The provocative findings presented in the manuscript by Mak et al.[7] raise a number of additional questions concerning the molecular and cellular basis of mate preference. Is the increased neurogenesis transient or sustained on continuous exposure to dominant male pheromones? What is the chemical identity of the male pheromone(s) that induce neurogenesis, and do female pheromones elicit similar effects on male neurogenesis and mating preference? In this respect, it is interesting that administration of prolactin increases neurogenesis in males[11], and male mice exposed to female pheromones show an increase in plasma LH levels[13]. Finally, it will be important to determine whether pheromone-induced neurogenesis in the hippocampus affects other behaviors, such as learning and memory, which are thought to be influenced by adult neurogenesis.

Another intriguing question arising from this story is whether human mating preference is influenced by pheromones or is dependent on pheromone-induced neurogenesis. The role of pheromones in modulating human

behavior is controversial, despite evidence that some types of behavior, including menstrual synchrony and suppression, are influenced by pheromones[14]. This skepticism arose, in part, because the vomeronasal organ, a chemosensory structure thought to mediate most pheromone action, is not functional in humans[15]. However, both male[8] and female sexual behaviors[7] in rodents have now been shown to be mediated through receptors in the MOE. As humans have a functional MOE, this raises the possibility that some types of human sexual behavior, or mate preference, could also be modulated by pheromones. The discovery of a second class of receptors in the MOE of mice with an orthologous receptor in humans[9] supports the hypothesis that sexual behaviors in humans, as in mice, may be influenced by pheromone receptor signaling in the MOE.

The present findings will undoubtedly stimulate research to identify male pheromones responsible for mate preference and to define the molecular mechanisms underlying pheromone-induced neurogenesis. The extent to which similar mechanisms exist in

humans will be a topic of continuing interest to scientists, the public at large and, assuredly, the $10 billion-per-year perfume industry.

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Walking the walk

R Christopher Miall

Central pattern generators provide the basic stepping pattern in walking, but cannot adjust for the environment. A new study of human locomotion shows a pattern of changes in independent neural controllers for left and right legs.

Walking around in the real world, as opposed to an uncluttered laboratory, requires flexible and adaptive fine-tuning of the basic alternating stepping pattern of our two legs. Think of Michael Jackson's moonwalk, the asymmetric gait of a hemiplegic or even the sharp cornering of a cockroach on a messy kitchen floor; they are all examples of highly adapted stepping patterns. Like all walking animals[1], the cockroach has a set of pattern generators that control the motion of each leg, which are coupled together to produce the alternating motion of left and right legs. For the animal to walk, however, these interconnected central pattern generators (CPGs) must be modulated to allow different stride lengths in each leg, different swing heights to step over obstacles, and so on. Individuals who have reduced sensory or motor function in the lower limbs following a stroke often relearn to walk with an unusual gait[2]. Though not optimal,

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their gait may be the only working solution that they have found. The moonwalking that Jackson popularized in 1983 is an even more unusual learned pattern. His ability to give a convincing impression of forward walking, while actually moving backward, apparently took many hundreds of hours of practice, and shows that the basic kinematic pattern of leg movements can be almost completely inverted, generating ground forces with the bent leg, while sliding the apparently supporting leg over the ground.

The locomotor CPG in the human spinal cord must be under continuous descending control, with visual, cutaneous, proprioceptive and vestibular signals influencing walking direction, adjusting stepping patterns, cueing the switch between stance and swing phases, maintaining postural control and so on[3,4]. In this issue, Choi and Bastian[5] demonstrate just how flexible human walking can be by using a 'split-belt' treadmill to enforce unusual walking patterns. The authors then tested the generalization of this adaptive change to explore how the CPG components for the two legs are interconnected.

The treadmill, like jogging machines in every modern gym, has a horizontally moving belt whose ground speed can be altered. Unlike gym machines, the split-belt treadmill has separately controlled belts for the left and right legs. Choi and Bastian[5], like others[6], demonstrate rapid adaptation of walking when one belt moves at twice the speed of the other. For example, participants were first trained to walk forward with the left leg on the slow belt and the right leg on the fast belt. After ten minutes, they were then tested on a tied-belt condition, with both belts moving at the same speed. Participants showed a clear aftereffect, with the right leg now overstepping compared with the left (**Fig. 1a**). However, when the participants were tested on backward walking, they showed no aftereffect at all. Moreover, the testing of backward walking in the tied-belt condition did not reduce the forward-walking adaptation. Hence, forward and backward walking are independent learning tasks, and adapting one does not affect the other.

Stepping patterns were quantified in terms of a phase difference between the two legs. In normal

locomotion, this is 0.5 (180° out of phase), with one leg swinging forward as the other leg is moved backward. Choi and Bastian[5] found a phase shift at the onset of the split belt, followed by a return to 0.5 with adaptation, and a phase shift in the opposite direction as an aftereffect. Similar, but proportionally larger, patterns of change were seen in step lengths: the distance between the heels at footfall. In the aftereffect, the fast leg steps too far ahead of the slow leg, giving the impression of a limp. Adaptation was symmetrical with respect to training direction, so training in backward walking showed a clear aftereffect when tested in the backward-walking tied-belt condition, but a period of tied-belt forward walking imposed between training and testing in backward walking did not show any effect of training in forward walking, nor did it reduce the learned effect.

Their most complex task involved hybrid walking, in which the split-belts moved at the same speed, but in opposite directions, so that subjects had to walk forward with one leg and backward with the other. Participants had to do something a bit like moonwalking: they alternately switched their support phase from the leg moving backward (as normal in forward walking) to the leg moving forward (as in backward walking). This led to a phase difference between the legs approaching zero, as both legs are moving in the same direction, but one in swing and one in stance. Subjects coped well with this task, and they then underwent training with one belt going twice as fast and in the opposite direction. Transfer of hybrid walking training was measured in tied-belt forward- and backward-walking conditions, as well as in the same-speed hybrid-walking condition. Testing the directionally specific effects on the individual legs revealed aftereffects of hybrid walking in both forward- and backward-walking tied-belt conditions, as predicted (**Fig. 1b**) because hybrid walking includes elements of forward and of backward walking. Moreover, these two postadaptation tests combined to wash out the adaptation, so that no remaining aftereffect was found in the final hybrid-walking test condition.

Thus, there is evidence of four functionally distinct systems: two directionally specific controllers for each leg. Their data is incompatible with a model (**Fig. 1c**) in which only the interactions between these four separate CPGs are modified by the adaptation process, whereas the CPGs themselves remain unchanged. What defines the 'direction specificity' of the controllers? Is there another set of controllers for sideways walking? Perhaps more realistically, are these controllers functionally separated by gait—is there one set for walking and another for running? In quadrupeds, walking, trotting
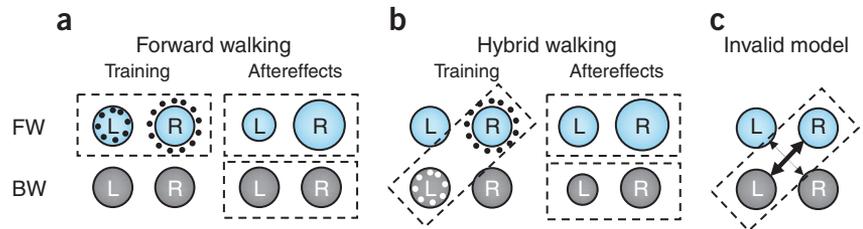
Figure 1 Four neural systems are postulated, controlling forward (FW) and backward (BW) walking in left and right legs. (**a**) In forward split-belt training, indicated by the dashed box, the right belt is faster than the left, inducing relative changes in the left and right forward-walking circuits (dotted circles). When walking on the tied-belt was tested after adaptation, an aftereffect was seen in forward walking, but not in backward walking. (**b,c**) In hybrid adaptive walking (**b**, diagonal dashed box), the left leg is on the slow backward belt and the right leg on the fast forward belt. This induced changes that were evident as aftereffects in both forward and backward walking, and that were compatible with this model of four functionally separate controllers, but were incompatible with a model (**c**, arrows) in which functional connections between these controllers are modified by learning.

and galloping are distinct patterns, as different as forward and backward bipedal walking. This predicts some interesting new experiments testing generalization of split-belt training across walking and running. In addition, coordination of these spinal circuits, and the switching between gait patterns, is heavily modulated by descending signals[1]. That is not directly demonstrated by Choi and Bastian's[5] work, but is consistent with a great deal of other work on quadruped locomotion[4]. It implies that the cognitive context[7] of the split-belt task might help to separate the functional circuits.

This leads to another important question that is raised by this new study[5]. If human locomotion is so adaptable, can tricks like the split-belt treadmill be used to enforce better gait patterns as part of a rehabilitation strategy; for example, after a stroke? So far, results from the same research group are encouraging[8], but leave a considerable ways to go. Despite split-belt training leading to a more symmetric pattern in the postadaptation stage, which shows that stroke patients retain the facility to adopt a more normal gait pattern, they revert to their asymmetric gait soon after the end of training. It is likely that they treat the adaptive experience as contextually separate from their normal walking experience. It will therefore be important to encourage generalization from the split-belt training to real-world walking[9]. Hence, an implicit training protocol that avoids explicit awareness or dual-task training, in which some other irrelevant task distracts attention from the walking, may increase transfer from the laboratory to the real world.

One interesting issue is what drives the de-adaptation process away from symmetry and back into the individual's adopted asymmetric pattern. If limb sensorimotor function after stroke is still impaired by reduced sensory or motor performance, then an asymmetric gait might be more effective, even if not normal.

However, if the de-adaptation is caused by residual long-term adaptive processes[10] that were not shifted during the brief exposure to split-belt walking, then maybe one can target that process, devising training protocols that reactivate and weaken those 'slow' memory traces[11] and trigger longer-lasting adaptation.

Another unusual extension of this work would be to use the split-belts to test the still uncertain links between upper- and lower-limb pattern generation. We do appear to use 'quadruped' locomotor patterns in some circumstances[12], as crawling infants or swimming adults, but the split-belt technique could allow for some interesting tests of interference between patterns of lower-limb gait and swing of the arms. For example, if the training causes an asymmetric aftereffect in the legs, is a complementary aftereffect seen in arm swing[13]? As further speculation, could some form of split-belt training that enforces a highly asymmetric arm swing be used to drive more effective, symmetric lower limb movement in rehabilitation patients? Most improbably, is there any hope for my disco dancing?

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