The nervous system uses nonspecific motor learning in response to uncertain perturbations

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Abstract

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 utilize 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 investigate 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 (Redding et al., 2005; Dionne and Henriques, 2008), 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) as well as 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. 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; but 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 investigate this problem (e.g., Scheidt et al., 2001; Baddeley et al., 2003; Fine and Thoroughman, 2007; Wei and Körding, 2009). The nature of perturbations
has not been systematically varied in this paradigm and little is known about how the nervous
c 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 employs a nonspecific adaptation strategy when it is uncertain about
perturbations of varying nature.

Methods
The present 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 details and then introduce Experiment 2 and its differences.

*Experimental procedure (Experiment 1)*

Eight naive 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 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 which 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 1008 reaching movements, resulting in approximately one hour of participation.

Insert Figure 1 here.

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 second 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. Then 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. Since the focus of the current study is on how subjects adapt to a previously experienced perturbation, this serves to minimize any response to ongoing perturbations.

Half of the movements were affected by one out of 6 possible perturbations that were randomly selected while 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 5 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 4N in the ramp condition and 8N 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 504 perturbation trials. 504 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 re-sampling 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:

\[ F = K \cdot \dot{x} + D \cdot v_x \]

Where \( \dot{x} \) 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 -6000 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 2000Hz to meet the high demands of producing realistic force channel. The error-clamping force channel effectively limited lateral deviation from a straight-line to about 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 ($y < 0.5$ cm and $>8$ cm) were excluded from the analysis. Due to 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 is 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 exclude only 3mm of the initial movement trajectory as the force channel constrained the initial drift and 8mm of the trajectory end owing to improved movement-termination judgment in the data acquisition program. Nevertheless, we argue that the exclusion of partial movement trajectory do not affect our investigation of trial-by-trial learning. Trials where the subject did not complete the full reaching movement in the $y$-direction were excluded (less than 5% of trials in both experiments). Position and velocity data that were directly available from data acquisition were filtered using a 4th order Butterworth low pass filter (cutoff frequency 12 Hz) before re-sampling to obtain spatial trajectories characterized by 200 points that are evenly spread in the $y$ direction. The velocity data was 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 show 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 pair-wise fashion among conditions. Since 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 investigate 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 as 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:

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

$X_{catch,i}$ is the acceleration/force trajectory in the catch trial for the $i^{th}$ condition and $X_{perturbation,i}$ is the acceleration/force trajectory from the corresponding perturbation trial. These two trajectories are available 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; $\alpha$ is a weighting variable characterizing how much influence the perturbation trial has on the compensatory response. We utilized expectation-maximization (EM) algorithm to fit each subject’s data separately. Visuomotor rotation was not included in this analysis since acceleration trajectories in this condition are fairly small around zero in Experiment 1 (see Fig 3A) and EM algorithm does not converge on these small values, while there is no force perturbation in Experiment 2. Thus, $\alpha$ is a 5 (conditions) $\times$ 1 vector and $X_{generic}$ is a time-series vector which has the same length as that of the acceleration/force trajectory. We are particularly interested in the absolute amplitude of $\alpha$: 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 (Krakauer et al., 1999;
Scheidt et al., 2001; Baddeley et al., 2003; Donchin et al., 2003; Lai et al., 2003; Osu et al.,
2003; Fine and Thoroughman, 2006; Cheng and Sabes, 2007; Fine and Thoroughman, 2007). 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.

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 have
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 investigated in the present paper; the later part of the movement relies on feedback-
based endpoint control to stabilize at the final goal (Dizio and Lackner, 1995; Sainburg and
Wang, 2002; Ghez et al., 2007; Scheidt and Ghez, 2007; Tseng et al., 2007). Based on these
everal studies, we postulate that the force measured in catch trial carries the signature of
feedforward learning in the early segment of the movement which progressively declines
towards 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 aftereffects 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 appear to adapt to the perturbations and exhibit aftereffects 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 (e.g., Scheidt et al., 2001; Fine and Thoroughman, 2006), and block-learning studies (cf. Kawato, 1999). In Experiment 2, the kinematic aftereffect in catch trials is absent as the force channel constrained most of trials within a 1mm-wide straight line (not shown).

Insert Figure 2 here.

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). Since 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 be roughly cosine shaped and towards 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). Lastly, 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 6 perturbations appear to produce a broad range of error information that the nervous system can incorporate in the adaptation process.

As the perturbation effects are largely symmetrical, we collapsed the movement trajectories averaging the aftereffect of the leftward perturbation with the negative aftereffect of the rightward perturbation (see Method). As such we reduced the number of conditions and can then 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): pair-wise 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 are high at 0.92 ± 0.01 (Fig 3C and 3D).

This coarse analysis thus suggest that visual errors resulted from different perturbations are quite distinct but trial-by-trial adaptation is rather insensitive to these distinct perturbations.

Insert Figure 3 here.

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 appear to be different in both amplitudes and shapes (Fig 4A-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, since 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 pair-wise 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).

Insert Figure 4 here.

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 find 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 since 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; one-sided paired t-test, p < 0.05), indicating the corrective responses are less different than the perturbation trials are. In Experiment 2, forces in 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 Method) in accordance to findings from recent studies (Dizio and Lackner, 1995; Sainburg and Wang, 2002; Ghez et al., 2007; Scheidt and Ghez, 2007; Tseng et al., 2007), the resultant forces appear to closely resemble those acceleration trajectories in Experiment 1; and more importantly, they also appear 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.

Insert Figure 5 here.

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 pair-wise 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 6A and 6B, respectively). Note the
correlation between the perturbation trial and the catch can not be calculated for visuomotor
rotation condition in Experiment 2 as there is no force trajectory for this perturbation (Fig 6B). If
responses to perturbations are specific, the highest correlation coefficient for each row (one 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 find that catch trials following a
visuomotor rotation correlated highest with almost all perturbation trials (Fig 6A). Catch trials
following half sine force perturbation correlated the second highest with 4 out of 6 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 as the
force trajectory for perturbation trials was the same across subjects. The average 95% confidence
interval of correlations in Experiment 1 (Fig 6A) was 0.051; while the average difference
between the largest correlation and the diagonal correlation was as large as 0.093 (excluding the
visuomotor rotation condition as it has the highest correlation value on the diagonal line).
Therefore this sanity check confirmed that the pair-wise correlation was indeed off-diagonal.
Taken together, these results further demonstrate that the compensations shown in the catch trials
are not specific to the perturbations.

Insert Figure 6 here.
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 Method). The weight ($\alpha$) 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 demonstrating the small or negligible contribution of specific force perturbations on the corrective responses.

The weight ($\alpha$) 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 $\alpha$ has the largest deviation from zero, has less than 5% probability of having an $\alpha$ that is more negative than -0.15 (bound obtained from Gaussian statistics). Similarly for each of other conditions, $\alpha$ 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.
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 investigate how different perturbation trials and their subsequent catch trials are by comparing their principal components. This comparison was not performed for Experiment 2 since perturbation forces were deterministic and we cannot calculate PCA analysis on perturbation trials. The PCA was performed on acceleration trajectories for each condition separately (data as shown in Fig 4 and Fig 5). For perturbation trials, the first and second components explain 81.0 ± 2.6% and 14.7 ± 2.1% of the total variance across conditions, respectively. For catch trials, the first two components explained 71.5 ± 3.1 % and 23.8 ± 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 employed in our experiment generated distinct perturbing effects and whether the corrective responses are indeed similar across these perturbations. To compare conditions using the principal component analysis, 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 degrees. On the other hand, if they are similar, the angle between components should be close to zero (Krzanowski, 1979). The pair-wise comparisons of 6 conditions yield 15 angles. If the first two largest PCA components are considered, perturbation trials yield an average angle of 13.3 ± 4.2° and catch trials yield 4.2 ± 0.8°. One-way ANOVA indicated that the angles between perturbation trials are significantly larger than those between catch trials (p < 0.005). In order to conclude that angles between catch trials are small while 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 regrouped into 6 conditions and
then relative angles were calculated based on this permutated data set. We performed this
calculation 1000 times. The average angle from the permutation test is 5.8° for perturbation
trials and 6.2° degrees for catch trials. For perturbation trials, the angle from the real data set is
significantly larger than the permutated one ($p < 0.0001$; $p$ 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 while 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 while
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 then 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 appear 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 ± 3.8% for acceleration and force trajectories, respectively). We
computed the error measures popular in studies of hand reaching, including end point 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 (zero 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 illustrated 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 non-specific 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 non-specific corrections would not be fundamental but rather the result of learning the
statistical distribution of perturbations. If meta-learning was the reason then the corrective
responses at the beginning of the experiment should be different from those at the end of the
experiment. We thus compared the pair-wise correlation between the first and the second trial,
the first and the middle trial and the first and the last trial. These 3 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 × 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 two experiments, respectively) nor interaction effect \((p = 0.96\) and 0.29) were significant. Secondly, we performed the decomposition analysis to parse each trajectory (the first, the middle and the last trial) into a generic component and a perturbation-specific component (see above and also in the Methods). The specificity should increase over these trials if meta-learning is in effect. However, again, two-way ANOVA over the weight of specificity \((\alpha)\) 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 appear that meta-learning strongly affected our results.

**Discussion**

We have used a random sequence of perturbations to analyze trial-by-trial adaptation. We have 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 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 the present study. We find 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 towards 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 (Pine et al., 1996; Ghahramani and Wolpert, 1997). 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 employed in this study. However, for the visuomotor rotation, there is no need to rely on proprioception as the perturbation is visual. Despite the typically high precision of visual information, the correction following 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 as such the subsequent compensation always opposes the direction of the
previous perturbation.

Sing and colleagues proposed that the lack of specific adaptation is due to the similarity
between seemingly different force perturbations in the context of muscle spindle signals (Sing et
al., 2009). This view is similar to our conjectures that limitation of the perceptual system is the
reason underlying the nonspecific response. However, as 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, only with wash-out trials (without force perturbations) and error-clamp trials in
between. Through meta-learning subjects in the Sing et al.’s study may have learned about the
way the experiment was evolving. As our study has an unpredictable distribution of perturbations
it turns out that 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 the
current study, we presented subjects with random perturbations, which rendered subjects with
large uncertainty about incoming perturbations which may have lead 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 (e.g., 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 perturbed subjects’ forward reaching movements either to the left or to the right by velocity-dependent force (Fine and Thoroughman, 2007). 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 and his colleagues (2009) recently examined how subjects adapted to visuomotor rotation perturbations where the angles of the rotation were unpredictable (Braun et al., 2009). They found that over a few learning trials subjects’ correction converged to stereotypical patterns. The results of these two studies, along with findings of the present study,
suggests 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 (Smith et al., 2006; Körding et al., 2007; Berniker and Körding, 2008). The observable learning effect is thus a combination of multiple processes. In the present 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 about 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) as it involves feedback-based correction at the end of reach. Instead, we are 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 force-field (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 have shown 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 show 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. 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 measured the activity of Purkinje cells in the
vermis of the oculomotor cerebellum when monkeys performed a saccadic adaptation task
(Soetedjo and Fuchs, 2006). 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 appears 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
depends 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 non-specific trial-by-trial adaptation to
specific blocked adaptation occur? Are there different brain areas involved? And, 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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Figure Caption

Figure 1: A). Sketch of the manipulandum and the experimental setup. B-G) Six 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 panel B) the X axis is for displacement and it is different from other panels where X axis is for applied perturbation force.

Figure 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 grey. The grey color shades stand for the standard error across subjects. Note in the first 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 1mm (not shown).

Figure 3: A) and C). The visual trajectories (in the lateral direction) in perturbation trials (A) and in catch trials (C) are plotted for different perturbation conditions separately. The black lines are the subject average and the grey shadowed areas (often tiny) indicate the standard errors 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 pair-wise 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 one-trial learning
across conditions. Data are from Experiment 1; Experiment 2 does not permit analyses of
trajectories as it constrained the lateral movements in catch trials by applying strong force
channels.

Figure 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 grey shades (not very visible) stand for the standard error 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 pair-wise 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.

Figure 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 grey shades stand for the standard error across subjects. B). The same
acceleration trajectories as shown in Panel 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 grey shades stand for the standard
error across subjects. The red lines denote the forces that are calculated by multiplying the raw
force with decreasing gains (see Method). D). The force trajectories as shown in panel C are
scaled according to their own range and stacked together. Each line is from a single condition.

Figure 6: A-B). Correlation coefficients of pair-wise correlation between perturbation trials and
catch trials are displayed as grey 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 pair-wise correlation, which lies on the diagonal
that is displayed as a grey dash line. The largest correlation and the second 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 zero
except the ramp condition for Experiment 1 and the triangle condition for Experiment 2. This
indicates that for most perturbations the first-trial adaptation is not specific.

Figure 7: A-B). The first principal components of acceleration trajectories (panel A, Experiment
1) and force trajectories (panel 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.
Displacement in Y (m)

Displacement in X (m)