Infants Adapt Their Stepping to Repeated Trip-Inducing Stimuli

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INTRODUCTION

To achieve functional walking, one must be able to adapt to changes in the external environment, such as changes in the terrain or the presence of obstacles. Ample evidence supports the ability of adult humans to adapt to sustained changes in the locomotor environment. For example, after a period of walking on a rotating disk, blindfolded human subjects showed curved walking trajectories when attempting to walk in a straight line (Earhart et al. 2001; Gordon et al. 1995; Weber et al. 1998). This phenomenon, called aftereffect, revealed the modifications of the motor program after exposure to sustained perturbations. Aftereffects have also been reported in other experimental conditions. After running forward on a treadmill, blindfolded subjects inadvertently jogged forward when asked to jog in place (Anstis 1995). Similarly, after running on a treadmill that sloped upward, the horizontal treadmill belt was perceived as sloping downward (Anstis 1995). Walking on a split-belt treadmill with the belts running at different speeds can also induce aftereffects. After a period of split-belt walking, subjects were asked to modify the belt speeds until the two belt speeds felt matched. A difference in speed between the two belts remained (Jensen et al. 1998). These data showed that the adult human locomotor system is capable of adaptive plasticity after sustained perturbations.

The results from the preceding studies are consistent with those obtained from experiments studying upper limb movements (Flanagan et al. 1999; Gondolfó et al. 1996; Martin et al. 1996a,b, 2002). With practice, adult humans were able to use a manipulandum to reach visual targets in the presence of a disturbing force field. The trajectory of the reach became similar to the control condition without the force field after some training. Interestingly, the movement trajectory became distorted immediately after the disturbing force fields were removed, revealing an aftereffect. The presence of aftereffects reflects the ability of adult humans to predict the disturbances and modify the motor program to cancel the effects of the perturbations (Gondolfó et al. 1996).

Reduced mammalian preparations also showed adaptation to repeated perturbations during walking. In decerebrate ferrets, decerebrate cats and spinal cats, when the swing phase of the forelimb was repeatedly perturbed by a bar (i.e., trip-inducing stimuli), the animal learned to increase the maximum height of the limb during the swing phase to avoid the obstacle. On removal of the obstacle, the high stepping persisted for several step cycles (Bloedel et al. 1991; Edgerton et al. 2001; Hodgson et al. 1994; Lou and Bloedel 1987). These results suggest that this particular form of learning does not require the cerebrum.

Would the developing human locomotor circuitry show similar phenomena? Human infants have been used as a model to study the control of walking before the descending tracts from the motor cortex are fully mature (Yang et al. 1998a). In this study, we examined whether human infants under the age of 1 yr adapt to repeated trip-inducing stimuli during the swing phase of stepping. Our data showed that the high stepping persisted for a few steps after the removal of trip-inducing stimuli, primarily in infants >9 mo of age. The results suggest that the locomotor circuitry in infants is capable of adaptive plasticity, but the plasticity is likely dependent on the maturation of specific neural structures. Preliminary results have been published in abstract form (Pang and Yang 2002).

METHODS

Subjects

The infants in this study were recruited through three local health clinics. Ethical approval was obtained through the Health Research Clinics of the University of Alberta. Ethical approval was obtained from the Corbett Hall, University of Alberta, Edmonton, Alberta, Canada T6G 2G4 (E-mail: jaynie.yang@ualberta.ca).

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Ethics Board, University of Alberta and Capital Health, Edmonton, Alberta. Parents were contacted by phone and instructed to practice stepping with the infant for 1–2 min daily because practice has been shown to increase the chance of obtaining good stepping in the laboratory (Yang et al. 1998a). We contacted the parent/guardian monthly to determine whether the infant was stepping. The infant was brought in for the experiment if the parent or guardian reported that the infant can make ≥10 consecutive steps, with support, at a time. Informed and written consent was obtained from the parent before the infant participated in the study. The experiments were conducted in accordance with the Declaration of Helsinki for experiments on human subjects. Thirty-three infants aged 5–11 mo (mean: 9.1 mo) were studied. All of the infants were born at term. None of the infants could walk independently at the time of the experiment.

Recording procedures

After the skin was cleaned with alcohol swabs, Kendall SOFT-E, pediatric (Ag/AgCl) electrodes were applied over four muscle groups in the left leg: quadriceps (Q), hamstrings (HAMS), tibialis anterior (TA), and gastrocnemius-soleus (GS). An electrogoniometer (Penny and Giles Computer Products, Biometrics, Blackwood Gwent, UK) was placed over the left knee joint to measure knee motion in the sagittal plane (flexion-extension). The goniometer was placed so that one arm was aligned with the longitudinal axis of the femur and the other with the lower leg. Adhesive skin markers were placed over the left side of the trunk just above the superior border of the iliac crest, the greater trochanter, the knee joint line, the lateral malleolus, and the lateral aspect of the fifth metatarsal-phalangeal joint of the left leg. The left view of the infant was recorded (30 frames/s) by using a video camera (PV-950; Panasonic, Secaucus, NJ).

A Gaitway treadmill system (Kistler Instrument, Amherst, NY) was used for all experiments. Beneath the treadmill belt were two force plates, one in front of the other, to measure vertical ground reaction forces during walking. The infant was held under the arms by one of the researchers or by a parent with one hand on each side of the infant’s upper trunk. The forearm of the individual holding the infant was supported to ensure that no movement was imposed on the infant. The infant was allowed to support its own weight as much as possible.

To prevent the infant and the adult holding the infant from seeing the baton that was used to induce tripping, a linen sheet was placed ~20 cm above the treadmill surface surrounding the infant. The speed of the treadmill belt was adjusted to obtain optimal stepping (between 0.22 and 0.31 m/s). Several trials of forward stepping were recorded for each infant.

Trip-inducing stimuli were applied manually. In previous animal studies (Edgerton et al. 2001; Lou and Bloedel 1987), disturbances were elicited by interjecting a bar into the path of the limb on each successive swing phase. Because the stepping pattern is more variable in infants, placing the bar in the same location would not have provided consistent perturbations. For example, the position of the limb varies mediolaterally with each step and the onset of the swing phase varies. For these reasons, the bar may make contact with different parts of the foot at different times in the swing phase. Therefore we applied the trip-inducing disturbances manually to make sure the perturbations were applied to the correct location of the foot (i.e., dorsum) at the desired part of the step cycle (i.e., early swing). An instrumental baton with a sponge-covered tip was used to briefly touch the dorsum of the left foot during the early swing phase. The baton was instrumented with a force transducer to measure the amount of force applied to the foot during the disturbance. In some trials, only one swing phase was disturbed. In other trials, the foot was touched for a few consecutive steps (varying from 2 to 6 steps, randomly). Typically, the mechanical stimulus induced a response (see also Lam et al. 2003a), called the stumbling corrective response by Forsberg et al. (1975), who first showed it in spinal cats. We observed whether high stepping persisted after the removal of the trip-inducing stimuli (i.e., aftereffect). Trials with trip-inducing stimuli were repeated as much as possible, depending on the tolerance of the infant.

Throughout the experiment, infants were distracted with games and toys. Each walking trial was typically 1–2 min long. The whole experimental session took ~1 h. Electromyography (EMG), signals from the baton, force plates, and knee electrogoniometer were amplified and recorded on VHS tape with a pulse code modulation encoder (A. R. Vetter, Redesburg, PA). All walking trials were videotaped. The video and analog signals were synchronized by a custom-made digital counter at a rate of 1 Hz. At the end of the session, the mass of each infant was recorded (range: 7.3–12.5 kg).

Data analysis

The data were analyzed off-line. The EMG data were high pass filtered at 10 Hz, full-wave rectified, and low-pass filtered at 30 Hz. The signals from the baton, force plates, and knee electrogoniometer were also low-pass filtered at 30 Hz. All the signals were then analog-to-digitally converted at 250 Hz (Axoscope 8; Axon Instruments, Foster City, CA).

The video data were reviewed to identify sequences of walking and disturbances. The corresponding analog data were then identified. The beginning of the stance and swing phases were determined by foot contact and toe off, respectively, as indicated by the force plate signals in conjunction with the video image. To obtain baseline measures of joint movements and toe clearance, 10 undisturbed steps were randomly chosen to serve as the control for each subject. For selection of successful disturbances, the following criteria were used: the force signal from the baton reached its peak during early swing phase (i.e., before the knee goniometer signal reversed from flexion to extension), the peak disturbance force exceeded 0.5 N because we found that a force of 0.5 N was sufficient to elicit a stumbling corrective response, and the sequence of the disturbances was followed by at least five consecutive undisturbed steps because we wished to determine the time course of any high stepping following the removal of the stimuli.

The peak force value recorded from the baton was used as a measure of the force applied to the foot during the disturbance. If more than one disturbance was applied in a trial, the peak force of each disturbance in that trial was summed and then averaged. This value served as an estimate of the average peak force applied to the foot for that particular trial. Because the disturbance was applied during the swing phase and the subsequent modifications in locomotor trajectory occurred primarily in the swing phase, the data analysis focused on the swing phase.

The force plate signals were analyzed to estimate the amount of body weight borne by the infant before and after the disturbances were applied. This was used to determine whether the person holding the infant inadvertently changed the amount of weight support during and after the disturbances. Changes in the amount of body weight support could influence the height of toe clearance. For each subject, the average force on the right leg during the left swing phase was computed for the control steps and the first post-disturbed step.

The relevant video data (i.e., the swing phases of the control steps, disturbed steps and 5 post-disturbed steps) were digitized from the videotape to the computer (Adobe Systems, Mountain View, CA). The positions of the joint markers were digitized manually using custom-written software programs (Frame Analyzer, Garand International Telecom). The position data were then filtered using a fourth-order Butterworth, dual-pass filter with a low-pass cut-off frequency at 4 Hz for the hip, 5 Hz for the knee, and 6 Hz for the ankle and toe (Winter 1990). The maximum toe height (as indicated by the position of the joint marker on the left 5th metatarsal-phalangeal joint), and the angles of the left hip, knee, and ankle joints were computed with custom-written software programs (MATLAB; MathWorks, Natick, MA).

We were also interested in determining whether the adaptive changes in movement pattern after the removal of the stimuli were...
reflected by changes in muscle activity. Mean EMG amplitude of the TA burst for the whole duration of the swing phase was calculated for the control steps and the five post-disturbed steps. If the TA EMG data showed considerable artifact or crosstalk with GS EMG, the data were discarded for this analysis. Concurrent activity in the two channels during times when the activity should be reciprocal (such as stance and swing phase of walking) was defined as probable crosstalk. The TA EMG data from one subject were eliminated as a result.

It is very difficult to record from the hip and knee flexor muscles from the infants because of the deep location of the muscles and the considerable amount of fatty tissue in the area, resulting in a small signal-to-noise ratio. To estimate the changes in muscle activity at the hip and knee joints during the swing phase, inverse dynamic analysis was performed to estimate muscle torques at the hip and knee.

For the video images, out-of-plane movements were determined by changes in the apparent lengths of the thigh and lower leg using the video data. If the apparent length of the thigh or lower leg varied by >10% during the swing phase, the step was eliminated from kinetic analysis. Only 9% of the steps were excluded as a result. Inverse dynamic analysis using a two-segment model (i.e., lower leg and foot were considered as 1 segment) was performed to calculate the hip and knee torques (Hoy and Zernicke 1986). This was reasonable because the mass of the foot and the force contribution from the ankle are very small in the swing phase (Schneider et al. 1990). The torque values were normalized to the mass of the infant (Winter 1991). Muscle torques were evaluated for all control steps and the first post-disturbed steps only because any adaptive changes in stepping would be most apparent in the first post-disturbed step. Because there was variability in the swing phase duration between and within subjects, the swing phase duration was normalized to allow data averaging and comparison between trials and between subjects. Custom-written software (MATLAB) was used for all evaluations.

Control experiments

Control experiments were conducted with five infants to make sure that the aftereffect was not due to heightened excitability of the infants caused by the repeated stimuli. EMG was not recorded and torque analysis was not performed in these infants. The trip-inducing stimuli were applied in the same way as previously described. In addition, separate trials were recorded in which mechanical taps were applied to the posterolateral aspect of the left thigh with the same baton. In both separate trials were recorded in which mechanical taps were applied to the hip and knee joints during the swing phase, inverse dynamic analysis was performed to estimate muscle torques at the hip and knee.

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Statistical analysis

For each trial, one-tailed t-tests were used to determine whether the maximal toe height for the first post-disturbed step was significantly higher than that from the averaged control steps. z score is a ratio of the difference in maximum toe height (between the 1st post-disturbed step and the averaged control steps) and the SD of the maximum toe height for the averaged control steps. An aftereffect was defined as a z score >1.645 (P < 0.05). If repeated trials were available, the z score for each trial was summed and averaged. The subject is considered to have an aftereffect if the average z score >1.645. One-way ANOVA was used to determine whether the force applied to the foot was significantly different between trials with different number of consecutive disturbances (varying from 1 to 6). χ² test of association was used to test the relationship between the incidence of aftereffect and number of perturbed step cycles. Because older (>10 mo) and younger infants (<8 mo) seemed to show a different response following the removal of trip-inducing stimuli, χ² test of association was also used to test whether there was an association between the incidence of aftereffect and the two different age groups.

Independent sample t-test were used to compare the coefficient of variation for the maximum toe height during the swing phase in the control steps for the two age groups. The two age groups compared were as defined in the preceding text (i.e., >10 and <8 mo). The coefficient of variation was defined as the ratio of SD over the mean for the 10 control steps.

Two-way ANOVA with a mixed design (i.e., containing both within and between subject factors) was used to determine whether there was a difference between the infants showing an aftereffect and those who did not in a number of measures: 1) the duration of the stance and the swing phase for the control, disturbed, and post-disturbed steps. 2) The average left TA EMG during the swing phase for the control and the first post-disturbed steps. And 3) the average vertical ground reaction force from the right leg during the left swing phase for the control and first post-disturbed steps.

To examine the time course of the aftereffect, a one-way ANOVA with repeated measures was used to compare the maximum toe height for the averaged control step and the five post-disturbed steps. A two-way ANOVA (completely randomized design) was used to determine whether the average peak force of the disturbances and the average maximum toe height for the disturbed steps were different between subjects who showed an aftereffect and those who did not. Trials with a single disturbance were not included in the preceding analyses because they produced very few aftereffects.

The statistical tests were conducted with mean values from each subject (i.e., averaged across all successful trials). An alpha value of 0.05 was set for all statistical tests. To reduce the probability of making a type I-error, the significance level was adjusted according to the number of comparisons for all post hoc tests (Glass and Hopkins 1996). Post hoc comparisons were made with the Bonferroni t-test.

RESULTS

Some infants showed high stepping after removal of trip-inducing stimuli

Some infants continued to show high stepping after the removal of the trip-inducing stimuli. An example is shown in Fig. 1, A–D. The black bars (Fig. 1A, between 3rd and 4th traces) represent the stance phases of the left leg, whereas the spaces between the bars represent the swing phases. The maximum toe height during swing phase is indicated (bottom trace) with each data point representing one step. The data points between the vertical dashed lines indicate the disturbed steps. In this particular example, three consecutive swing phases were perturbed (see the corresponding force signal from the baton, middle bottom). The left leg reacted to the perturbations by producing high steps as indicated by the maximum toe height (bottom) and the increase in knee flexion angle (2nd trace). The duration of the swing phase was concurrently prolonged in the disturbed steps. The maximum toe height did not return to the control value until the third post-disturbed step. The stick diagrams show the trajectory of the left leg for the last undisturbed step (pre-disturbed step; Fig. 1B), the first disturbed step (Fig. 1C), and the first post-disturbed step (Fig. 1D). It is obvious that the movement pattern was modified in the first post-disturbed step when compared with the pre-disturbed step.

On the other hand, some infants did not show any aftereffect after repeated trip-inducing stimuli. An individual example is shown in Fig. 1, E–H. In this case, six consecutive swing phases were perturbed (Fig. 1E). Similar to the previous example, the infant reacted to the disturbances by producing high steps accompanied by a prolongation of the swing phase.
However, immediately after the removal of the disturbances, no high stepping was observed. The maximum toe clearance for the first post-disturbed step immediately returned to control value. The stick figures illustrate the whole movement pattern. High stepping was elicited by the disturbance (Fig. 1G). The movement trajectory for the first post-disturbed step (Fig. 1H) was very similar to that for the undisturbed step (Fig. 1F), indicating the absence of an aftereffect.

The group data indicated that all infants reacted to the disturbances by producing high steps. The prolonged swing phase of the disturbed limb was accompanied by a concomitant increase in the stance phase on the contralateral limb so that an alternating stepping pattern was preserved (not shown). Because the response of the contralateral limb is consistent with other disturbances we have used to prolong the swing phase (Pang and Yang 2001; Yang et al. 1998b), no further analysis was done. The response immediately after the withdrawal of the disturbances differed between infants. The maximum toe height during the swing phase was substantially increased in infants with an aftereffect (15 subjects) for the first and second post-disturbed steps compared with control steps (Fig. 2A). For infants without an aftereffect (18 subjects), the maximum toe height only showed minimal increase for the first and second post-disturbed steps. Post hoc comparisons revealed a significantly higher toe clearance in infants who showed an aftereffect compared with those who did not for the first post-disturbed step.

The swing phase was prolonged significantly during the disturbed steps for both groups of infants (Fig. 2B). For the first post-disturbed step, the swing phase was slightly prolonged.
and the stance phase slightly shortened in both groups of infants. There were no differences in the stance or swing phase durations between the two groups of infants in any of the steps.

Number of consecutive disturbances affected the appearance of an aftereffect

Figure 3A shows the relationship between the number of consecutive disturbances applied in a given trial and the percentage of trials in which an aftereffect was successfully induced. Data from all infants are included. When a single swing phase was perturbed, aftereffects were rarely seen. As the number of consecutive disturbances was increased to two, aftereffects were observed more frequently. The success rate of inducing an aftereffect remained more or less the same as the number of consecutive disturbances was further increased up to six. There was a significant association ($\chi^2$ test of association, $P < 0.05$) between the number of perturbed step cycles and the incidence of an aftereffect. The average peak force applied to the foot was the same regardless of the number of consecutive disturbances (1-way ANOVA), so the ineffectiveness of inducing aftereffects by a single perturbation is not due to differences in force (Fig. 3B).

Age affected the incidence of obtaining an aftereffect

The most interesting finding was a correlation between the presence of an aftereffect and age. Data were pooled for all trials with two or more disturbances in an infant because there was no difference in the response between disturbances of two or more (number of trials per subject: median: 5, mean: 6). The pooled data were plotted so that the horizontal axis represents the age of the infants while the vertical axis indicates the average $z$ score for maximum toe height in the first step after the disturbance was removed (Fig. 4). Each data point represents the averaged data from one infant; --- indicates the $z$-score value of 1.645. Data points above the line indicate a significant aftereffect. Despite variability between subjects, the $z$ scores showed a tendency to increase with age. Most of the infants $>9$ mo of age (71%) and few of the infants $<9$ mo of age (20%) demonstrated an aftereffect.

The infants were further divided into two groups: those $<8$ mo and those $>10$ mo (Fig. 5). For each group, the number of disturbances...
infants with and without an aftereffect was plotted against the number of consecutive disturbances applied in a given trial (number of trials per subject for each category of disturbance: median: 2, mean: 2). For the younger infants, aftereffects were rarely seen regardless of the number of disturbances applied (Fig. 5A). In contrast, for the older infants, the probability of obtaining an aftereffect was increased if more than one disturbance was applied (Fig. 5B). There was a significant difference in the incidence of obtaining an aftereffect between the two groups of infants for trials in which three or more consecutive disturbances were applied ($\chi^2$ test of association).

Possible confounding factors

Could the difference in obtaining an aftereffect result from the difference in the amount of force applied to the foot? The pooled data (Fig. 6A) showed that there was no significant difference in force between the infants with an aftereffect (●) and those without an aftereffect (○) regardless of the number of consecutive disturbances applied (2-way ANOVA). Is it possible that the two groups of infants responded to the disturbances differently and as a result exhibited differences in the aftereffect? The maximum toe height achieved was compared between infants that showed an aftereffect and those that did not. There was no systematic trend in this comparison, although in two comparisons (i.e., 4 and 5 consecutive disturbances) the two groups were significantly different (Fig. 6B).

Did the experimenter impose changes to the infant’s weight support that might account for differences in the post-disturbed steps? For the infants without an aftereffect, the average force borne by the right leg during the swing phase of the left leg was $36.3 \pm 3.1\%$ body wt (means $\pm$ SE) during the control steps, which was not significantly different from that during the first post-disturbed steps ($34.7 \pm 2.8\%$ body wt). Similar findings were obtained in infants with an aftereffect (control steps $= 38.0 \pm 3.1\%$ body wt, 1st post-disturbed steps $= 36.5 \pm 3.2\%$ body wt). There was also no difference in the walking speed between the two groups (average speed of 0.26 m/s for infants without an aftereffect and 0.25 m/s for infants with an aftereffect). Therefore neither changes in body-weight support nor treadmill speed could account for the different responses in the two groups of infants.

Could the relationship between the $z$ score and age be due to a less variable stepping pattern in the older infants? Presumably, a less variable stepping pattern would result in a smaller SD and thus a higher $z$ score. The first post-disturbed step showed an average increase in toe clearance from the control steps of 4.5 cm for the older infants, which was two times higher than the younger infants (2.1 cm). The mean SD of the maximum toe height for the control steps was 1.4 cm [coefficient of variation (CV) = 0.39] and 1.7 cm (CV = 0.42), respectively, for the infants $>$10 mo and those $<$8 mo. Thus the stepping of the younger infants was only slightly more variable than that of the older infants. The coefficient of variation was not significantly different between the two groups (independent sample $t$-test). Therefore the difference in variability of stepping could not explain the different response in the two age groups.

Time course of the aftereffect

Pooled data across subjects who showed an aftereffect indicated that the aftereffect was relatively short-lived, varying from one to two step cycles (ANOVA with repeated measures) regardless of the number of perturbed step cycles. Figure 7 illustrates the maximum toe clearance for the infants who showed an aftereffect following the application of two and six disturbances. The averaged control steps, disturbed steps, and the five post-disturbed steps are shown. After the trip-inducing stimuli were removed, high stepping persisted for another one to two step cycles before the toe clearance returned to the control value.

Kinematics

Kinematic analysis revealed that the high stepping after the removal of the trip-inducing stimuli was produced by an increase in hip and knee flexion. Poold data for the trials in
which two to six consecutive swing phases were disturbed is illustrated in Fig. 8. Hip angle (Fig. 8, A), knee angle (Fig. 8, C and D) and toe height (Fig. 8, E and F) are plotted against the percentage of normalized swing phase duration (0% represents toe-off, whereas 100% represents foot-floor contact). For those infants who did not demonstrate an aftereffect (Fig. 8, left), the hip and knee angle and toe height for the first post-disturbed steps (thick lines) were quite similar to those for the control steps (thin lines). Slight increase in knee flexion and toe clearance is noted, however, probably because a number of infants in this group showed an increase in maximum toe height but barely missed the significance level of 0.05 (see Fig. 4). In contrast, for those infants who demonstrated an aftereffect, the movement during the swing phase of the first post-disturbed step was characterized by an increase in hip and knee flexion (Fig. 8, right). Note that the knee flexion angle peaked slightly earlier than the hip flexion angle.

Muscle torques

The aftereffect was also seen as an increase in hip and knee flexor muscle torques during swing phase. The average hip and knee muscle torque profiles during the swing phase are shown in Fig. 9. For infants without an aftereffect, the hip and knee torque profiles for the first post-disturbed steps (thick lines) were quite similar to those for the control steps (thin lines; Fig. 9, A and C). In contrast, for infants with an aftereffect, there was a large increase in the hip flexor torque during the whole swing phase, accompanied by a small increase in the knee flexor torque in the early part of the swing phase (Fig. 9, B and D).

The mean amplitude of the left TA EMG burst during the whole swing phase was also measured. Overall, there was no significant increase in TA EMG amplitude between the averaged control step and the first post-disturbed step for infants with an aftereffect and those without (not shown).

Control experiments

Five infants participated in the control experiments. All of the five infants reacted to the trip-inducing stimuli to the dorsum of the foot by increasing their toe clearance during the swing phase ($z$ score $= 7.1 \pm 1.5$, means $\pm SE$). In contrast, none of the infants responded to the thigh stimulation by producing high steps ($z = 0.2 \pm 0.1$). More importantly, while four of five infants showed an aftereffect in the first post-disturbed step after the trip-inducing stimuli were removed ($z = 5.8 \pm 2.0$), none of these infants showed an aftereffect following the removal of thigh stimulation ($z = 0.5 \pm 0.3$). The average force applied to the dorsum of the foot ($3.4 \pm 0.4$ on September 27, 2016 http://jn.physiology.org/ Downloaded from J Neurophysiol • VOL 90 • OCTOBER 2003 • www.jn.org

FIG. 7. Time course of aftereffect. A: data from the infants who demonstrated an aftereffect after 2 consecutive disturbances are shown ($n = 10$). The control step (C), disturbed steps (- - -) and post-disturbed steps (post) are shown. The trip-inducing stimuli clearly caused an increase in maximum toe height during the swing phase. The maximum toe height remained significantly above the control value for another 2 steps after the withdrawal of the disturbances. B: data from the infants who showed an aftereffect after 6 consecutive disturbances ($n = 7$). The maximum toe height remained above the control value for another 2 steps after the withdrawal of the disturbances.

FIG. 8. Kinematics changes associated with an aftereffect. Left: the data for those infants who did not show an aftereffect, right: the data for those who showed an aftereffect. The changes of hip angle (A and B), knee angle (C and D), and toe height (E and F) are plotted against the time during the normalized swing phase (0% represents toe off; 100% represents toe contact). In each diagram, the thin solid line indicates the control step (with the light gray shade representing 1 SE). The thick solid line represents the 1st post-disturbed step (with the dark gray shade representing one standard error). For the infants who did not show an aftereffect, the hip and knee motion as well as toe trajectory for the 1st post-disturbed step only showed minor changes compared with the control steps. In contrast, for the infants who demonstrated an aftereffect, there was a large increase in hip and knee flexion, accompanied by an increase in toe clearance for the 1st post-disturbed step.
The coefficients of variation of the maximum toe trajectory were very similar between the two age groups. Finally, the control experiments indicated that it is unlikely that the after-effect was due to an increase in general excitability produced by repetitive mechanical stimuli. In summary, the presence of aftereffects in infants cannot be attributed to methodological problems.

**Modifications in the movement pattern in response to repeated stimuli**

All infants reacted to the disturbances by enhancing flexion, resulting in high steps (i.e., stumbling corrective response) (see also Lam et al. 2003a). However, the response differed between infants immediately after the disturbances were withdrawn. Some infants modified their motor program with repeated stimuli to the dorsum of the foot (i.e., aftereffect). The modified movement pattern is very similar to the high steps generated during the disturbed steps (Fig. 1, C and D). Moreover, the movement pattern resembles the “elevating strategy” in adult humans when the dorsum of the foot strikes an obstacle during early swing phase (Eng et al. 1994). Similar to adult humans, the response in human infants is characterized by an increase in hip and knee flexion in the swing phase (Fig. 8, B and D), thereby increasing the foot clearance (Fig. 8F). The kinematic changes result from an increase in hip and knee flexor torque (Fig. 9, B and D). The modification in the movement pattern is functionally appropriate in that it increases the foot clearance to avoid the obstacle (Eng et al. 1994).

**Are lower centers of the human CNS capable of adaptive locomotor plasticity?**

Decerebrate ferrets and cats showed high stepping immediately after the removal of repeated trip-inducing stimuli (Bloedel et al. 1991; Lou and Bloedel 1987), indicating that this form of learning does not require the cerebrum. When the cerebellum was also removed from decerebrate ferrets, they showed the same learning behavior, although the movement was reported to be more disorganized (Bloedel et al. 1991). This finding suggests that the cerebellum, while necessary for coordination of smooth movements, is not essential for this type of learning either. In addition, it has been reported that spinal cats show the same phenomenon (Edgerton et al. 2001; Hodgson et al. 1994). Unfortunately, only single-subject data were presented in their reports. It is thus difficult to determine whether aftereffects can be consistently obtained in all spinal cats. Whether the mature spinal cord is capable of this form of learning remains an open question.

It has been well known that the isolated spinal cord is capable of other forms of learning as demonstrated in experiments studying habituation and sensitization of spinal reflexes and classical conditioning (reviewed in Patterson and Grau 2001; Wolpaw and Tennissen 2001). Operant conditioning of spinal reflexes in intact animals also involves plastic changes at the spinal level (reviewed in Wolpaw and Tennissen 2001). Moreover, the spinal cord is also able to learn specific functional tasks (i.e., stepping, standing) depending on the specific training regimen (De Leon et al. 1998a,b; Edgerton et al. 1992, 1997; Viala et al. 1986). After peripheral nerve injury, spinal cats are capable of significant locomotor recovery (Bouyer and
Adaptation to Trip-Inducing Stimuli

Rossignol 1998; Bouyer et al. 2001; Carrier et al. 1997). More recently, Timoszyk et al. (2002) demonstrated evidence of learning in spinal rats subjected to sustained loading. Therefore spinal learning can occur under many different experimental conditions.

It has generally been assumed that the stepping response in human infants is largely controlled by the brain stem and the spinal cord (Forsberg 1985; Peiper 1963). The cerebrum and its descending motor pathways to the spinal cord are not mature before the age of 1 yr as demonstrated by histological (Altman and Bayer 2001; Brody et al. 1987; Kinney et al. 1988; Yakovlev and Lecours 1967), electrophysiological (Crum and Stephens 1982; Evans et al. 1990; Eyre et al. 1991; Issler and Stephens 1983; Koh and Eyre 1988; Muller et al. 1991; Nezu et al. 1997; O’ Sullivan et al. 1981; Vecchierini-Blineau and Guheneuc 1981) and radiological studies (Barkovich et al. 1988; Dietrich et al. 1988; Holland et al. 1986). Therefore based on our results, it is reasonable to suggest that the human subcortical locomotor circuitry is also capable of adaptive plasticity just as in lower mammals.

What is intriguing in our results is the relationship between the incidence of aftereffects and age. Infants >10 mo of age were much more likely to show aftereffects than infants <8 mo (Fig. 4 and 5). We have demonstrated that methodological factors are highly unlikely to have accounted for these differences (see preceding text). Thus we are left with the possibility that other factors that change with age such as maturation of the nervous system, changes in body dimensions, or experience with stepping facilitate this form of learning. Previous exposure to similar repetitive perturbations is extremely unlikely because none of the infants could walk independently at the age of 1 yr as demonstrated by histological studies. Thus we are left with the possibility that other factors that change with age such as maturation of the nervous system, changes in body dimensions, or experience with stepping facilitate this form of learning.

The maturation of certain neural pathways may also be essential for this type of learning. Although animal studies have shown that the cerebrum is not required for this type of learning (Edgerton et al. 2001; Hodgson et al. 1994; Lou and Bloedel 1987), the specific brain stem or spinal pathways involved in this type of learning have not been identified. Some studies suggested that the cerebellum is important for motor learning during perturbed locomotion (Earhart et al. 2002; Yanigihara and Kondo 1996). In contrast, Bloedel et al. (1991) found that decerebrate animals could still adapt to trip-inducing stimuli 2 mo to 1 yr after a cerebellarotomy. Although this finding shows that the cerebellum is not absolutely essential for adaptation to repeated trip-inducing stimuli, it does not rule out the possible involvement of the cerebellum in intact animals. As infants approach 1 yr of age, many neural structures are maturing, including the cerebrum, the corticospinal tract and the lateral cerebellar hemispheres (Barkovich et al. 1988; Brody et al. 1987; Kinney et al. 1988; Yakovlev and Lecours 1967). It is possible that the maturation of these structures contribute to the learning effects reported here. Moreover, we do not know whether there are other maturational changes in the spinal cord that are important for this type of learning. So, while it is clear there are age-related changes in an infant’s ability to demonstrate this form of learning, we cannot address the cause for these changes in our study. Further animal work would be one way to determine the neural substrate for this type of learning.

In an earlier study from this laboratory, Lam et al. (2003b) used a different protocol to determine if learning occurred in young infants. In that study, sustained loading of a lower limb was used. Contrary to the current findings, the previous one did not show an age-dependent effect. We feel that this difference is likely related to the difference in protocol of the experiments. When a weight was attached to an infant, the response to the weight is less certain (i.e., he/she could respond vigorously by using more flexor activity, or respond minimally and drag his/her foot more). This option may have resulted in greater variability. In this study, the infants had no choice but to respond to the disturbance because the stumbling-corrective response is a reflex. Thus all infants responded and indeed responded in a similar way. The current protocol therefore is much more robust at showing learning if it was present.

In summary, the results suggest that the locomotor circuitry in humans is capable of short-term adaptive plasticity, before the onset of independent walking. The increased incidence of aftereffect with increasing age indicates that neural maturation or experience may be some of the contributing factors that enable the adaptation.

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