, respectively. For catch trials, the first two components explained 71.5 ± 3.1 and $23.8 \pm 3.4\%$ of the total variance, respectively. Hence most of variance in the acceleration profile can be explained with two PCA components for our data set. Central to our study, we want to know whether perturbations used in our experiment generated distinct perturbing effects and whether the corrective responses are indeed similar across these perturbations. To compare conditions using PCA, a standard procedure is to calculate the angles between these PCA components. If these conditions are very different, the components should orient orthogonal to each other with an angle close to 90° . On the other hand, if they are similar, the angle between components should be close to zero (Krzanowski 1979). The pairwise comparisons of six conditions yield 15 angles. If the first two largest PCA components are considered, perturbation trials yield an average angle of $13.3 \pm 4.2^\circ$ and catch trials yield $4.2 \pm 0.8^\circ$. One-way ANOVA indicated that the angles between perturbation trials are significantly larger than those between catch trials ($P < 0.005$). To conclude that angles between catch trials are small, whereas the angles between perturbation trials are large, we performed permutation test to see what angles can be expected from a random set of acceleration trajectories. All the acceleration trajectories in the analysis above were randomly re-grouped into six conditions, and relative angles were calculated based on this permuted data set. We performed this calculation 1,000 times. The average angle from the permutation test is 5.8° for perturbation trials and 6.2° for catch trials. For perturbation trials, the angle from the real data set is significantly larger than the permuted one ($P < 0.0001$; the P value is calculated as percentage of angles from permutation tests that are larger than the angle from real data set; this definition of P value is more appropriate as it does not require an assumption of normality). For catch trials, the angle from the real data set is near the 95% percentile of the angles from permutation test ($P > 0.95$). This indicates the angles between perturbation trials are indeed large, whereas the angles between catch trials are indeed small. Taken together, by comparing the acceleration trajectories from different conditions using PCA, we found that perturbation trials are rather distinct, whereas the corresponding corrective responses are rather similar.

If the nature of a random perturbation has no impact on the form of the corrective response, we may ask which aspects of movement errors give rise to the observed responses. The kinematic errors (Fig. 3) and the forces (by experimental design) experienced by subjects for different perturbations are dramatically different and may be correlated with adaptation. To quantify this, we performed a linear regression between various kinds of error measures (see METHODS) and the first

principal component of the acceleration/force trajectory in catch trials. The reason to use the first PCA component is that the acceleration/force profiles from different conditions seem to be scaled versions of the same trajectory and the first PCA components, which presumably indicate the amplitude of scaling, captures most of the variance (71.5 ± 3.1 and $60.3 \pm 3.8\%$ for acceleration and force trajectories, respectively). We computed the error measures popular in studies of hand reaching, including endpoint error, maximal lateral deviation from a straight line, deviation from a straight path at the time of maximal velocity, integral of deviations from a straight line, directional error at the time of maximal velocity, maximal lateral force applied (0 for visuomotor rotation condition), and maximal lateral acceleration. Surprisingly, none of these correlations yielded significant results, and this result was consistent across all subjects. We also correlated the first principal component to all possible combinations of two different error measures. No systematic results could be found. This lack of correlation can be shown by the scatter plots, where the first principal component is plotted as a function of some selected error measures (Fig. 7). This, from yet another angle, suggests that subjects' response to perturbations is not specific and largely independent of the type of perturbation experienced.

The brain may not generally use nonspecific adaptation in the cases we studied, but it might gradually learn to use them over the course of the experiment (meta-learning). If this is the case, the nonspecific corrections would not be fundamental but rather the result of learning the statistical distribution of perturbations. If meta-learning was the reason, the corrective responses at the beginning of the experiment should be different from those at the end of the experiment. We thus compared the pairwise correlation between the first and second trials, the first and middle trials, and the first and last trials. These three correlation coefficients serve as measures of how similar later after-effects are with earlier ones. Meta-learning should lead to decreasing correlation over time. For both experiments, two-way ANOVA (3 timing \times 6 conditions) did not identify evidence of learning with the main effect of timing ($P = 0.58$ and 0.32 for *experiment 1* and *experiment 2*, respectively). Neither main effect of perturbation conditions ($P = 0.61$ and 0.34 for 2 experiments, respectively) nor interaction effect ($P = 0.96$ and 0.29) was significant. Second, we performed the decomposition analysis to parse each trajectory (the 1st, the middle, and the last trial) into a generic component and a perturbation-specific component. The specificity should increase over these trials if meta-learning is in effect. However, again, two-way ANOVA over the weight of specificity (α) did not find any significant effect on timing ($P = 0.24$ and 0.86 for *experiment 1* and *experiment 2*, respectively), perturbation ($P = 0.07$ and 0.96), and their interaction ($P = 0.23$ and 0.99). Note that the analyses of meta-learning here also did not find any significant difference between perturbation conditions, in accordance to various results reported above. It does not seem that meta-learning strongly affected our results.

DISCUSSION

We used a random sequence of perturbations to analyze trial-by-trial adaptation. We found that corrections from trial to trial depend on the main direction of a perturbation but are similar regardless of the nature of the previously experienced

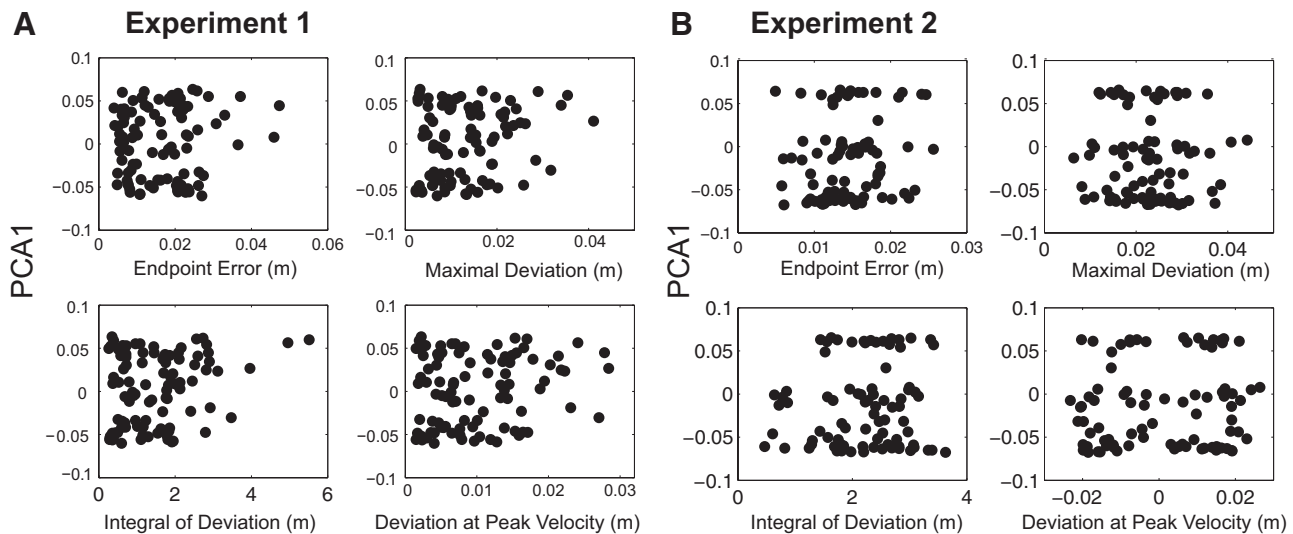


FIG. 7. *A* and *B*: the 1st principal components of acceleration trajectories (*A*, *experiment 1*) and force trajectories (*B*, *experiment 2*) in catch trials are plotted against error measures in its preceding perturbation trials. These error measures, shown by different subplots, include the movement endpoint error, the maximal lateral deviation of the hand from the straight path, the integral of the deviation over the movement, and the deviation at the peak velocity of the reach, respectively. There is no visible dependence of between the trajectory and these error metrics.

perturbation. This finding suggests that the responses to random perturbations are nonspecific to the form of the perturbation, at least for the diversified position-dependent force perturbations and visuomotor rotation explored in this study. We found that the shape and magnitude of these nonspecific responses are not significantly correlated with a number of error measures in the previous trial. Our results thus indicate that, during trial-by-trial adaptation with random perturbations, although the nervous system learns to oppose perturbations, it does so in a manner that is independent of the specific nature of the perturbations.

Our findings differ from the predictions of typical state space models in trial-by-trial adaptation (Baddeley et al. 2003; Donchin et al. 2003; Fine and Thoroughman 2007). These models usually assume that the nervous system linearly adapts to each movement error. When the same perturbation is applied repetitively, these models generally predict an exponential learning curve toward complete adaptation, which has been observed in various motor adaptation studies. With block learning, subjects can produce forces that very well cancel force perturbations such as a velocity-dependent force field (Shadmehr and Mussa-Ivaldi 1994; Thoroughman et al. 2007), position-dependent force field (Tong et al. 2002), and altered inertial property of the limb (Krakauer et al. 1999). They can also produce movements that cancel a visual perturbation such as a visuomotor rotation (Ghahramani and Wolpert 1997; Pine et al. 1996). For trial-by-trial adaptation to perturbations of varying nature, state space models similarly predict a partial learning for each perturbation and a small adaptive response as a function of the perturbation. However, our study did not find any miniature mirroring of the preceding perturbation in adaptive responses. The spatiotemporal features of these responses remain rather stereotypical for different perturbations. Multiple factors might contribute to this nonspecific adaptation to random perturbations, which we will discuss in the following paragraphs.

One relevant factor may be limitations of the perceptual system (proprioception in particular) for sensing the perturbing

force. This may prevent the brain from estimating the exact form of a perturbation in a single trial. This can be the case for the five position-dependent force fields used in this study. However, for the visuomotor rotation, there is no need to rely on proprioception because the perturbation is visual. Despite the typically high precision of visual information, the correction after a single visuomotor rotation was still partial and, more importantly, indistinguishable from corrections for other perturbations. This suggests that, when the perturbation is perceived precisely, the nervous system still seems uncertain about the perturbation. On the other hand, it is relatively easy for the nervous system to detect the direction of the perturbation because the subsequent compensation always opposes the direction of the previous perturbation.

Sing et al. (2009) proposed that the lack of specific adaptation is caused by the similarity between seemingly different force perturbations in the context of muscle spindle signals. This view is similar to our conjectures that limitation of the perceptual system is the reason underlying the nonspecific response. However, contrary to our finding of similar adaptation to different perturbations, they found that distinct force fields (position-, velocity-dependent, or combinations of both force fields) could induce different first-trial learning patterns. One possible reason for this discrepancy is that they presented a type of perturbation intermittently, with wash-out trials (without force perturbations) and error-clamp trials in between. Through meta-learning, subjects in the study of Sing et al. may have learned about the way the experiment was evolving. Because our study had an unpredictable distribution of perturbations, in our case, meta-learning should favor a behavior in which learning largely goes away, which we did not observe. As a result, subjects in their experiment could compensate for different perturbations without much uncertainty about the nature of the perturbation. In this study, we presented subjects with random perturbations, which rendered subjects with large uncertainty about incoming perturbations, which may have led to the observed nonspecific adaptation.

The lack of specificity in trial-by-trial adaptation might suggest that forming an accurate internal model needs repetitive exposure to the same perturbation. In perturbation studies with block design, subjects gradually change their compensation (in terms of movement trajectory or force profile) to “mirror” the perturbation (Shadmehr and Mussa-Ivaldi 1994), indicating that forming an internal model involves an incremental learning process. It has been recently proposed that an optimal strategy for motor adaptation demands estimation of perturbations, a process that involves a statistical inference based on noisy percepts (Berniker and Körding 2008). In this model, a sequence of trials is needed for the nervous system simply to be able to determine the nature of a perturbation. Our results suggest that the brain cannot adapt well if multiple exposures to a single type of perturbation are interspersed by other perturbations.

Two other studies on motor perturbation provided indirect support for the statistical inference account for estimating perturbations. Fine and Thoroughman (2007) perturbed subjects' forward reaching movements either to the left or to the right by velocity-dependent force. For some conditions the directions of random force perturbations were either equally likely or biased to one side. For the other condition, the direction of the perturbation was fixed but the occurrence of the perturbation was varied from rarely to more often. They found that adaptation to perturbations were more pronounced when the perturbation were more biased to one direction or applied more frequently. From our statistical account, this increasing directional bias and occurrence of the perturbation make the nervous system more certain about the form of the perturbation. In turn, the nervous system is more ready to adapt to the perturbations. Braun et al. (2009) recently examined how subjects adapted to visuomotor rotation perturbations where the angles of the rotation were unpredictable. They found that over a few learning trials, subjects' correction converged to stereotypical patterns. The results of these two studies, along with findings of this study, suggest that the perturbation itself is not the only determinant for adaptation and the statistical property of the perturbation sequence also shapes the compensatory response.

Previous studies have suggested that motor learning involves multiple processes adapting at different rates to disturbances of comparable time scales (Berniker and Körding 2008; Körding et al. 2007; Smith et al. 2006). The observable learning effect is thus a combination of multiple processes. In this study, the perturbations vary frequently from trial to trial and potentially lead to learning that is dominated by fast responses. We provide evidence that adaption on this fast time scale is nonspecific to the spatiotemporal pattern of the perturbation but rather consistent for countering the direction of the perturbation.

The finding of nonspecific adaptation also has implications for error reduction that are commonly reported in motor adaptation studies. A general finding in blocked-designed studies is that the second trial after initial exposure to a perturbation, the trial equivalent to the catch trial of our trial-by-trial design, already exhibits substantial improvement in performance. For example, the initial error after imposing visuomotor rotation perturbation is reduced by ~40% in a single trial (Krakauer et al. 1999). Similarly, in a reaching experiment without perturbations, 46% of endpoint error is corrected in the second trial

(van Beers 2009). In our study, we did not evaluate the error reduction (endpoint errors for example) because it involves feedback-based correction at the end of reach. Instead, we were interested in how much people learn from random perturbations and how much they shape their correction accordingly in the following trial. Interestingly, the trajectories of catch trials have minimal resemblance to the spatiotemporal signature of perturbations. This result thus suggests that large error reduction in initial learning does not necessarily require formation of a “partial” internal model of the just-experienced perturbation. Feedback-based error correction can be a large contributor to the error reduction in early learning.

Our results also suggest that the first reaction of the nervous system to perturbations is to act to impede their influences, regardless of the exact nature of the perturbation. Indeed, such behavior has been shown during adaptation of reaching movements in an unstable forcefield (Osu et al. 2003). Osu et al. found that subjects would move their hands in the opposite direction of the previous perturbing force, even though this strategy was inappropriate and would lead to movement errors. It was only after extensive training that they were able to reduce errors by increasing the impedance of the arm. The sensitivity to the direction but not the nature of the perturbation is consistent to the finding that after-effects during trial-by-trial adaptation are categorical (Fine and Thoroughman 2006). All perturbations in that study were brief force pulses pushing the hand to the left or right randomly at different locations on the movement trajectory. The compensatory response in the next trial was also found to be in the opposite direction of the perturbation without dependence on the location and the magnitude of perturbation. However, here we showed that such stereotypical trial-by-trial adaptation is not only relevant for force pulses applied at different positions along a movement trajectory but also for a wide range of different perturbations. Most interestingly, our study also showed that adaptation to visuomotor rotation, a perturbation having no external force applied and thus leading to no perturbed spindle signals, is indistinguishable from adaptation to various force fields.

Recent findings of complex spike activity of Purkinje cells in cerebellum might serve as the neural basis of a categorical adaptation strategy. The cerebellum has long been associated with motor adaptation, and complex spike activity has been postulated to be error signals that drive the adaptation (Marr 1969). Soetedjo and Fuchs (2006) measured the activity of Purkinje cells in the vermis of the oculomotor cerebellum when monkeys performed a saccadic adaptation task. In this adaptation task, the visual target jumped during saccades and the monkey adapted to this perturbation gradually over trials (McLaughlin 1967). Similar to the perturbations used in our reaching experiment, their perturbations were also randomly presented in two opposite directions. They found that complex spike activity of adaptation-related Purkinje cells was highly modulated by the direction of the error. However, the complex spike activity did not show consistent changes when the error was progressively reduced over adaptation to repetitive perturbations. It seems that the error signal driving the adaptation is insensitive to the error size but sensitive to the direction of the perturbation. This is consistent with our behavioral findings that hand movements always oppose the previous perturbation directionally but do not depend on the nature of the perturbation. If the same complex spike activity pattern can be found

during adaptation of voluntary reaching movements, it will not only provide neurophysiological underpinnings for our findings, but also speaks to a common role of complex spikes in motor adaptation across various tasks and motor effectors.

This experiment aimed at examining how subjects exhibit specific adaptation to different types of perturbations in a trial-by-trial paradigm. We instead found that, under these conditions, subjects adapt to perturbations in a nonspecific way. This study raises a good number of questions. For instance, how does the transition from nonspecific trial-by-trial adaptation to specific blocked adaptation occur? Are there different brain areas involved? How could current models of motor adaptation, such as state space models, be modified to fully account for these results? Answers to these questions will constitute new constraints on the mechanisms used by the nervous system for motor adaptation.

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DISCLOSURES

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

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