prepared for Caucasian faces (students at St Andrews University, 25 male, age 19–23 years, mean 21.0 years; 30 female, age 19–22 years, mean 20.6 years). Photographs were converted to digital format (Kodak Photo-CD) and 174 feature points on salient facial landmarks (for example, nose-tip) were defined manually for each face[14,15]. The average face shapes of the male and female Japanese and Caucasian face subsets were calculated from the feature points. The position of eye centres was standardized for corresponding average male and female face shapes. Each original face image was then warped to the shape of the corresponding average face and the resultant reshaped face images were blended together by averaging colour and intensity values of pixels at corresponding image locations[14,15] (Fig. 1). The vector difference between corresponding feature points on the male and female averages was increased or decreased by 50% to create feminized and masculinized shapes. The image of the composite face was then warped into these new face shapes to create image pairs with identical texture but enhanced or diminished sexually dimorphic differences in face shape. The size of all male and female face images was matched by standardization of inter-pupil distance. The resulting composite images were cropped around the face and faded into a black background (Fig. 2). Cropping removed the hair, ears and neck, which were not consistent in shape or visibility in component images because of differing hairstyles and clothing.

Procedure. A Silicon Graphics Indigo^2 Maximum Impact (4 MB TRAM) was used to create smooth continua between 50% masculinized and 50% feminized face pairs (Fig. 2) as the end points, and the cropped average as the midpoint. The point along a shape continuum was controlled interactively by the position of the computer mouse. The appropriate image was calculated in real-time using texture mapping hardware. Stimuli were presented in 24-bit colour at the centre of an 800 × 800 pixel window. Fifty Caucasian subjects (research staff and students from St Andrews University; age 19–31 years, 25 female) and 42 Japanese subjects (research staff and students from ATR and Doshisha University; age 18–44 years, 19 female) were instructed to select the most attractive face from the continuum. Each continuum was presented twice to allow left/right counterbalancing of the end points, making a total of eight trials in randomized order.

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Separate body- and world-referenced representations of visual space in parietal cortex

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In order to direct a movement towards a visual stimulus, visual spatial information must be combined with postural information[1]. For example, directing gaze (eye plus head) towards a visible target requires the combination of retinal image location with eye and head position to determine the location of the target relative to the body. Similarly, world-referenced postural information is required to determine where something lies in the world. Posterior parietal neurons recorded in monkeys combine

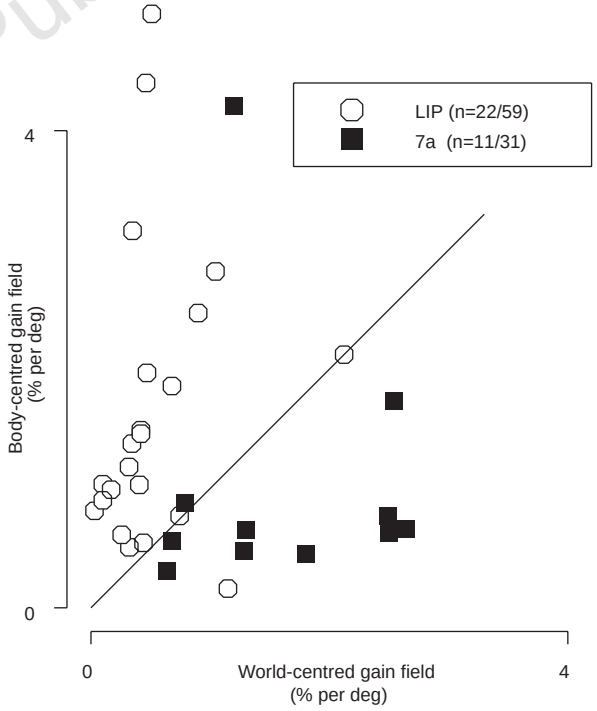

Figure 1 LIP responses (open circles) were modulated by body- but not world-referenced target location; 7a responses (filled squares) were modulated by world- but not body-referenced location. Visually evoked or delayed saccades were made after combined head-and-body rotation in the dark (world-referenced modulation), or after an equal counter-rotation of the body under a stable head. The absolute value of the gain field is shown for cells whose responses during and immediately after visual cue presentation depended on either body- or world-referenced head position (Student's t-test, $P < 0.05$; 33 of 90 cells). Cells above the diagonal line had stronger body-referenced modulation; cells below the line had stronger world-referenced modulation. Only two 7a cells fell above the line, and only two LIP cells fell below the line, indicating that body- and world-referenced modulation were well segregated by area (see Table 1).

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visual information with eye and head position[2–4]. A population of such cells could make up a distributed representation of target location in an extraretinal frame of reference[4–7]. However, previous studies have not distinguished between world-referenced and body-referenced signals[4,8]. Here we report that modulations of visual signals (gain fields) in two adjacent cortical fields, LIP and 7a, are referenced to the body and to the world, respectively. This segregation of spatial information is consistent with a streaming of information, with one path carrying body-referenced information for the control of gaze, and the other carrying world-referenced information for navigation and other tasks that require an absolute frame of reference.

Head position can be referenced to either the body or to the world. A body-referenced frame could derive from neck proprioception, or from efference copy of neck-muscle motor commands. World-referenced gain fields could derive from vestibular or visual signals. Parietal cells might use just one of these frames of reference; both frames could coexist on the same population of cells; or the two frames could be coded by two distinct cell populations[9–12].

We devised three tests to distinguish between these possibilities in rhesus macaques. To isolate body-referenced gain fields, visual responses to targets presented at identical retinal locations were compared after the body had been counter-rotated underneath the head to one of 2–7 positions (body-under-head rotation); after counter-rotation, the head was always at the same angle with respect to the world, but at different angles with respect to the body. To isolate world-referenced gain fields, responses to retinally identical targets were compared after the head and body had been rotated together to one of the same 2–7 positions (body-plus-head rotation); after combined rotation, the head was always at the same angle (0°) with respect to the body, but was at varying angles with respect to the world. Finally, for active head rotation, responses to retinally identical targets were compared after the animal had oriented its head to one of 2–5 positions; after active head rotation, head position varied with respect to both the world and the body.

We recorded from 288 cells in two macaques. Every trial began with an interval of central fixation followed by a peripheral target, always at the same retinotopic position. One animal made an immediate saccade to the target (231 cells), and the second memorized the target's location and acquired it after a short delay (57 cells). Responses to retinally identical targets were compared on interleaved trials following different head and body movements.

First we investigated whether head position was encoded with respect to the body or world. Ninety cells were tested using interleaved body-under-head and body-plus-head rotations. Many cells showed either body- or world-referenced gain fields, but few cells showed both. In addition, cells with body- and world-referenced gain fields were anatomically segregated. In cortical area LIP, 22 of 59 cells showed significant ($P < 0.05$) modulation for at least one of the two rotations: 20 body-referenced, one world-referenced, and only one mixed body- and world-referenced. In area 7a, 11 of 31 cells showed significant modulation: nine world-referenced, one body-referenced, and one mixed.

The segregation of body-referenced gain fields in LIP and world-referenced gain fields in 7a is shown in Fig. 1. Each point represents a cell with significant modulation in at least one rotation, coded by area. Gain fields were quantified by the mean percentage change in response to a 1° change in body-under-head (ordinate) or body-

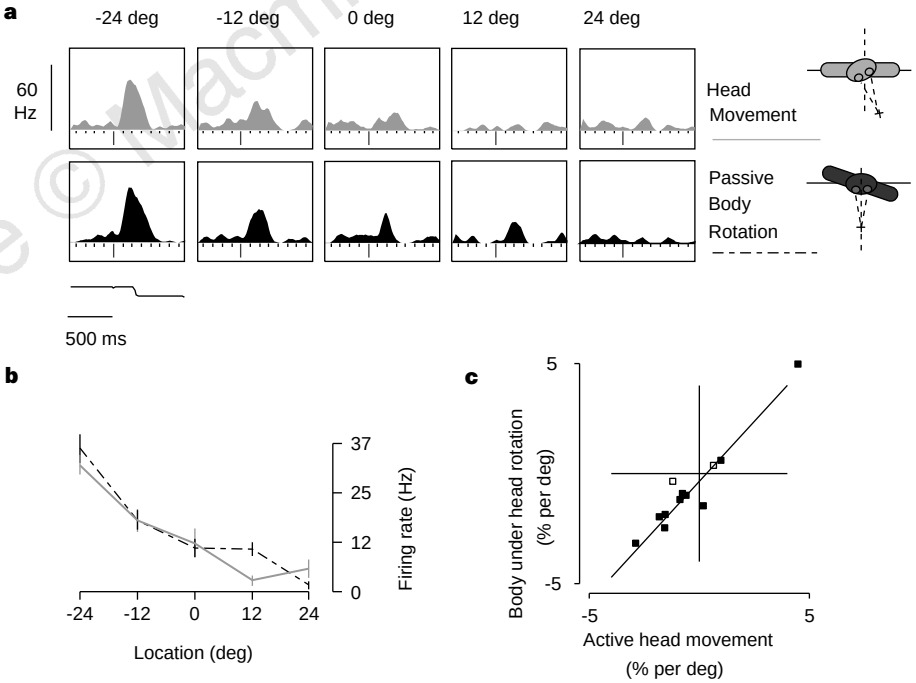

Figure 2 Head-position gain fields in LIP were accounted for by body-referenced modulation. **a**, On interleaved trials, animals made identical visual saccades from five different initial fixation points using two different head and body postures. Half of the saccades occurred with the body straight ahead and the head turned to one side (top row), the other half with the head straight ahead and the body turned to one side (bottom row). For each inset, data from eight saccades were smoothed and aligned on target presentation (large tick). An example eye-position trace is shown at the bottom left. **b**, The modulation resulting from changing both head-on-body and head-in-world position (solid grey line) was nearly identical to the gain field resulting from changing only head-on-body position (broken black line). Gain-field strengths (4.0 and 4.2% per deg, respectively) were calculated by fitting a least-squares regression to the mean discharge 50–450 ms after target appearance. Error bars show ±1 s.e.m. **c**, Similar results were obtained in the 10 out of 27 LIP cells tested with significant body-referenced gain fields (filled squares); the gain field obtained by varying head position only with respect to the body and not with respect to the world (ordinate) equalled that produced by changing both body- and world-referenced head position (abscissa). The line shows the result of a least-squares linear regression of the data (1.06 ± 0.10, not significantly different from 1 [$P = 0.56$]; $r^2 = 0.92$). Two additional cells had significant gain-field modulation for the active head but not the body-under-head rotation (open squares). Least-squares regression through all 12 cells yielded a regression coefficient of 1.09 ± 0.09 ($P = 0.34$; $r^2 = 0.52$).

plus-head position (abscissa), performed in the dark. Most 7a cells fell beneath the diagonal, indicating that world-referenced gain fields were systematically stronger than body-referenced gain fields. Most LIP cells fell on or above the diagonal, indicating that body-referenced gain fields were systematically greater than or equal to world-referenced fields. Out of 31 7a and 59 LIP cells tested, only two cells showed significant effects in both reference frames. In a separate series of experiments in which only head-plus-body rotation was performed (see Table 1), world-referenced modulation was more than twice as frequent in 7a than in LIP (40% versus 18% of cells, respectively), and the mean absolute modulation in cells with significant effects was approximately 50% greater in 7a than in LIP (1.71 ± 0.17 versus 1.11 ± 0.13% modulation per degree of head rotation, mean $\pm$ 1 s.e.m.).

Thus, when the head was repositioned with respect to the body, visual responses in LIP were modulated. When the head was repositioned with respect to the world, visual responses in 7a were modulated. However, active head movements typically displace the head in both frames of reference. The next two experiments examined gain-field modulation when the head was actively rotated with respect to both the body and the head.

In LIP, body-referenced gain-field effects could entirely account for the modulation seen after active head rotations (Fig. 2). Gain fields were compared after body-under-head and active head rotations. The top row of peristimulus time histograms in Fig. 2a shows visual responses to targets presented after an active head rotation to one of five positions. With the head turned to the left, target appearance elicited a robust response. With the head turned to the right, a retinotopically identical stimulus elicited no response. The bottom row shows that gain fields obtained after counter-rotating the body under the head were virtually identical (Fig. 2b), indicating that the gain field seen for this neuron after active head movement could be explained completely by body-referenced head position information, with little or no contribution from vestibular signals. Equal contributions from efference copy signals under both conditions cannot be ruled out, because it is possible (although unlikely) that the animal actively assisted during the body-under-head movement.

Most LIP cells had body-referenced gain fields (Table 1). Gain fields measured after active head and body-under-head rotations are compared in Fig. 2c. Of 27 cells, 12 showed a significant effect for at least one rotation. A regression analysis failed to show a difference between the two conditions, showing that LIP gain fields were driven primarily by body-referenced signals, with little or no contribution from world-referenced vestibular signals, even during active head movement (least-squares regression coefficient: 1.09 ± 0.09; $r^2 = 0.95$).

In a third experiment, we investigated whether world-referenced gain fields in 7a could entirely account for the modulation seen after active rotations of the head relative to the body. Although we found no effect of passive rotation of the body under the head, it is possible that proprioceptive or efference copy signals might nonetheless influence 7a cells when delivered in conjunction with a vestibular signal. Gain fields obtained after active head rotation were compared with those obtained after body-plus-head rotation. World-referenced signals account for only part of the effect during active head rotation (Fig. 3). Of 102 cells tested, 57 showed significant gain fields in at least one condition. Regression analysis revealed a coefficient relating the two gain fields of 0.61 ± 0.10, with a large amount of residual variance ($r^2 = 0.40$). Of these 57 cells, 18 showed significant modulation after active head but not after passive body-plus-head rotation, suggesting an influence of proprioception or efference copy. Alternatively, the faster speed of head rotation in the active head rotation task might have produced a more robust vestibular signal.

To confirm the vestibular origin of world-centred gain-field modulations in 7a, we compared responses after small rotations ($\pm$6–12°), either above (10° per s^2) or below (0.04–0.08° per s^2) the vestibular threshold. In six of seven cells, gain fields appeared after rotation above but not below threshold, strongly suggesting a vestibular input. In the absence of direct connections with the brainstem vestibular nuclei, the origin of this input could be either cortical or subcortical from vestibular-related areas. Because the vestibular canals signal angular velocity, whereas gain fields depend

Table 1 Cells in LIP and 7a with signifciant body- or world-referenced gain fields

Area	Task	Total	Body	World	Both (mixed)
LIP	Memory saccades (world plus body)	32	10	0	1
	Visual saccades (world plus body)	27	10	1	0
	Visual saccades (world only)	50		9	
	Total		20 of 59 (34%)	10 of 109 (9%)	1 of 59 (2%)
7a	Memory saccades (world plus body)	25	0	7	0
	Visual saccades (world plus body)	6	1	2	1
	Visual saccades (world only)	148		60	
	Total		1 of 31 (3%)	69 of 179 (39%)	1 of 31 (3%)

In LIP, most head-position gain fields were body referenced; in 7a, most were world referenced. Few cells showed mixed effects. The use of memory or visual saccades yielded similar results. Cells were tested for either both world- and body-referenced effects (world plus body) or for world-referenced effects alone (world only). The distribution of cells with significant effects as a function of anatomical area was statistically significant (chi-squared test on body-referenced modulation: $\chi^2 = 9.09, 1$; $P = 0.0026$; chi-squared test on world-referenced modulation, with Yates' correction: $\chi^2 = 12.271, 1$; $P = 0.00046$).

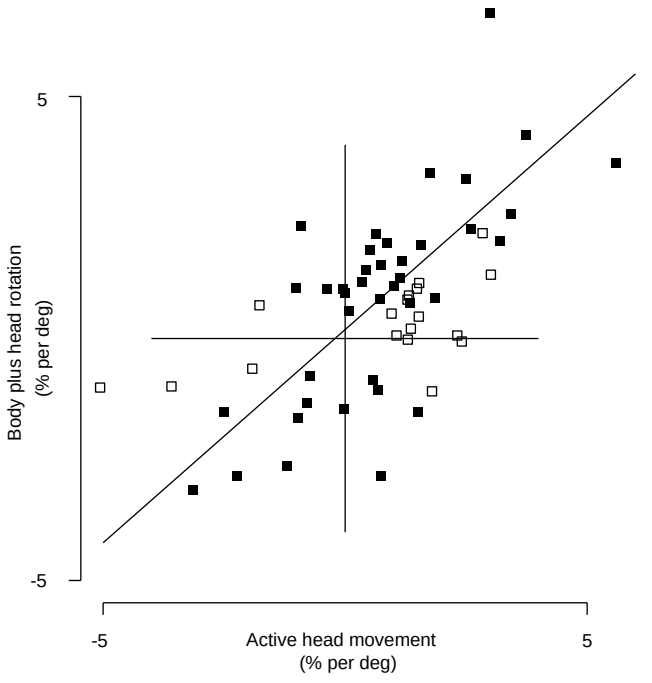

Figure 3 The 7a world-referenced gain field modulation did not fully account for modulation seen after active head movements. Gain-field modulation strengths are compared for body-plus-head (ordinate) and active head rotation (abscissa). Of 102 cells, 39 showed significant world-referenced gain-field modulation after body-plus-head rotation (filled squares). The solid diagonal shows least-squares linear regression through these data (0.88 ± 0.14, not significantly different from 1 [$P = 0.39$]; $r^2 = 0.52$). An additional 18 cells had significant gain-field modulation for the active head but not the body-plus-head rotation (open squares). Least-squares regression through all 57 cells yielded a coefficient of 0.61 ± 0.10 ($P < 0.01$; $r^2 = 0.40$).

on position, a mathematical integration of the afferent vestibular signal would be required[13]. Note that the efference copy of a velocity command would require a similar integration[14].

LIP is more closely associated than 7a with saccadic eye movements. LIP projects more heavily upon the frontal eye field than does 7a, and LIP responses are more often presaccadic than 7a responses[15,16]. Electrical microstimulation of LIP elicits saccadic eye movements, whereas stimulation of 7a does not[17,18]. LIP, but not 7a, has been shown to play a specific role in saccadic eye-movement intention[19]. The finding of body-referenced modulation in LIP is surprising, because retinotopic (eye-referenced) target location would suffice for planning eye movements. However, emerging evidence suggests that the apparent emphasis on the coding of eye movements in isolation may be an artefact of using a head-fixed preparation. Primates normally move their head and even their trunk to shift their gaze, so gaze centres in the primate may control more than just the eye[20]. Our finding of body-referenced modulation of visual signals in LIP is consistent with a more general role in directing gaze to visible and remembered targets.

Area 7a projects heavily to the parahippocampal gyrus and the presubiculum, regions known in primates to be involved in the generation of topographical memory, and in rats to be involved in world-referenced navigation[21–24]. The finding of world-referenced gain fields in 7a is consistent with a role in such functions. Some cells in primate hippocampus are activated when the animal gazes in a particular world-referenced direction; such a pattern of activation could result from world-referenced gaze direction provided by area 7a[25].

A population code can store information from several frames of reference[4,7], yet we have shown that body- and world-referenced information is largely segregated in parietal cortex. A similar anatomical segregation occurs in the coding of spatial information for directing eye versus arm movements[19]. Although it is clear that anatomical segregation based on function occurs in motor areas, it has been argued that segregation in striate and extrastriate cortex is based instead on the sensory properties being analysed[26], or on very general functional grounds[27]. We propose that, in posterior parietal cortex, information is segregated based on the specific functional role it will serve. The segregation of neck proprioceptive and vestibular information related to head movement is particularly noteworthy given that these two signals appear to be combined as early as the vestibular nuclei[28]. Segregation in the cortex may reflect different computational constraints on information processing, and may thereby increase computational efficiency and help avoid the 'curse of dimensionality' that results when attempting to code many variables within a single group of cells. □

Methods

Rotations. Data were recorded from four hemispheres of two adult male rhesus macaque monkeys. A computer-controlled, motorized machinist's turntable was used to align the turntable in the world, to which the animal's body was loosely coupled. (Both animals were under constant infrared video observation to check that the animal did not twist excessively relative to the turntable, and the second animal was equipped with a shoulder harness that completely eliminated such movement.) A pair of computer-controlled brakes acting on the head-holder allowed head fixation relative to either body or world. With neither brake engaged, the head was free to rotate ±45 degrees in the yaw plane, and to move up and down ±0.5 cm. Animals viewed a panel of light-emitting diodes, and were trained to orient their heads towards a blinking target and to make eye movements to the locations of visible and remembered steady targets. In some experiments (such as the memory saccade data of Fig. 1), all body and head movements were passive, and different postures were achieved by sequences of turntable rotations with appropriate braking. In other experiments (such as those of Figs 2 and 3), active head movements were used instead of the brake system. In this case, passive body rotations were followed by active orienting head movements. Rotations typically required from 1.5 to 3 s to complete. The positions of the eyes, head and body were electronically monitored and recorded.

Neuronal recording. Preferred vectors of isolated cells were selected from 8 possible saccade directions and 1–2 amplitudes. The preferred vector was then used to test visual saccade responses carried out at 3–5 different gaze positions, or memory saccade responses carried out at 2 different gaze positions. Different gaze positions were established by presenting a fixation target aligned with the head after positioning the head and body in one of three postures: body straight and head deviated eccentrically; body deviated eccentrically and head aligned with body; or head straight and body deviated. Typically, 8–12 trials were performed using each gaze position from each of 2 or 3 different postures. In 14 cells, individual trials were completely randomly interleaved; in 5 cells, different postures were tested in separate blocks of trials; and in the remaining cells, 2–4 target presentations were performed after each (randomly interleaved) change in posture. These differences did not systematically affect our results. For every cell, equal numbers of oppositely directed saccades were interleaved to ensure attention to retinotopic target location. Body rotations were performed in the dark or light; saccade performance and data collection occurred only in darkness.

Data analysis. Gain fields were calculated by fitting a least-squares regression to spike rate. In memory trials, rate was measured during and immediately after visual stimulus presentation (50–350 ms after the onset of a 100-ms cue). In visual saccade trials, rate was measured in a computer-selected 400-ms interval referenced between 250 and 600 ms after cue presentation; the same interval was used for all trial types from a single cell. Similar results were obtained using a fixed, presaccadic interval. LIP and 7a were distinguished by position and depth of the recording site, and by the character of cellular responses[16]. Assignments to either LIP or 7a were always made before testing for the coordinate frame, and all analyses were performed in an area-blind manner.

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Spatial exploration induces a persistent reversal of long-term potentiation in rat hippocampus

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Experience-dependent long-lasting increases in excitatory synaptic transmission in the hippocampus are believed to underlie certain types of memory[1–3]. Whereas stimulation of hippocampal pathways in freely moving rats can readily elicit a long-term potentiation (LTP) of transmission that may last for weeks, previous studies have failed to detect persistent increases in synaptic efficacy after hippocampus-mediated learning[4–6]. As changes in synaptic efficacy are contingent on the history of plasticity at the synapses[7], we have examined the effect of experience-dependent hippocampal activation on transmission after the induction of LTP. We show that exploration of a new, non-stressful environment rapidly induces a complete and persistent reversal of the expression of high-frequency stimulation-induced early-phase LTP in the CA1 area of the hippocampus, without affecting baseline transmission in a control pathway. LTP expression is not affected by exploration of familiar environments. We found that spatial exploration affected LTP within a defined time window because neither the induction of LTP nor the maintenance of long-established LTP was blocked. The discovery of a novelty-induced reversal of LTP expression provides strong evidence that extensive long-lasting decreases in synaptic efficacy may act in tandem with enhancements at selected synapses to allow the detection and storage of new information by the hippocampus.

To study the effects of processing new information on the persistence of LTP in the hippocampus, we chose a task that is known to involve activation of this brain region, exploration of a new environment[8,9]. Familiar and novel environments consisted of two boxes that were clearly distinguishable on the basis of lighting (familiar, bright versus novel, dim; see Methods). We chose to use the darker box as the novel environment because of the well known preference of rats for dimly lit areas, thereby increasing the likelihood of exploratory behaviour and minimizing the likelihood of aversive reactions (such as neophobic behavioural freezing) in the new environment. Behavioural (reduced exploration; see Methods) and electrophysiological (reduced hippocampal activation; see below) evidence that this type of exploration was accompanied by the acquisition of information about the new environment was found when the animals were reintroduced to the box on the following days.

Experiments were carried out on freely behaving animals that had been habituated over a period of 2 weeks to the recording procedure and the familiar box. Once baseline synaptic transmission, as measured by the amplitude of the field excitatory postsynaptic potential (EPSP), was found to be stable over a period of at least 3 days, high-frequency conditioning stimulation was applied to the test pathway in order to induce LTP. The conditioning stimulation used in these studies (10 trains of 20 pulses at 200 Hz) was sufficient to elicit a relatively large potentiation of synaptic responses that remained constant over the subsequent 4-h recording period if the animals were kept in the familiar box (see Fig. 1a legend for

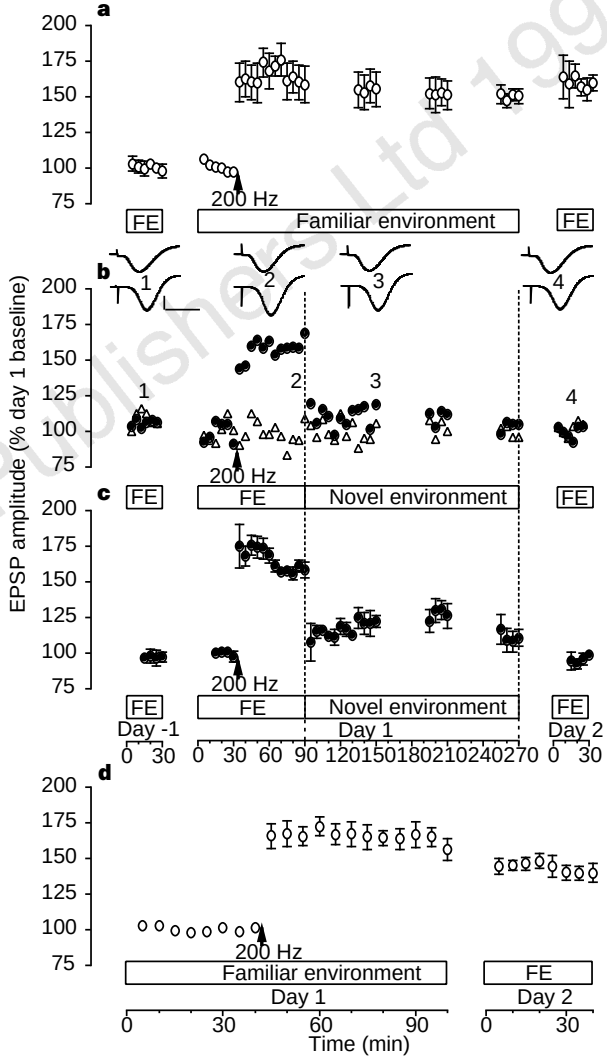

Figure 1 Exploration of a novel environment rapidly reverses LTP. **a**, High-frequency (200 Hz, arrow) stimulation induced stable LTP when induced and recorded in a familiar environment (FE). The amplitude of the field excitatory postsynaptic potential (EPSP) was significantly increased to 158.3 ± 12.9, 155.4 ± 12, 151.1 ± 9.9 and 159.7 ± 5.8% of baseline at 1, 2, 4 and 24 h after the conditioning stimulation (values are 5-min averages ± s.e.m., $P < 0.01$, $n = 9$). **b**, **c**, LTP was rapidly reversed when the animal was placed in a novel environment 1 h after the application of the high-frequency stimulation. Although the EPSP amplitude was increased at 1 h (159.8 ± 5.4), on introduction to the new environment (NE) synaptic responses returned towards baseline values, reaching 123.8 ± 4.2% at 2 h and 111.9 ± 5.9% at 4 h ($P > 0.05$ compared to baseline and $P < 0.01$ compared to potentiated level at 1 h or the level of LTP in controls; $n = 5$). LTP was still absent 24 h later when recorded in the familiar environment (98.5 ± 1.7%). **b**, Example of a two-pathway experiment. Test (black circles and lower traces) versus ipsilateral non-tetanized control pathway (white triangles and upper traces). Horizontal bar, 10 ms; vertical bar, 2 mV. **d**, Handling the animals by removing them from the familiar box to their home cage 1 h after inducing LTP had no significant effect on the magnitude of LTP when measured 24 h later in the familiar box (156 ± 7.6 and 139.8 ± 6.3% of baseline at 1 and 24 h after the conditioning stimulation; $P > 0.05$ compared to controls; $n = 5$).