

Involvement of the autonomic nervous system in motor adaptation: acceleration or error reduction?

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Abstract In the last few decades motor adaptation was extensively studied observing the invariant features of reaching movements. In a parallel neurobehavioral line of research emotional learning was studied under the umbrella of the ‘two-factor theory of learning’. In this study we explore the relation between motor learning and the autonomic response (heart rate, HR) of subjects performing point to point reaching movements holding a computer mouse. We consider two alternative outcomes: one is that autonomic response correlates with the learning rate and the second is that the autonomic response correlates with the residual error at the steady state. Eighteen subjects performed reaching movements under perturbed visual feedback demonstrating learning and after effects of learning. The hand movement as well as an Electrocardiogram signal were recorded throughout the training and carefully analyzed offline to extract the trial by trial error as well as the heart period. The results show clear correlation between the change in HR and the residual error but no correlation between the change in HR and the learning rate supporting the second alternative that the sensitivity to errors but not the learning rate correlates with the autonomic response. A control group of another seven subjects

underwent the same experiment without the perturbed visual feedback. This control group showed no change in the HR. Further studies are required to validate this hypothesis and unravel the mechanism by which the autonomic response correlates with the residual motor error.

Keywords Perturbation · Reaching movement · Adaptation · Motor learning · Emotional learning · Internal model · RR intervals · HR response

Introduction

The nervous system receives sensory information from the environment and generates motor commands in processes that involve real time feedback and learning. These processes were extensively explored by observing fast reaching movements in humans who were additionally challenged by perturbation forces (Lackner and DiZio 1994; Shadmehr and Mussa-Ivaldi 1994; Wolpert et al. 1995; Flash and Gurevich 1997; Donchin et al. 2003; Karniel and Mussa-Ivaldi 2003; Scheidt et al. 2005; Thoroughman and Taylor 2005). The authors of the textbook about these studies convincingly contend that “all learning depends on motor learning” (Shadmehr and Wise 2005). This study intends to explore in humans the possible relation between emotional learning, as represented by the activity of the autonomic nervous system, and motor learning of arm reaching movements during adaptation to visual perturbation.

Rapid reaching movements are usually well characterized by invariant features of the hand trajectory, a roughly straight line path and a bell shaped speed profile (Morasso 1981; Flash and Hogan 1985). In order to preserve these invariant characteristics under force perturbations the brain

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adapts and demonstrates learning and after-effect of learning (Lackner and DiZio 1994; Shadmehr and Mussa-Ivaldi 1994; Flash and Gurevich 1997). Similar learning phenomena are also observed when the visual feedback is altered in tasks requiring movement of a computer mouse from point to point (Wolpert et al. 1995).

To explain this adaptive behavior it was suggested that the brain represents the environment, e.g., by an internal inverse model, in order to generate the required motor command. A few computational models were proposed to describe these phenomena (Inbar and Yafe 1976; Wolpert et al. 1998; Bhushan and Shadmehr 1999; Gribble and Ostry 2000; Karniel and Inbar 2000; Wolpert and Ghahramani 2000) and it was suggested that the cerebellum is the locus of this adaptive controller (Schweighofer et al. 1998; Kawato 1999; Barlow 2002; Imamizu et al. 2003). All of these models include an adaptive controller and a learning algorithm which modifies the controller in the right direction to reduce the tracking error (the difference between the actual and the intended trajectory). Figure 1 describes this kind of controller in a block diagram, which also includes the possible role of the autonomic response in either modifying the learning rate or modifying the sensitivity to small errors.

The literature dealing with simple motor learning procedures, such as reaching movements, is typically oblivious to the involvement of the emotional-autonomic activity in the learning process. In contrast, autonomic–motor interaction was demonstrated in context of neurobehavioral studies under the umbrella of the ‘two-factor theory of learning’ (Lennartz and Weinberger 1992). This theory predicts that coping with challenging event proceeds through two successive stages of learning. In the first stage, the challenging event triggers unconditioned emotional–autonomic responses and promotes fast acquisition of conditioned emotional–

autonomic responses. These autonomic responses are believed to modulate the level of arousal, redirect the attention and enhance the salience of the relevant information (Davis 1992). By these means, the autonomic responses facilitate the typically slow acquisition of motor responses during the second stage of learning. Eventually, motor responses adapt in the sense that they resolve the challenging situation. Recently, we proposed that the two-factor theory of learning should be supplemented with a third stage during which availability of adaptive motor responses promotes the extinction of the emotional–autonomic responses (Mintz and Wang-Ninio 2001). Such three stage sequence of learning was found particularly relevant for explanation of the interaction between the amygdala-based emotional-fear learning and cerebellar-based amygdala motor learning in animals (Weisz et al. 1992; Mintz and Wang-Ninio 2001; Neufeld and Mintz 2001). Amygdala-based emotional learning (first stage) accelerated, and lesions of the amygdala delayed, the cerebellum-based eyeblink conditioning (second stage) in animals. Successful acquisition of the eyeblink response was associated with extinction of the emotional response (third stage).

In this study we explore the relation between motor learning and the autonomic response (heart rate, HR) of subjects performing point to point reaching movements holding a computer mouse under conditions of perturbed visual feedback. Based on the above ‘three factors theory’, we hypothesize: (a) initiation of the no-perturbation reaching movements will trigger autonomic response which will be extinguished following acquisition of the adaptive movement, (b) initiation of perturbations of the visual feedback will reinstall the autonomic response, which will be again extinguished following motor adaptation. Finally, (c) we expect that the intensity of the autonomic responses will be positively correlated with the quality of motor learning. In a first order approximation, the learning curve could be simulated by a first order differential equation resulting in an exponential decay described by two parameters, the learning rate (or time constant) and the final residual error at the steady state. Under the assumption of casual relation between the autonomic response and the motor learning, one possible influence of autonomic responses is modulation of the motor learning rate; a second alternative is modulation of the sensitivity to the error signal (see Fig. 1).

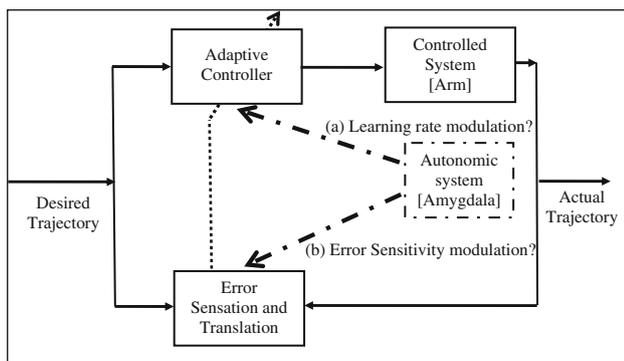


Fig. 1 Motor learning and the autonomous system. We consider two alternatives for the involvement of the autonomous system in motor learning: It can either modulate the learning rate (a) or modulate the sensitivity to small errors (b). The first alternative predicts correlation between the autonomous response (measured here by changes in heart rate) and the motor learning rate and the second predicts correlation between the autonomous response and the final residual motor error

Methods

Subjects

Twenty-five subjects participated in this study after providing their written informed consent. The experimental

group consisted of 17/1 male/female students or faculty 24–42 years of age. The control group consisted of 6/1 male/female students or faculty 25–36 years of age. All were experienced right hand computer users with normal or corrected vision and no reported motor disorders. The experimental protocol was approved by the local Helsinki committee.

Procedures

Subjects were tested individually in the Tel Aviv University Biomedical Signals & Systems Laboratory. They signed the informed consent form and ECG electrodes were applied. Subjects were seated in front of a computer monitor and were instructed about their goal in a simple computer sensory-motor task without revealing the function of the visuomotor transformations. Following the task completion subjects were asked to fill in a short questionnaire.

The sensory-motor task

The task was to hold an optic computer mouse with the right hand and use it to move a cursor from a starting to target locations on a 17" computer screen with refreshing rate set at a 100 Hz ('MS Windows' feature). A wooden board (60 × 80 cm h/w) was used as a mouse pad. It was leaned upon the edge of the table and subject's laps at comfortable angle (range 0–10°) to allow a wide range of hand/mouse movements. The mouse served as the motor extension of the subject's hand and the associated cursor position served for analysis of the hand movements.

Instructions

Subjects were provided with the following instructions: at start, please position the cursor inside the green circle on the left side of the monitor and click on the mouse's left button turning the circle blue (origin). After a 2 s delay, a green circle (target) will appear on the right side of the monitor. Your task is to move the cursor and position it inside the target circle and then to click again on the left button. The right circle will turn blue, the left circle will disappear and reappear after 2 s at the same location as a green target circle. Please repeat the mouse 'move and click' operation towards the pop-up green target circles until the game ends while observing the following constraints:

- Each 'move and click' trial will be rewarded by five points only if: (a) the delay from the pop-up of the target circle to 'click' was shorter than 1.3 s, and, (b) the 'click' was performed with the cursor inside the target circle. Response delay was presented on the

screen by time management indicator designed as a small rectangle frame filled by red color with the passage of time (Fig. 2).

- No reward will be provided for trials with a 'click' outside of the target circle and 5 points will be deducted on trials with a delayed 'click'.
- Please keep the cursor inside the origin circle in-between the 'move and click' trials.
- Please do not rise up the mouse above the wooden board during the 'move and click' trials. You may do so only during the 2 s waiting periods.
- The entire game would take less than 10 min.

Financial reward was provided to motivate good performance. The game consisted of 104 trials with a maximal possible score of 520 points. Subjects were notified that 10 NIS will be granted for a score > 250, 15 NIS for a score > 350, 25 NIS for a score > 450 and 50 NIS will be granted for a score > 500.

Timeline

1. *No-perturbation trials*: Trials 1–36 included no perturbation of the cursor movement.
2. *Perturbation trials*: Trials 37–92 (excluding trials 71 and 78) included vertical perturbation of the cursor movement. This perturbation was excluded from the control experiment.

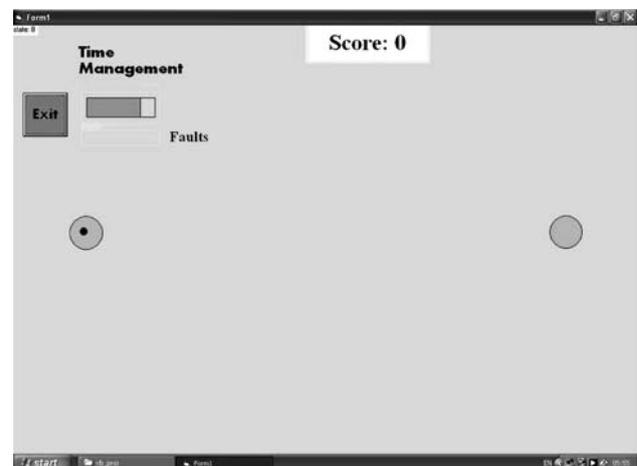


Fig. 2 The task on-screen layout. The two circles changed their designation as 'origin' and 'target' over successive trials; blue and green, respectively. Subjects received on-line feedback on their performance. The 'Time Management' indicator visualized the updated passing time on each trial. The 'Faults' indicator showed the number of trials on which the performance exceeded the 1.3 s threshold duration. The 'Score' indicator showed a cumulative gain of points. The 'exit' button was operational only at the end of the game, after the completion of 104 trials

3. *Catch trials*: Trials 71 (left to right) and 78 (right to left) included no perturbation of the cursor movement (i.e., similar to the no-perturbation trials).
4. *After-effect trials*: Trials 93–104 included no-perturbation of the cursor movement (i.e., similar to the no-perturbation trials).

The graphical application

The game was programmed with a “Visual Basic Studio VB6.0” application. The game was presented over the whole monitor screen ranging 1,024/768 pixels (Fig. 2). The upper left screen corner was defined as $[x, y] = [0, 0]$ and the centers of the two circles (2.6 cm in diameter, and designated interchangeably as ‘origin’ and ‘target’ circles on successive trials) were positioned at $[x_a, y_a] = [106, 346]$ and $[x_b, y_b] = [906, 346]$. The monitor scale conversion was 1 cm = 30.2 pixels implying that the horizontal distance between the two circle centers was 26.5 cm, i.e., 800 pixels. The cursor was shaped as a small dark-blue circle, 0.6 cm in diameter. Its position was refreshed at a rate of 200 Hz (‘MS Windows’ feature) and its x, y center was continuously sampled at a rate of 100 Hz.

Perturbation of cursor position

Perturbation trials included a slight vertical perturbation of the cursor directed to the right of the hand direction. While the cursor perturbation took affect, the ‘original’ cursor reflecting the hand/mouse movement became invisible and only the ‘perturbed’ cursor was seen on screen. In order to prevent perturbation effects during the waiting phases between movements, the perturbation did not start with the onset of each movement, but rather started a small distance from the origin circle, based on the x coordinate of the original cursor. For L → R (i.e., left-to-right) movements the perturbation started from $x_{\text{threshold}} = 256$ coordinate, and for R → L (i.e., right-to-left) movements the perturbation started from $x_{\text{threshold}} = 756$ coordinate. The relation between the perturbed cursor coordinates $[x', y']$ and the original cursor coordinates $[x, y]$ is expressed by Eqs. 1 and 2, for L → R and R → L movements, respectively.

$$\begin{aligned} x' &= x \\ y' &= \begin{cases} y & x \leq 256 \\ y + \alpha \cdot (x - 256) & x > 256 \end{cases} \end{aligned} \quad (1)$$

$$\begin{aligned} x' &= x \\ y' &= \begin{cases} y & x \geq 756 \\ y - \alpha \cdot (756 - x) & x < 756 \end{cases} \end{aligned} \quad (2)$$

The vertical perturbation amplitude α value was set in pilot study to a level of 1/6, small enough to prevent the

awareness of the subjects to its existence. This perturbation wasn’t present during the control group experiments.

Behavioral data analysis

Analysis focuses on the movement path, which was challenged by the perturbation factor. Subjects’ natural hand movements are expected to be horizontal with no diagonal motion. In contrast, during the perturbation trials hand movement angle is expected to be different than 0. For correct directing of the perturbed cursor towards the target circle, the final perturbed cursor coordinates $[x'_f, y'_f]$ should match the target circle coordinates as exemplified for L → R movements by Eq. 3. Therefore, the final original cursor coordinates $[x_f, y_f]$, i.e., the final hand position at the end of the movement, should obey Eq. 4 according to the vertical perturbation equations.

$$x'_f = 906 \quad y'_f = 346 \quad (3)$$

$$\begin{aligned} x_f &= 906 & y_f + \alpha \cdot (x_f - 256) &= 346 \\ y_f &= 238 \end{aligned} \quad (4)$$

The same calculations are obtained for the R → L movements as presented by Eq. 5:

$$\begin{aligned} x_f &= 106 & y_f + \alpha \cdot (756 - x_f) &= 346 \\ y_f &= 454 \end{aligned} \quad (5)$$

Hence, for L → R movements the path of the original cursor (i.e., hand path approximation) is expected to be diagonal directed with a slight upward angle to meet the final coordinates $[x_f, y_f] = [906, 238]$. For R → L movements the path of the original cursor is expected to be diagonal directed with a slight downward angle to meet the final coordinates $[x_f, y_f] = [106, 454]$. The initial angle of the original-invisible cursor path was identified as the β angle created by the imaginary line connecting the original cursor coordinates at Ro with the origin circle coordinates related to the horizon as illustrated in Fig. 3, for each hand movement. Ro is a varied distance from the origin circle, where the original cursor position was found 200 ms after it crossed the coordinates where the perturbation started to take affect. The 200 ms delay was chosen to be short enough to minimize the corrective hand movements due to the visuomotor feedback (Keele and Posner 1968; Beggs and Howarth 1970; Paillard 1996), and to be long enough to allow good evaluation of the feed-forward model learning process.

Hand movement compensation level (i.e., ‘learning’ function) was defined as the tangent value of the β angle, i.e., $\tan(\beta)$. β was considered negative if the hand path direction turned to the left side of the horizon, related to the starting point location.

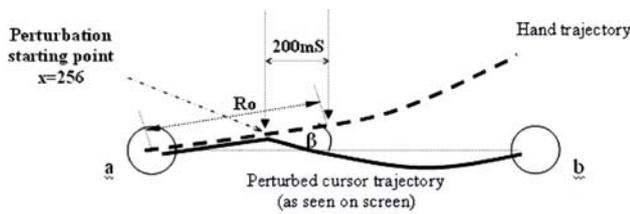


Fig. 3 Example for β angle calculation for L \rightarrow R movement. Perturbed cursor trajectory is presented as *solid line*. Hand trajectory on the board is transformed to the screen coordinates as *dashed line*. β is the angle between the imaginary *horizontal line connecting circles 'a' & 'b'*, and the imaginary line connecting the origin circle 'a' with the original cursor position 200 ms after it crossed the $X = 256$ horizontal coordinate (i.e., at distance of R_0 from 'a' center point). This angle indicates the size of the hand movement path deviation from a horizontal straight path, while compensating for the perturbation

Theoretically, the ideal $\tan(\beta)$ for the perturbed movements (i.e., $\tan(\vartheta)$) can be calculated assuming a straight hand path from the origin circle towards the final coordinates $[x_f, y_f]$. This straight hand path will move the on screen cursor (i.e., the perturbed cursor) straight towards the target circle.

$$\text{For L} \rightarrow \text{R movements : } \tan(\vartheta) = -\frac{y_b - y_f}{x_b - x_a} = -0.135 \tag{6}$$

$$\text{For R} \rightarrow \text{L movements : } \tan(\vartheta) = -\frac{y_f - y_a}{x_b - x_a} = -0.135 \tag{7}$$

The ideal $\tan(\beta)$ of the whole experiment is presented by Eq. 8.

$$\text{ideal } \tan(\beta) = \begin{cases} 0 & \text{Movement\#} \in [1-36, 71, 78, 93-104] \\ -0.135 & \text{Movement\#} \in [37-70, 72-77, 79-92] \end{cases} \tag{8}$$

The individual 'learning function' was defined as $\tan(\beta)$, and the individual 'ERR function' (i.e., error function) was defined by Eq. 9 for each trial.

$$\text{ERR function} = |\tan(\beta) - \text{ideal } \tan(\beta)| \tag{9}$$

ERR function analysis focuses on the perturbation trials 37–70 only, excluding trials 71–80 during which the $\tan(\beta)$ might have been influenced by the 'catch trials'. Each subject ERR function is expected to be represented by a downward curve during the perturbation trials that may be roughly considered to meet an exponential behavior, according to Eq. 10.

$$\text{ERR}(i) \approx \text{ERR}_\infty - (\text{ERR}_\infty - \text{ERR}_0) \cdot e^{-\frac{i-l}{\tau}} \quad i = \text{trial number } l + 1 \dots m \tag{10}$$

$l = 36$

ERR_0 , ERR_∞ and m are individually defined based on the curve of ERR function results, according to Eqs. 11–13.

$$\text{ERR}_0 = \tan(\theta) + E[\text{ERR}(27 \dots 36)] \tag{11}$$

$$\text{ERR}_\infty \equiv \text{ERR}_{\min} = \min(E[\text{ERR}(j \dots j + 9)]) \quad 37 < j < 61 \tag{12}$$

$$m = j \Big|_{E[\text{ERR}(j \dots j + 9)] = \text{ERR}_{\min}} \tag{13}$$

The τ value of each subject was estimated by 'exponential regression' for the i variable based on Eqs. 10–13.

Hence, the performance of individual subjects during the perturbation trials can be characterized by two characteristic values:

1. τ : expresses the rate of the feed-forward motor adaptation.
2. ERR_{\min} : expresses the minimum adaptation error, calculated (according to Eq. 12) as the minimum value of averaged ERR of any 10 consecutive trials during the perturbation trials.

Validation of behavioral data analysis

In order to verify that the results do not depend on the apparent peculiarity of the data analysis, two alternative analysis methods were applied. First, 'learning function' was recalculated as the vertical deviation of the original cursor at the middle of the path between the circles per trial, $y_m = y|_{x=506} - 346$, instead of the angular error described above. The rest of the analysis was similar to the above, deriving new values for τ and ERR_{\min} . Second, the individual τ and ERR_{\min} were estimated by simple 'exponential regression' for perturbation trials 37–70 without pre-evaluating ERR_∞ as the minimal error in ten consecutive trials.

ECG recording

The ECG signal was monitored through electrodes applied to the right shoulder and to the left lower abdomen. The signal was amplified and low-pass filtered by a hardware 4th order Sallen-Key filter with 40 Hz cutoff. Then, it was digitally sampled by "LabView 7" application through an A/D converter at a rate of 250 Hz. Data was stored for a pre-task baseline period of 30 s and for a period of 350–380 s of the task.

Filtering

A sixth order Butterworth band-stop filter suppressed the 49.5–50.5 Hz frequencies and a sixth order Butterworth

high-pass filter suppressed the wondering D.C. effect below 1 Hz.

Detection of ‘R’ peaks

The ‘R’ peaks were identified based on time domain analysis in the form of mathematical correlation between a model of ‘P-QRS-T’ pattern and the original ECG channel. Times of successive ‘R’ peaks (i.e., $R(i)$) and duration of RR intervals (i.e., $RR(i)$) were stored.

RR interval analysis

Based on the biphasic RR response hypothesis, i.e., initial RR-decrease followed by an RR-increase, RR intervals were averaged across segments of 30 s, as follows:

1. RR_{baseline} represents the mean RR during the pre-task 30 s period.
2. $RR_{\text{min } 0}$ represents the minimal value of mean RR per 30 s period during the no-perturbation trials.
3. RR_0 represents the mean RR per 30 sec period just ahead of ‘perturbation onset’.
4. $RR_{\text{min } 1}$ represents the minimal value of mean RR per 30 s period during the perturbation trials.
5. RR_1 represents the mean RR per 30 s period toward the end of the perturbation trials just ahead of the first catch trial.

Since the timing for RR-decrease response varied between subjects, $RR_{\text{min } 0}$ and $RR_{\text{min } 1}$ were computed as described above, thus the values of RR-decrease and RR-increase were $RR_{\text{min } 0} - RR_{\text{baseline}}$ and $RR_0 - RR_{\text{min } 0}$, respectively during the no-perturbation trials, and were $RR_{\text{min } 1} - RR_0$ and $RR_1 - RR_{\text{min } 1}$, respectively during the perturbation trials.

Results

Hand kinematics

In line with previous reports (e.g., Wolpert et al. 1995; Nijhof 2003), subjects performed roughly rectilinear path with a bell shaped speed profile and demonstrated adaptation to the visuomotor perturbation. Planar trajectories and velocities profiles are illustrated in Appendix A (Fig. 8), which also deals with the relation between the cursor movements and the hand/mouse movements. Figure 4a presents the $\tan(\beta)$ values of the original cursor for all the movements of a typical subject from the experimental group. During the no-perturbation trials, $\tan(\beta)$ gradually converges to the ideal 0 value, which is the shortest path to the target circle. With the start of the

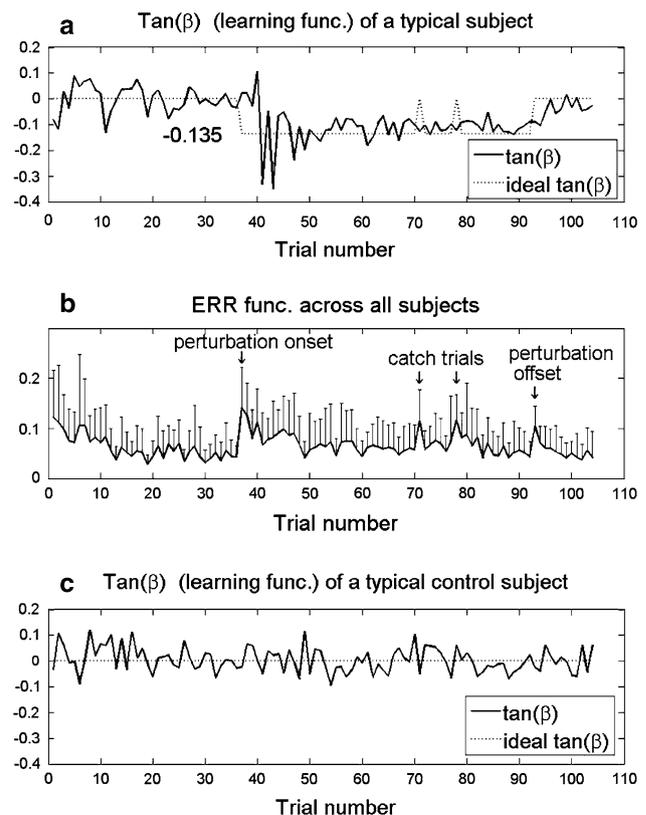


Fig. 4 **a** The tangent of angular hand deviation from a straight line, $\tan(\beta)$, on the 104 trials (the 52 L \rightarrow R trials and the 52 R \rightarrow L trials) of a typical subject. The ideal $\tan(\beta)$, namely the angular tangent of hand deviation required to move the cursor in a straight line towards the target circle, is marked in dotted line on no-perturbation, perturbation and after-effect trials. **b** The distance between actual and ideal arm movements (i.e., $|\tan(\beta) - \text{ideal } \tan(\beta)|$), ERR values (mean \pm SD) averaged across all subjects. **c** The tangent of angular hand deviation from a straight line, $\tan(\beta)$, on the 104 trials (the 52 L \rightarrow R trials and the 52 R \rightarrow L trials) of a typical subject from the control group

perturbation trials, $\tan(\beta)$ decreases, reflecting movement opposite to the perturbation direction, and gradually converges to the ideal $\tan(\beta) = -0.135$, thus compensating for the vertical perturbation. $\tan(\beta)$ seems to be insensitive to the catch trials indicating a feedforward control. Finally, during the after-effect trials $\tan(\beta)$ gradually converges to the initial 0 value. Figure 4c presents the $\tan(\beta)$ values of the original cursor for all the movements of a typical subject from the control group.

Figure 4b presents the group error index (difference between $\tan(\beta)$ and the ideal direction, named ERR, see ‘‘Methods’’). One can see that during the no-perturbation trials, the ERR converged to about the ideal level of performance right after trial 10. During the perturbation trials the ERR converged to the best level of performance much slower, only after about 30 trials. Figure 5 shows the results of t tests which were applied on the $\tan(\beta)$ values to

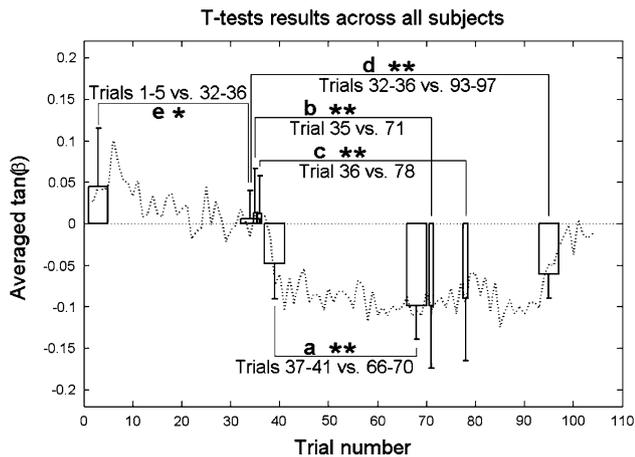


Fig. 5 The tangent of angular hand deviation from a straight line, $\tan(\beta)$, values (mean \pm SD) were compared by t tests, displayed over a dotted line representing the averaged $\tan(\beta)$ across all subjects. **(a)** motor adaptation demonstrated by comparison of the initial (37–41) vs. late (66–70) perturbation trials showing compensation for the cursor perturbation. **b, c** Motor adaptation demonstrated by comparison of the R \rightarrow L (35) and L \rightarrow R (36) catch-trials versus final no-perturbation trials 35 and 36. **d** Adaptation demonstrated by comparison of the initial ‘after effect’ trials (93–97) versus final no-perturbation trials 32–36. **e** Initial motor adaptation demonstrated by comparison of the initial (1–5) versus late (32–36) no-perturbation trials. * $P < 0.05$, ** $P < 0.001$

demonstrate motor adaptation during the no-perturbation and perturbation trials. Values of $\tan(\beta)$ were significantly lower on catch trials and after-effect trials in comparison to final no-perturbation trials ($P < 0.001$). Also, $\tan(\beta)$ values were lower on late versus initial perturbation trials ($P < 0.001$).

The subliminal nature of the perturbation was verified by the negative answer of all subject to the question “Have you noticed any unusual behavior of the computer mouse during the experiment?” presented to each subject in a questionnaire after the completion of the experiment.

Heart period presented as RR intervals

RR intervals in a representative subject are presented in Fig. 6a across the three periods of the task:

No-Perturbation trials: RR decreased initially and then increased to a level slightly above the baseline level.

Perturbation trials: RR decreased gradually below the baseline level just ahead of the first catch trial, and stayed at that level until the end of the perturbation trials.

After-effect trials: RR increased gradually to a baseline level.

The group RR indices are presented in Fig. 6b.

RR intervals in a typical subject from the control group are presented in Fig. 6c.

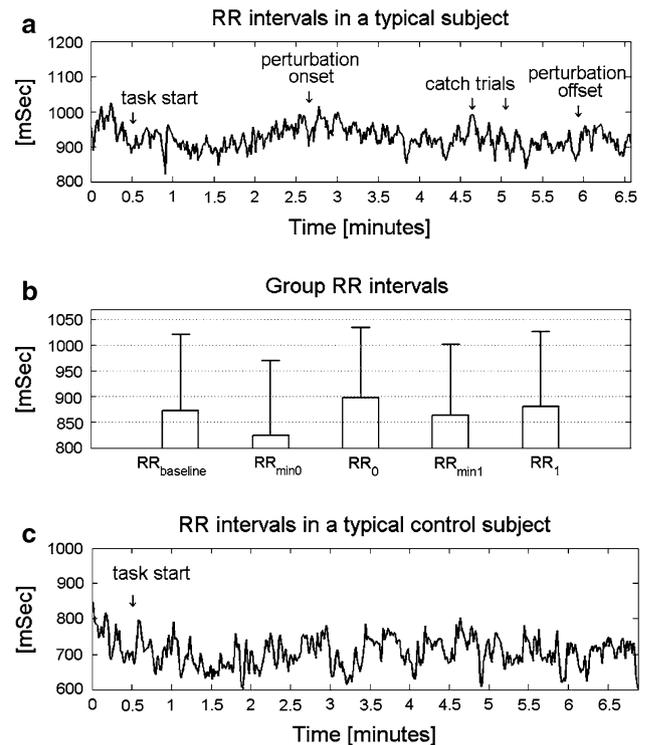


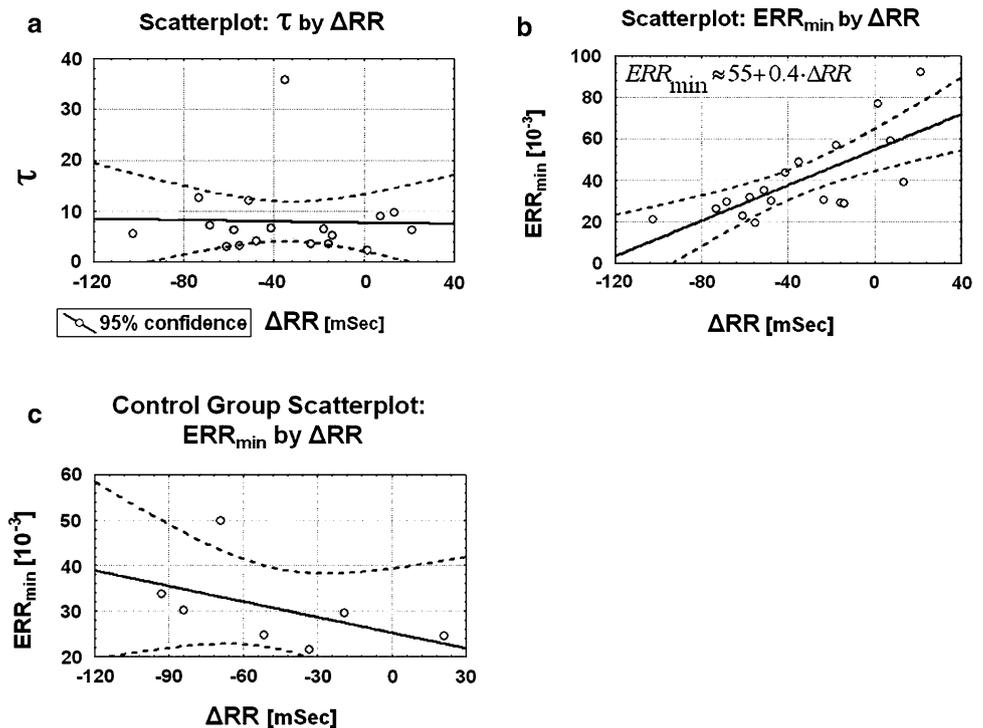
Fig. 6 **a** RR intervals of a typical subject (I.L.) across whole experimental duration. **b** Indices of group RR intervals (mean \pm SD) averaged across specific segments of 30 s across all subjects. **c** RR intervals of a typical subject (M.S.) from the control group

Correlation between indices of motor adaptation and RR intervals during the perturbation trials

Involvement of the autonomic system in the adaptation to the sensory-motor task was assessed by computing the correlation by linear regression between maximal decrease in RR ($\Delta RR = RR_{\min 1} - RR_0$) during the perturbation trials 37–70 and the two indices of motor adaptation during the same trials. Indices of motor adaptation were the τ and ERR_{\min} , expressing the rate of the feed-forward learning during the perturbation trials and the minimum error level reached in the process of learning, respectively.

Correlation between τ and ΔRR was not significant ($R^2 = 0.0$; $P > 0.92$; Fig. 7a), suggesting that the rate of motor learning is independent of the decrease in RR during the perturbation trials. Correlation between ERR_{\min} and ΔRR was significant ($R^2 = 0.52$; $P < 0.001$; Fig. 7b), implying that the lower errors in motor learning are associated with more profound decrease in RR during the perturbation trials. The two validation methods yielded similar results. When behavioral analysis was based on the ‘medial vertical deviation’ learning function, the correlation between τ and ΔRR was not significant ($R^2 = 0.05$; $P > 0.37$), and the correlation between ERR_{\min} and ΔRR was significant ($R^2 = 0.45$; $p < 0.003$). When both τ and

Fig. 7 Linear regressions across all subjects of **a** τ versus ΔRR and **b** ERR_{\min} versus ΔRR , during the perturbation trials, and **c** ERR_{\min} versus ΔRR of the control group. τ and ERR_{\min} [10^{-3}] represent the rate of motor adaptation and the minimum adaptation error, respectively, and ΔRR represent the maximal decrease in RR during the perturbation trials



ERR_{\min} values were estimated by exponential regressions, the correlation between τ and ΔRR was non-significant ($R^2 = 0.1$; $P > 0.2$), and the correlation between ERR_{\min} and ΔRR was significant ($R^2 = 0.49$; $P < 0.001$).

Referring to the control group, the correlation by linear regression between ERR_{\min} and ΔRR was not significant ($R^2 = 0.23$; $P > 0.25$; Fig. 7c).

Discussion

Subjects demonstrated clear motor adaptation in a task that required reaching movements under visuomotor perturbation. The present study explored for the first time the involvement of the autonomic nervous system in motor learning during hand reaching movement. The study demonstrated that the autonomic reactivity in the form of HR acceleration correlated with reduced final residual motor error but not with the motor learning rate.

Motor adaptation

Reaching movement is an elementary movement, which is the basis for more complex movements and therefore it was intensively investigated in the recent studies of the motor system (Shadmehr and Wise 2005). We tested a simple point-to-point reaching movement and introduced a perturbation in the form of a visuomotor transformation between the hand movement (the computer mouse) and the

cursor on the screen. The visuomotor transformation was designed to be rather small in order to avoid conscious perception of the perturbations. The subliminal nature of the perturbation was confirmed by the subjects' reports in response to the questionnaire. Under these conditions, we observed the well documented results of similar motor adaptation studies, namely the movements of the cursor from the origin to the target gradually became closer to a straight line. We observed these adaptation phenomena of reduction in the initial angle between the hand movement and a straight line in the no-perturbation phase and more profoundly in the learning phase during the visuomotor perturbation. This basic phenomenon of motor adaptation to visual perturbations was observed in previous studies under various conditions (e.g., Wolpert et al. 1995; Krakauer et al. 2000; Wang and Sainburg 2004).

Autonomous response to motor adaptation task

The sequence of no-perturbation followed by perturbation trials imposed a simple and fast form of motor adaptation followed by a longer motor re-adaptation process, respectively. Both instances of adaptation are a form of procedural (Krebs et al. 2001), subliminal learning. Nevertheless, like other procedural learning tasks (Fairclough et al. 2005), the no-perturbation and perturbation trials were associated with characteristic HR response. Such HR responses were not observed in the control group experimental trials.

The series of unperturbed trials were associated with fast acceleration followed by deceleration HR response. The subsequent perturbation trials were associated with slowly developing acceleration but only short and small deceleration response. This deceleration pattern did not replicate the consistent deceleration response to the final unperturbed trials. Future study will test whether the deceleration process to perturbation trials was blocked by the catch trials that followed closely the peak of the acceleration period. Cumulatively, we suggest that simple demand for motor adaptation, even if induced by subliminal sensorimotor perturbation, provides a sufficient challenge to trigger autonomous response in a form of HR acceleration.

Relation between autonomous response and motor adaptation

By adding the autonomous measure to the typical motor adaptation task one can sequence the learning process according to the predictions of the ‘three factors theory of learning’ (Mintz and Wang-Ninio 2001). Indeed, in most subjects as well as in the average response we recognized three stages of learning during the unperturbed trials. In the first stage, subjects rapidly acquired the HR acceleration response, already to the very first trial. In the second stage, subjects adapted gradually their motor response during the first 10–15 trials, while preserving the original level of HR acceleration. Finally, in the third stage, subjects maintained the adaptive level of motor performance associated with progressive HR deceleration.

In response to the perturbation trials, subjects reacted with gradual and ostensibly parallel HR acceleration and motor adaptation. This dynamics of the two measures prevents clear separation between the first and the second stages of learning. Nevertheless, we could confirm the hypothesis that the intensity of the autonomic responses is positively correlated with the quality of the motor adaptation. Quality of motor adaptation may be expressed as a shift of the learning curve to the left or as elevation of the asymptotic level of the learning curve (i.e., accelerated rate of learning or decrease in performance errors, respectively; see Fig. 1). Results suggested that increase in HR acceleration is associated with reduced final level of motor errors. This could be caused by increased sensitivity to errors which instructs the learning system to rest only at lower values of the errors (as suggested in Fig. 1).

This clear correlation between the HR acceleration and final level of motor errors could be explained by many possible mechanisms. It is therefore important to note that the hypothesis about sensitivity to errors (Fig. 1) is only one possible interpretation consistent with the data and further studies in various conditions of anxiety, attention,

reward, fatigue etc. are required to unravel the underlying mediators behind the observed correlation.

Computational models

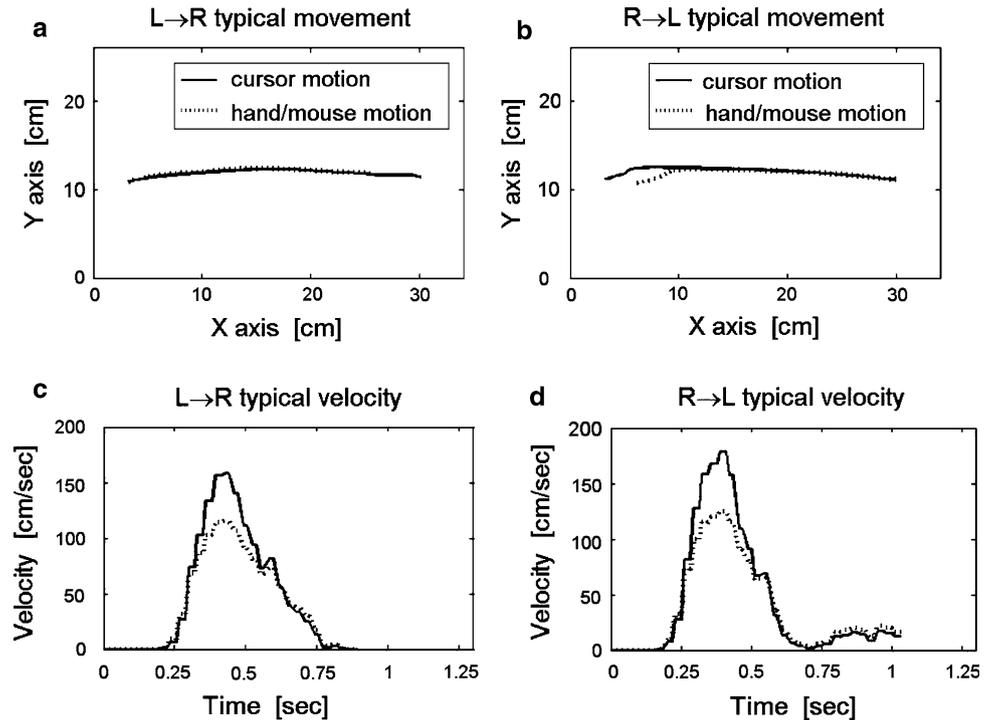
The study of arm reaching movements have recently been accompanied by computational models improving the predictive capabilities of scientific theories in this field of research (Jordan 1996; Kawato 1999; Wolpert and Ghahramani 2000). In a first degree of approximation, all computational models include a learning mechanism typically derived from a gradient decent algorithm, minimizing error function of the performance. In the study of adaptation to force perturbations two such models have been proposed (Thoroughman and Shadmehr 2000; Scheidt et al. 2001), both predict an exponential learning curves. Since this first degree approximation contains two parameters (learning rate and asymptotic residual error) we explored the possible correlation between these parameters and the autonomic response of the subjects as measured by changes in the HR. In neuroscience, when two alternatives are being posed, frequently, the result supports both alternatives to some extent. Therefore we were truly content to observe the significant correlation between the HR acceleration and the residual motor error and more so the lack of any correlation between the HR acceleration and the learning rate. Although correlation should not be mixed with causal relation, the former supports the latter, therefore we can interpret this surprising result as indicating that the sensitivity to errors but not the learning rate is modulated by the autonomic response. Further studies are required to replicate this result in other motor tasks and explore this relation in more details to consider more sophisticated computational models, such as the recent second order model suggesting two time scales (Smith et al. 2006). The mechanism by which the autonomic response is correlated with the residual motor error is an open question posed at the door of biologists.

Appendix

Linearization of cursor versus mouse velocity

The position of the cursor on the monitor served to define the position of the mouse/hand on the board. However, as occurs with standard computer mouse, the transformation between the velocity of the hand/mouse on-board (\vec{V}_h) and the on-screen cursor velocity (\vec{V}_c) is not linear. In addition, the on-screen cursor speed had been set to slow speed (The new mouse speed was set to ‘1’ through

Fig. 8 **a** and **c** Typical single L → R, and **b** and **d** typical single R → L movements' trajectories and velocities. The *continuous lines* refer to the cursor, and the *dotted lines* refer to the calculated hand/mouse motion. The hand path is fairly straight and the velocity is roughly bell shaped



'windows' SPI_SETMOUSESPEED function) to force wide hand movements by the subjects. In an ad hoc calibration test of the practical hand movement range of $V_h = 0\text{--}120$ cm/s we observed a fine fit to simple quadratic relationship between cursor velocity and hand velocity as presented by Eq. 14. Precise analysis of hand velocity according to the recorded original cursor velocity, should consider the inverse transformation assuming that there was no distortion in the angle of the velocity vector.

$$V_c \approx 0.0063 \cdot V_h^2 + 0.65 \cdot V_h \quad (14)$$

Considering only the positive solution one can solve for the inverse transformation as follows:

$$V_h \approx -51.95 + \sqrt{2661.2 + 158.73 \cdot V_c} \quad (15)$$

This corrective action was done off-line to approximate the original mouse/hand movements. No linearization correction was implemented on-line, thus keeping the nonlinearity of the velocity transformation, as in a standard mouse cursor behavior, during the game. Figure 8 presents the planar trajectories and velocities of the cursor and the hand/mouse motion, during two typical no-perturbation trials movements (R → L and L → R). The cursor velocity recordings served to calculate the hand/mouse velocity by applying the inverse transformation described by Eq. 15. In addition, assuming no distortion in the angle of the cursor velocity vector in respect to the angle of the hand velocity vector, the Cartesian vectors of \vec{V}_h were calculated (i.e., V_{hx} and V_{hy}). Since the sampling rate of the cursor position was constant, the Cartesian

coordinates of the hand/mouse position (i.e., X_h & Y_h) can be calculated according to Eq. 16.

$$X_h(t) = X_h(t=0) + \int_0^t V_{hx} \cdot dt \quad (16)$$

$$Y_h(t) = Y_h(t=0) + \int_0^t V_{hy} \cdot dt$$

Although there is a quite difference between the velocity of the cursor and the velocity of the hand/mouse motion, their path are rather similar (straight line) and their velocity profiles are bell shaped. Due to the similarity in the path we assume that the cursor location and deviation from straight line represents the hand's deviation from a straight line.

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