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RESEARCH ARTICLE

Y. Hatada · R.C. Miall · Y. Rossetti

Two waves of a long-lasting aftereffect of prism adaptation measured over 7 days

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Abstract Prism adaptation is a useful paradigm to study the integration and reorganization of various sensory modalities involved in sensory–motor tasks. By prolonging the prismatic aftereffect and well-timed observation, we aimed to dissociate the components and mechanisms involved in human prism adaptation by their differential decay and development time courses. Here, we show that a single session of prism adaptation training, combining small increments of prism strength below the subjects' awareness threshold, during a pointing task with a free walk session with total prism exposure duration of 75 min, generated a surprisingly long-lasting aftereffect. The aftereffect was measured by the magnitude of the proprioceptive shift (assessed by straight-ahead pointing in the dark) for 7 days. An aftereffect was observed, which lasted for more than 6 days, by a single prism adaptation session. The aftereffect did not decay gradually. Unlike previous descriptions, the aftereffect showed two separate time-courses of decay and increase. After a significant initial decay within 6 h, the aftereffect *increased* again from 1 day up to 3 days. The novel decay and delayed development profile of this adaptation aftereffect suggests two separate underlying neural mechanisms with different time scales. Our experimental paradigms promise to reveal directly the temporal characteristics of early versus late long-term neural plasticity in complex human adaptive behavior.

Keywords Prism adaptation · Aftereffect · Visuo–motor · Sensory–motor · Plasticity

Introduction

Adapting to optically shifting prism glasses involves the spatial adjustment of eye–hand coordination (Welch 1978, 1986; Redding and Wallace 1997a; Redding et al. 2005). The adjustment is thought to have two main mechanisms: strategic and adaptive components (Redding and Wallace 1996). Initially, subjects cognitively adjust their pointing using visual feedback, a strategic component. Then, through repeated pointing at the correct location, there are changes within the neural adaptive components. When the glasses are removed after adaptation, subjects make opposite pointing errors, thus exposing a compensatory aftereffect.

Recent research plasticity at various levels (i.e., molecular, cellular, systematic and behavioral), with functional observation or interference at various time ranges, has revealed correlated processes at several levels, using time as the reference. Early versus late long-term plasticity of molecular and cellular mechanisms was found to correlate with behavioral changes that ranged from an hour to days and months (Ito 2001; Kandel 2001).

A study reported the duration and decay pattern of aftereffects, following a single session of prism adaptation for days. Klapp et al. (1974) reported significant aftereffects, measured by open loop mid-sagittal thrusting, lasting for at least 1 day, following a single 36 min prism adaptation with the same mid-sagittal thrusting. The aftereffects reduced rapidly on the first day, and then appeared to decrease very gradually over the remaining period of 2–4 weeks. Klapp et al. (1974) used the same methods for prism adaptation and aftereffect measurement. This may have caused a long-lasting

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Y. Hatada (✉)
Institute of Cognitive Neuroscience, University College London,
17 Queen Square, London, WC1 N 3AR, UK
E-mail: y.hatada@psychol.ucl.ac.uk

R.C. Miall
Behavioural Brain Sciences, Psychology,
University of Birmingham, Birmingham, UK

Y. Hatada · Y. Rossetti (✉)
Espace et Action, UMR-S 534 INSERM-UCBL,
16 avenue Lépine, Case 13, 69676 Bron, France

Y. Hatada · Y. Rossetti
Institut Fédératif des Neurosciences de Lyon,
Lyon Cedex 03, France

context-dependent aftereffect. Others reported long-lasting aftereffects, but not by repetitive measurements. Lackner and Lobovits (1977) reported aftereffects at 24 h following 10 min 20 D prism adaptation. Yin and Kitazawa (2001) reported arm-specific aftereffects in a monkey, lasting 72 h following 500 trials of rapid reaching for 30 min with 15 D displacement. Both hands were used in this study with opposite shifting prisms: first the left arm was adapted to rightward displacing prisms by 500 times reaching and then the right arm was adapted to leftward displacing prisms by 500 times straight-ahead reaching. The left arm showed a leftward shift and the right arm showed a rightward shift. Other gradually decaying long-lasting aftereffects were reported after long continuous adaptation training (e.g., Hay and Pick (1966), who reported 10 days aftereffects after 42 days continuous adaptation). Recently, unilateral neglect patients showed sensory–motor and cognitive aftereffects for a few days, following a few minutes of adaptation training (Rossetti et al. 1998; Farne et al. 2002; Pisella et al. 2002). Neglect patients, however, have various lesions that making the systematic study of aftereffects difficult.

Hence, in order to study the underlying mechanisms of visuo-sensory spatial reorganization involved in the prism adaptation, we attempted to prolong the aftereffect in healthy subjects, following a single session of adaptation to allow the possible dissociation of adaptation components based on their different time course of development in the aftereffects. During training, we used pointing targets that were laterally separated from the mid-sagittal plane (straight-ahead) used during the pointing tests. Only a single session of prism training was used in order to have a relatively precise knowledge of the onset of the adaptation aftereffects. To achieve prolonged aftereffects, we combined several adaptation procedures, shown individually, to generate positive effects. First, prism strength was progressively increased using sub-awareness level increment steps (Jakobson and Goodale 1989; Michel 2003; Calabria et al. 2004) to reduce strategic adjustment components (Redding and Wallace 1996). Second, the exposure duration and number of pointing movements was increased (Yin and Kitazawa 2001) and the adaptation procedure was spaced with short breaks (distributed practice: Taub and Goldberg 1973). Third, free motion was included (Redding and Wallace 1985) after subjects reached a significant level of finger-pointing adaptation, to further reinforce adaptation (Redding and Wallace 1997a, 2002). Fourth, left-shifting prisms were used, which generated larger aftereffects of shift in line bisection than right-shifting prisms (Colent et al. 2000) did, perhaps due to hemispheric asymmetry (Butler et al. 2004).

Here, we present the evidence for two separate waves of prism adaptation aftereffects lasting hours and days, measured by straight-ahead pointing, following a single session of prismatic exposure in healthy subjects. The aftereffects initially decayed to non-significant levels at 6 h, but then increased to significance for upto 7 days. These findings will be discussed in relation to neurobiological mechanisms. Experimental procedures such as ours help improve the understanding of multi-modal integration and plasticity at a more global level, involving multiple interactive mechanisms.

Methods

Apparatus

The same experimental setup was used during both the prism adaptation training and the aftereffect measuring sessions. A subject was seated at a fixed position, relative to the measurement apparatus (Rossetti et al. 1998), with the head stabilized by a chin rest. For comfort, the height and position of the chair was adjusted to bring the measurement table just below chest level. During all pointing tasks and prism adaptation training, the subjects rested their left hand on their left thigh. At the start of each pointing movement, the right hand's index finger rested on the table in front of the subject close to chest level at a non-visible position. The pointing direction was measured using a touch tablet that registered the position of an index finger thimble. The measurement was expressed in angular degrees of deviation from the mid-sagittal axis.

Prism adaptation training

Table 1 shows the prism adaptation training procedure. Seven different wedge, left-shifting, glasses were used for this prism exposure, with shifts of 2, 4, 6, 8, 10, 12 and 15°. The glasses were put on and taken off while the subject's eyes were closed. While wearing the glasses, the subject was asked to point, at a comfortable speed with the right index finger, at two fixed targets already marked on the apparatus board, which were 10° right and left from the mid-sagittal point and 50 cm in front of the subject. Pointing to the two targets was performed in random order under the instruction of the experimenter. After a total of 20 target-pointing movements (10 right and 10 left targets), there was a 5-s pause before the same training procedure was repeated (i.e., 2×20 points with the same glasses). These 40 trials were repeated with progressively increasing prism strengths from 2 to 15°. With the final 15° prism glasses, the 40 trials were repeated twice (i.e., 4×20 points). Finally, the subject walked out from the laboratory in our institute while wearing 15° prism glasses for a session of whole body exposure lasting 45 min, during which he could see his own hand and body and walked and pointed in his normal environment.

Table 1 Training procedure and measurement sequence

Event sequence	**Stage of training**		Measurements						
	Prism state	**Pointing at target**	**Straight ahead pointing**	Passive straight ahead test	Visual straight ahead test	Open loop pointing	Land Mark Test	Line bisection	Task
		with visual feedback	**eyes closed**	two directions	two directions	Eyes open in dark			Condition
Pre-test Baseline	Off		**10 trials**	2x10 trials					Eyes closed
					2x10 trials	10 trials	42 trials	10 trials	Eyes open
Prism adaptation training procedure	**Exposure 2º**	**40 trials**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 4º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 6º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 8º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure10º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 12º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure15º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 15º	**40**							
	Off		10*						Eyes closed
						10*			Eyes open
	Exposure 15º	**Free walk 45 min**							
Post-tests (0hr)	Off		**10 trials**	2x10					Eyes closed
					2x10	10	42	10	Eyes open
Post-tests (2hr)	Off		**10 trials**	2x10					Eyes closed
					2x10	10	42	10	Eyes open

The same measurements as above were repeated at 4, 6 h and 1, 2, 3 and 7 days after returning to a normal environment
Only data from the pre- and post-test straight-ahead pointing measurements, using the right arm (bold), are included in the present report. Dark gray shading prism adaptation procedure. Light gray shading period without exposure to the normal visual environment. Visual straight-ahead was measured by judgment of an LED, moving at a constant 3°/s speed from left to right. Passive proprioceptive mid-sagittal measurement was taken by judgment, during passive arm movement at 10°/s from left and right. The Land Mark Test measures allocentric object symmetry. Line bisection measures egocentric object symmetry. Pre- and post-test straight-ahead, passive proprioceptive mid-sagittal judgment, open-loop pointing and line bisection measures were obtained with both arms.

[a] During prism adaptation (*) only right arm was used

Measurement of prism adaptation aftereffects

The first measurement was performed before adaptation training, to provide a baseline. Between each level of prism exposure, adaptation was also monitored with straight-ahead pointing and open loop pointing (without visual feedback). Following the prism adaptation procedure, the adaptation aftereffects were measured at 0 h

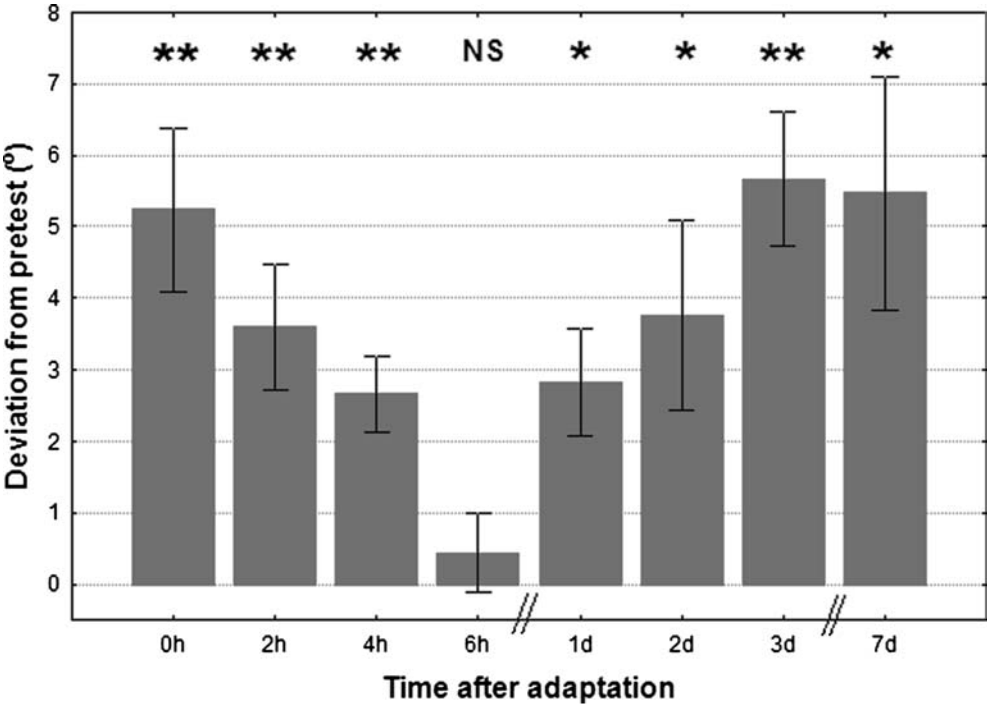

Fig. 1 Shift of prism adaptation aftereffects, measured by mid-sagittal pointing (averaged data of eight subjects). Means/SEM of deviation from pre-test measures. *Asterisk* indicates significant deviation was tested by unilateral student *t* test against a single value of zero with Bonferroni correction (*$P \leq 0.10/3$, **$P \leq 0.05/3$)

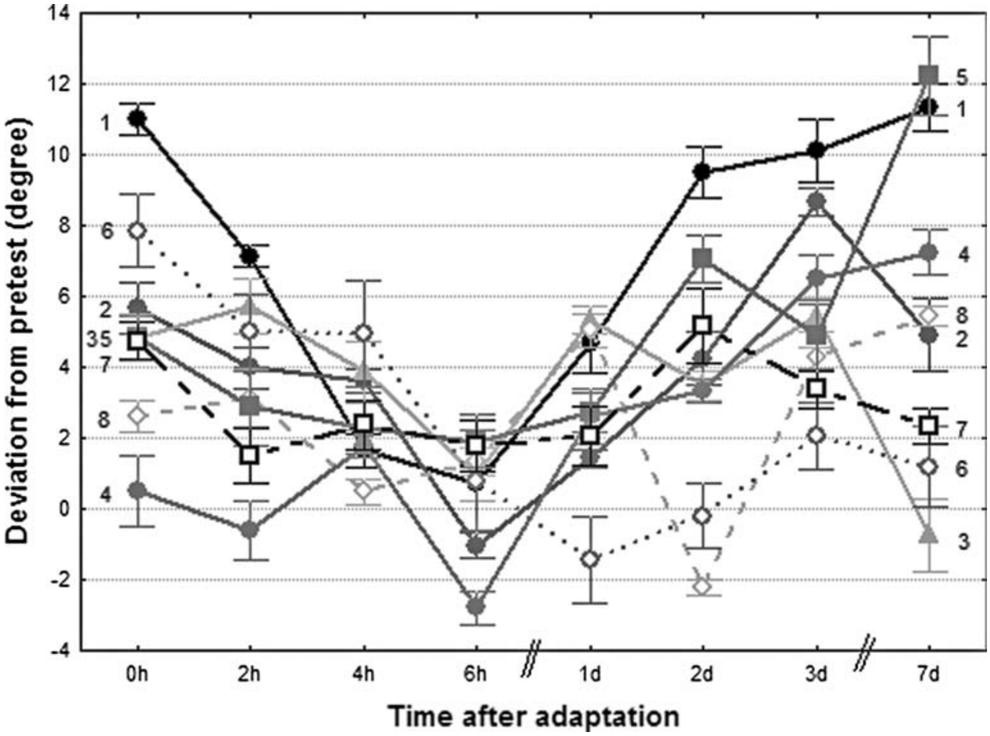

Fig. 2 Data of the eight subjects in Fig. 1. Individual means/SEM of deviation from pre-test measurements. Three cases (*dotted lines*) did not show a minimum value at 6 h

(immediately after the whole set of prism adaptation training and a few minutes rest in total darkness, before exposure to any vision at all), and at 2, 4 and 6 h for 1, 2, 3 and 7 days after the final removal of the 15° prism glasses (see Table 1). The subject pointed at a comfortable speed, with his index finger in his subjective mid-sagittal plane toward the far side of the apparatus board level, without visual feedback. Each measurement included ten trials. All measurements were done with eyes closed and the subjects were not given any feedback on the accuracy of their responses. Other measurements were taken for completeness but are not the main focus here. Due to the complexity of this experiment, these results will be shown in separate papers with focused themes.

Table 2 Individual data

Subject	Max. of first wave		Min. between two waves		Max. of second wave	
	Mean	SEM	Mean	SEM	Mean	SEM
1	10.98	0.45	0.72	0.50	11.33	0.68
2	5.66	0.71	−1.05	0.36	8.46	0.42
3	5.73	0.78	0.64	0.65	5.47	0.47
4	1.81	0.39	−2.80	0.49	6.93	0.65
5	4.66	0.58	1.91	0.74	12.21	1.11
6	7.86	1.02	−0.90	1.21	2.05	0.95
7	4.75	0.50	1.75	0.66	5.16	1.05
Total	5.92	1.08	0.04	0.64	7.37	1.36

Seven individuals' means/SEM at the maximum of the two waves and at the minimum between them: subject 8 had three waves and is excluded from this analysis. The minimum values were observed at 6 h for 5 of 7 subjects. For subject 6, the minimum was at 1 day. For subject 7, the deviations did not differ significantly during 2 h to 1 day so the minimum was taken at 6 h

Subjects

Eight healthy and normal-sighted subjects were used for this study. All of them were right-handed (3 females, 5 males, 22–45 years). In accordance with the French law, ethical approval was gained individually before their attendance for the experiments.

Results

Straight-ahead pointing shows a long-lasting rightward shift for more than 7 days with two separate waves in hours and days

Figure 1 shows the group mean deviation of post-test sessions from pre-test, in order to see the magnitude of the aftereffect shift and the level of separation between the two waves. The training procedure immediately generated a rightward shift of about one-third (5.23 ± 1.14° (SE)) of the maximum 15° prism optic shift. This large aftereffect then decayed, within 6 h, to the pre-test level (0.41 ± 0.56° (SE)). However, it was followed by a second shift that started to increase again after day 1 and showed a maximum rightward shift of 5.67 ± 0.94° (SE) at day 3. This significant aftereffect was still observed (5.47 ± 1.63° (SE)) on the last measurement at day 7. Interestingly, the magnitude of this second wave was as high as that of the first wave. A repeated-measures ANOVA, with eight time points as within-subject factors, revealed a significant main interaction with time ($F(7, 49) = 3.631$, $P = 0.003$). Additional tests assessed whether these after-effects significantly deviated from zero. Unilateral student *t* tests were used to compare each post-pre value with the zero value. Independence of the 8 post-test measurements was assessed by a principle components analysis. This analysis revealed that 80.6% of the variability of the data could be accounted for by three principle components (with eigenvalues more than 1.0) indicating that there were three independent components. Using the Bonferroni correction (unilateral $P = 0.10/3 = 0.033$), the magnitude of the post-test deviation was significant for 7 out of 8 measurements (0 h: $P < 0.003$; 2 h: $P < 0.005$; 4 h: $P < 0.002$; 1 day: $P < 0.007$; 2 days: $P < 0.025$; 3 days: $P < 0.001$ and 7 days: $P < 0.012$). Only the measurement at 6 h was non-significant($P < 0.459$).

These results reveal a new finding, suggesting that the aftereffect following our adaptation session showed an initial decline over the first few hours, as previously reported, but also showed a re-development of the aftereffect over the next few days, returning to as high a level after 3 days as was seen immediately after the adaptation session. The aftereffect was still significant after 7 days.

The reduction of the aftereffect from 0 h was tested by Dunnett's post hoc tests at seven time points. We use Dunnett's post-hoc test since this is a stringent post hoc test for comparing multiple group data with a reference group data and takes into account repetitive measurements. The analysis revealed a significant reduction of aftereffects at only one out of seven time points, at 6 h ($P < 0.002$ by Dunnett's post hoc tests from 0 h) throughout 7 days of aftereffect observation. Hence, the decay of the aftereffect was much slower than previously reported.

Individual data show two waves of shift in hours and days separated by a dip of shift around 6 h

Figure 2 shows the magnitude of deviation, from pretest measurements, for the eight participants. In spite of the variability of individual patterns, the reduction of the aftereffect at about 6 h is clearly seen in most subjects. A significant and long-lasting rightward shift can be identified in each individual, together with a dip at between 4 h and 1 day.

Table 2 shows the mean maximum shift of both waves and the mean minimum shift between the two waves, measured for the separate individuals and then averaged over seven subjects. One subject (subject 8 in Fig. 2) had three peaks in the aftereffect curve and is excluded from this analysis. After defining the individual minima between the two waves, the maxima from the two separate waves were taken for each subject. Five out of seven subjects had their minimum value at 6 h. The dotted lines in Fig. 2 indicate the two cases that do not fit this pattern. Subject 6 had the minimum at day 1 and so the minimum was taken from this data instead. Subject 7 had a long dip between 2 h and 1 day, after a quick decay from initial values, so that although the minimum was at 2 h, the separation between the two waves was taken at 6 h. The average minimal shift obtained between the two waves was 0.04 ± 0.64° ($n = 7$). This value was not significantly different from zero ($t(6) = 0.058$; $P = 0.96$).

Discussion

Our results revealed a new, biphasic time-course of decay and an increase of aftereffects in hours and days, respectively, was seen within a long-lasting prism adaptation aftereffect over 7 days.

Two waves of aftereffect with different time scales

The initial shift, immediately following prism adaptation training, was gradually lost, becoming non-significant within 6 h. This initial trend may classically have been interpreted as a simple and finishing de-adaptation. However, the lateral shift increased again, reaching a significant level on day 3, without any additional adaptation training. We will refer to the aftereffect before 6 h as ‘‘the first wave’’ and the significant shift from 1 to 7 days as ‘‘the second wave’’.

Usually, the adaptation aftereffects have been reported to decay exponentially (e.g., Hay and Pick 1966; Klapp et al. 1974; for reviews, see Welch 1978; Redding and Wallace 1997a). In the past there have been reports of occasional delayed increases, referred to as ‘‘reminiscence’’, in prism adaptation aftereffects (Taub et al. 1966; Goldberg et al. 1967; Choe and Welch 1974; Welch 1978). In each of these cases, the rare delayed increase occurred 15 min or less after the end of adaptation training. While the reason for the unreliability (since they could not be reproduced) of the reminiscence in these studies is not known, the consolidation of context-dependent specific learning and learning effects, due to repetitive measurements, were suggested (Welch 1978; Redding et al. 2005). These reports of reminiscence were on a different time scale from the two waves in our present study, which occurred over hours and days.

What elements contribute to increased duration of prism adaptation aftereffect?

We used gradual increments in the prism strength, with sub-awareness steps of 2–3° (Michel 2003; Calabria et al. 2004; tested aftereffect of 5 D prism displacement by Jakobson and Goodale 1989), from 2 to 15° in seven steps. This awareness threshold was determined based on the skin conductance level on the left index finger when one of the 0, 2, 8° prisms was randomly applied to one eye, while the other eye was closed, and subjects pointed at a target with their right hand. The results showed that there was no significant difference between 2 and 0°, but there was a significant difference for the 8° prism (Calabria et al. 2004). Although each prism strength increment in our experiment was of the sub-awareness level, subjects might have noticed the accumulated shift toward 15° more than the lower degree ranges, due to the presence of stronger visual distortion. It is possible that the final 3° increase, from 12 to 15° in one step, may have been noticeable, based on Calabria et al.’s data (Calabria et al. 2004). Gradual increments were previously found to generate larger instantaneous shifts in visual rotation (Kagerer et al. 1997) or movement amplitude (Ingram et al. 2000). Reduced awareness of the increment of prisms should increase the aftereffects of the adaptive component by reducing the contribution of conscious strategic adjustment components in the initial adaptation (Jakobson and Goodale 1989; Redding and Wallace 1996), as it is the case in unilateral neglect patients (Rossetti et al. 1998; Farne et al. 2002). Second, during the free-moving exposure period, subjects walked and used both hands in goal-directed ecological tasks. It may also be crucial that this free-exposure condition, which is known to increase the visual components of adaptation (Redding and Wallace 1985), was introduced only after a significant proprioceptive adaptation level was reached through finger-pointing (Hatada and Rossetti 2004a, b). Therefore, it could produce a reinforcement of the adaptive components, rather than the strategic effect that might be expected with the immediate onset of prism exposure (Redding and Wallace 1996). Third, prism glasses producing a left optical shift were previously found to generate a stronger aftereffect in line bisection measurements than prism glasses producing a right shift (Colent et al. 2000), perhaps due to CNS hemispheric asymmetry (Butler et al. 2004). Fourth, adaptation training was interspersed with 5 s breaks in the middle of each training block, since spaced training trials produce larger aftereffects than massed training (Taub and Goldberg 1973). Finally, we increased total prism exposure to 320 pointing movements (Yin and Kitazawa 2001) and for 75 min.

This study did not focus on determining the critical factors for prolonging aftereffects, but rather used the prolonged aftereffects to study the decay time course of prism adaptation components. Understanding the contribution of individual adaptive factors to prolonging aftereffects, leading to the first and second waves, will require studies in the future.

Could this long-lasting aftereffect be a specific context-dependent phenomenon?

It has been suggested that the test room and apparatus, the unusual task of sagittal pointing in the dark room or other elements of the aftereffect measurements might cause subjects to recall the context of the prism adaptation, which would cause retrieval of context-specific learning for the straight-ahead test (Welch 1986; Redding and Wallace 2005; Redding et al. 2005). Context-dependent consolidation was suggested as an explanation for the delayed increase (reminiscence) in the other studies, where this was unreliably found to sometimes occur in an unreproducible manner (e.g., Goldberg et al. 1967; Taub and Goldberg 1973) in the time range of 1 h (reviewed in Welch 1978).

However, this seems an unlikely explanation for our results. First, our test measurements of the aftereffects share little task context with the pointing performed during prism exposure, reducing the probability of a task-context-dependent artifact (Redding et al. 2005). During prism adaptation, subjects pointed to two given lateral targets, 10° right and left from the midline, with visual feedback. In contrast, straight-ahead pointing during aftereffect measurements was done with eyes closed and pointing at a subjective (“imagined”) mid-sagittal point (Redding and Wallace 2002, 2003, 2005). Second, the insertion of a 45-min session of unrestricted free-moving exposure may also have reduced specific context-dependent artifacts. Third, it is difficult to explain the loss of significant aftereffects at 6 h, in terms of context effects, since the measurement at 6 h was done in the same context. There is no obvious reason why the context-effect would be lost for 1 day and then gradually regain in magnitude. Also, other aftereffect measures showed specific decay and develop curves independently from each other. The passive arm mid-sagittal judgment by arm movements, from two opposite lateral positions, showed shifting aftereffects in only one of the two movement directions (Y. Hatada et al. submitted). Therefore, we believe that the aftereffect seen here is a component-specific aftereffect.

What mechanisms might produce two separate aftereffect waves?

The decline of the first wave of aftereffect is not unexpected and is in line with other reports of adaptation aftereffect decay. However, the return of the aftereffect over the next few days was unexpected.

Fatigue-related factors

The gradual decay in straight-ahead pointing, over the first 6 h, might be thought to be due to fatigue-related factors, recovering after sleep. However, it seems unlikely that fatigue would result in a return to pre-test performance, with small variability, rather than a general increase in the variance of the pointing direction. It also seems unlikely that fatigue should be so prominent, while testing at 6 h, when compared with immediately after the extensive adaptation session: there were repeated 2-h intervals between the tests at 0, 2, 4 and 6 h that should have provided rest.

Sleep effect

One potential factor leading to the returned aftereffect may be the effect of sleep. Previous studies reported that sleep enhances the effects of learning (for review, see Walker and Stickgold 2004). Since the break between the two waves coincided with a sleep period, sleep needs to be considered, and the return of the aftereffect might reflect sleep-mediated consolidation of the memory or context-dependent cues. However, a number of studies failed to show a sleep effect for the consolidation of adaptation against opposing or perturbing tasks (e.g., Goedert and Willingham 2002; Caithness et al. 2004). Robertson et al. (2004) showed that implicit sequence motor-learning depended simply on the duration after the learning session, regardless of sleep; whereas explicit learning was NREM sleep-dependent. We used an implicit adaptive procedure; therefore, the sleep-dependent components may be weak, if present. However, the effect of sleep on prism adaptation has still to be clarified.

Neuronal mechanisms

It is already well known that cellular plasticity involves two different kinds of mechanisms, with time scales relevant to our study. The first, with a range of hours, could be controlled by second messengers and kinases in cytoplasm, within existing synapses (early long-term plasticity (e-LT*P*); here *P* “plasticity” may include potentiation, facilitation or depression (for reviews, see Ito 2001; Kandel 2001). The second level could be late long-term plasticity (l-LT*P*), depending on gene transcription and translation, leading to stable morphological changes, including new synaptic connectivity (Kandel 2001). During the interval between e-LT*P* and l-LT*P*, adaptation-specific inputs at subsets of synapses can be maintained for a few hours via synapse-specific “tagging” (Martin and Kosik 2002).

In vivo and in vitro studies in Aplysia showed that early- and late-LTF (facilitation), expressed bi-phasically, is correlated with memory: the duration of e-LTF was between 1 and 6 h and for l-LTF, between 10 h and a few days (Sutton et al. 2001). Over the same time scale, in vitro time lapse video-enhanced-microscopic studies showed that new neuronal branches could grow at a rate of about 40 μm/day, from pre-existing synaptic varicosities (Hatada et al. 2000), followed by maturation into fully functional synapses over 24 h (Hatada et al. 1999). In vertebrates, the formation of new synapses also requires structural molecules to be transported and become functional. In large dendritic trees, e.g., in Purkinje neurons or long axons of cortical pyramidal neurons, this transport could take some time: the anterograde transport for actin filaments is 0.4–5.0 mm/day (Oblinger and Lasek 1985). These plastic modifications can be local, occurring post-synaptically at dendritic spines or in wider areas through pre-synaptic modifications (Chklovskii et al. 2004), with a time delay that is likely to be larger. Therefore, if the expression of e-LT*P* is short-lasting, due to a weak input, there could be a gap, which becomes noticeable at the behavioral level before the onset of l-LT*P*, as seen between our first and second wave. The fact that the second wave was still observed after more than

6 days suggests that it is supported by a stable neural network formation or modification.

Natural decay and unlearning

There have been only few studies that attempted to test the time course differences between natural decay and unlearning and their results are inconclusive (Hamilton and Bossom 1964; R.B. Welch et al., unpublished manuscript). Both studies looked at short durations, of less than 15 min and their results contradicted each other. In the former study, both natural decay and unlearning showed a reduced magnitude of aftereffects, but there was no significant difference between the two. Natural decay was the condition of sitting in complete darkness quietly and unlearning was the condition that subject moved their arms forward and backward with visual feedback for 15 min after adaptation. The latter study, by contrast, showed no decrease in aftereffects by natural decay, but found a significant decrease in aftereffects by unlearning, within 10 min. Our results show a significant reduction of aftereffect, relative to immediately after the prism adaptation at 0 h (tested by Dunnett's), only at 6 h throughout 7 days of observation. So, the decay of our aftereffects was much slower than that of the previous two studies.

The prismatic aftereffect is commonly thought to be under constant de-adaptation pressure during exposure to the normal environment after adaptation. For the proprioceptive component measured by straight-ahead pointing, however, this may not be the case. During the adaptation procedure, subjects were not allowed to see the starting position of their hand whereas, during normal life, people can usually see their hand in their peripheral vision and adjust their hand path accordingly. It has been shown that the aftereffect is very small or zero if subjects are allowed to see their starting hand position during the prism adaptation procedure (Redding and Wallace 1996, 1997b). Therefore, normal, everyday reaching and pointing, which includes vision of the starting position of the hand, may be exerting only a very weak de-adapting pressure on the proprioceptive sense. The initial decay of aftereffects during the first couple of hours, which has been interpreted as de-adaptation, could, in fact, have more to do with the natural decay of e-LT*P*, which encodes the modification/remapping for straight-ahead pointing due to the adaptation training. In this view there would again be no need to assume context-dependent learning in order to explain the second wave of aftereffects, since there is only a very weak de-adaptation pressure. Both the decay of the initial first wave of adaptation and the rise of the second wave would be consequences of the underlying neural mechanisms e-LT*P* and l-LT*P*. During the normal interaction after prism adaptation, subjects could unconsciously have been using more online arm movement corrections. Subjects certainly did not report being aware of correcting their arm movements during the 7 days following the prism training.

Possible interaction between different CNS areas

Finally, it is possible that the two wave patterns of plasticity may not necessarily be expressed in the same CNS areas, but is transferred between two different CNS regions, as suggested from animal studies (Takehara et al 2003; Boyden et al. 2004). The transfer between different CNS regions (e.g., cerebellum, hippocampus and prefrontal cortex), through dynamic interaction, has been reported in the time range of l-LTP, after eye blink conditioning in rats (Takehara et al. 2003). Ablation revealed that memory consolidation required the cerebellum throughout the 4 weeks of study, whereas the hippocampus was required more during the earlier period and medial prefrontal cortex more during the later period (Takehara et al. 2003). In mice, spatial memory crucially depends on the hippocampus at day 1, but on the parietal cortex, among others, at day 30 (Maviel et al. 2004). Therefore, the two waves in our aftereffects are not necessarily expressed at the same CNS regions, regardless of the uncertain sleep effects.

Studies with cerebellar legion patients show that these patients show an adaptive performance to prisms, but no aftereffects, indicating that the expression of adaptation aftereffects requires the cerebellum (Weiner et al. 1983; Martin et al. 1996; Baizer et al. 1999; Pisella et al. 2005). Clower et al. (1996) showed the selective activation of regional blood flow at the posterior parietal cortex, contralateral to the reaching limb involved in prism adaptation. Clower et al. (2001, 2005) reported the connection between the cerebellum dentate nucleus and the inferior parietal lobule of the posterior parietal region via the thalamus. Therefore, in a similar manner as reported in the example above, these areas may be involved in the two–wave pattern of plasticity via secondary induction. During new skill learning, cerebellar activity shifts from the cerebellar cortex to areas of the cerebellar dentate nucleus within the learning session (Imamizu et al. 2000). Although the neural mechanisms underlying prism adaptation and its long-lasting aftereffects is not yet well understood, these neural networks, between Purkinje cells at cerebellar neuclei, the thalamus and parietal cortex, including pre-motor (Kurata and Hoshi 1999), primary motor, primary sensory cortex, could be the locations for plastic modification through e-LT*P*, l-LT*P* underlying the adaptation aftereffect.

Conclusion

Although there is still a huge gap between our understanding of the system's behavior and the underlying complex neural mechanisms, these temporal coincidences and the universal nature of cellular mechanisms could be useful tools to bridge these two levels. Our paradigm promises an experimental approach that may reveal the temporal characteristics of e-LT*P* and l-LT*P* in complex human adaptive behavior.

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