initially random formation of putative synapses followed by the retraction of all filopodia that failed to make contact—thus, synapses appear to stabilize dendrites.

The study by Niell et al.1 is perhaps the first to actually watch potential synapse loss during synaptogenesis in the CNS. As in cultured neurons5, the authors found that synapse disassembly, suggested by a significant decrease in PSD-95-GFP puncta fluorescence, seemed to take place before dendrites retracted. Why would synapse disassembly cause dendritic terminals to retract? One possibility is that resources needed to maintain or extend new dendrites may be limited; therefore, retraction in regions with undesired inputs would facilitate dendritic extensions elsewhere. Reiterations of this process would tend to bias dendritic elaboration and growth toward regions containing appropriate presynaptic terminals. The current live-imaging study thus supports this 'synaptotrophic model' put forth a number of years ago based on electron microscopy observations12. This model might explain, in part, how asymmetrically organized dendritic arbors are established in some sensory systems such as the retina and barrel cortex where preferred afferents are organized into specific subregions of the tissue2,14. Further live-imaging studies of dendritic behavior and synapse development, in circuits where one can distinguish between appropriate and inappropriate presynaptic terminals, should provide a deeper insight into how some connections are maintained and others eliminated. Given that zebrafish are an excellent model for studying circuit development in vivo, such imaging studies using this model system will undoubtedly be fruitful.

Just one word: plasticity

Andrew R Blight

A new study shows that after injury of the corticospinal tract in the rat spinal cord, spontaneous recovery of function involves extensive plastic changes in the connectivity of multiple types of neurons distributed throughout the central nervous system.

The ability of the adult mammalian central nervous system (CNS) to recover from injury is sometimes remarkable and at other times frustratingly limited, but in either case it remains poorly understood. Nowhere has the frustration and lack of understanding been greater than in the case of the injured spinal cord, where limitations on recovery seem particularly severe. Plasticity of connections in the spinal cord provides some capacity for adaptation to injury1,2 and represents a target for therapeutic manipulation3,4. When one pathway from the brain to the motor systems of the spinal cord is interrupted, another parallel pathway can take over the role of the missing projection, by a process of collateral sprouting. In this issue, Bäreyre et al.5 demonstrate a surprisingly extensive capacity for spontaneous functional reorganization in spinal circuits. This plasticity does not occur at one level of the neural network, but crosses over to parallel pathways and extends to both upstream and downstream components.

Andrew R. Blight is at Acorda Therapeutics, Inc., 15 Skyline Drive, Hawthorne, New York 10532, USA.

e-mail: ablight@acorda.com

new connections that were lost during this time projected to short propriospinal neurons, whose axons remain within the cervical spinal cord. Connections to long propriospinal neurons, projecting to the motor pools of the lumbar cord, apparently most useful, were retained. The investigators were then able to show that the long propriospinal axons themselves increased their projections in the lumbar motor pool. To provide additional evidence that a new intraspinal pathway had been formed by this combination of first- and second-order sprouting, they did transynaptic retrograde tracing by injecting pseudorabies virus into the hindlimb muscles. They saw a 4–5 fold increase in the labeling of pyramidal cells in the motor cortex, lumbar motoneurons and cervical propriospinal interneurons, which project either to cervical or lumbar motor pools. The precise nature of neuronal projections, including the branching site of new collaterals and the degree to which synapses are formed directly on motoneurons is not entirely clear and much more complex than illustrated here. After dorsal hemisection of the lower thoracic spinal cord, involving complete transection of the dorsal corticospinal tract, increased synaptic projection (blue) was seen from hindlimb motor cortex to long propriospinal interneurons projecting to lumbar motor pools (1), from those same propriospinal neurons, within the lumbar motor system (2), at 3 weeks after injury, from hindlimb motor cortex to short propriospinal interneurons within the cervical cord (3, though many of these presumably inappropriate connections appeared to be lost again at 12 weeks); and from forelimb motor cortex to hindlimb motor pool (4), most likely through sprouting at the level of propriospinal neurons in the cervical cord. Pronounced sprouting was not seen from the ventral CST (5), though some sprouting may occur, based on earlier findings with cervical transection of the CST injury.

Partial functional recovery of the hindlimb placing responses developed gradually over the weeks after the CST lesion, consistent with a functional benefit of the increased cortico-spinal connection. Unilateral transection of the pyramidal tract in the brainstem produced a significant loss of that recovery on the affected side, indicating that the recovery of placing was dependent on new projections of the CST. The increased projection from cortex to lumbar motor systems was also confirmed electrophysiologically. Microstimulation of the cortex produced hindlimb muscle activation in uninjured animals and, at slightly higher threshold and latency, in animals at 12 weeks after injury, but not in animals after only 3 days or 3 weeks of recovery. Again, this electrophysiological recovery could be abolished by a second, unilateral transection of the CST in the brainstem.

One additional finding emerged from the studies. Retrograde labeling with pseudorabies virus from the periphery revealed an ‘upstream’ reorganization of corticospinal connections. Approximately a quarter of the labeled neurons in the cortex of animals recovering from the dorsal CST lesion were outside the normal hindlimb area; most were found in the forelimb area of the cortex, but a few came from outside the motor representation altogether. Therefore, the processes of reorganization started by the dorsal hemisection spread well beyond the neurons that were directly damaged, including other pathways within the local spinal cord, the target motor systems in the lumbar cord, and related populations of cells in the motor cortex of the brain.

Changes in connectivity are likely to be even more widespread than the Bareyre et al. study has revealed. Compensatory sprouting of the ventral CST has already been detected in cervical cord, and is likely to occur in this model too, though it was not possible to resolve such changes here, perhaps because of the modest contribution of the ventral CST to the hindlimb motor system. There are also likely to be changes in other ascending and descending projections that were not examined, but which are damaged by the hemisection lesion. Some of these may contribute to the overall functional recovery that is seen. This, however, does not diminish the remarkable extent and apparent functionality of the changes that were measured.

The human CNS may be very different in its responses to injury, as compared to the rat. Nonetheless, there is evidence of widespread reorganization of connections in human CNS derived from studies in people with spinal cord injury. Precise interpretation of these changes is difficult, given the complexity and severity of spinal lesions in such cases.

The signaling process responsible for these widespread changes is not at all clear. Still more obscure is the mechanism that allows newly formed connections to be retained or lost, based on their overall usefulness, as seems to be the case with the new connections to the short propriospinal interneurons. If a feedback mechanism exists to signal whether a neural connection is ‘right’ or ‘wrong’, it seems to require integration at the very highest level. Intuitively, such a mechanism seems to be in action under conditions, such as amateur athletics, that test the performance of our sensorimotor systems. This is expressed with characteristic remorse by the poet Philip Larkin as he describes tossing an apple core at a waste basket:
Understanding awareness: one step closer

Steven J Luck

Attention enhances neural and behavioral responses to visual objects, but how does this affect our conscious perception? Attending to an object increases our subjective experience of stimulus contrast, reports a study in this issue.

In this issue, Carrasco and colleagues\(^1\) provide a step toward a richer and yet still rigorous description of awareness. This study addresses phenomenological experience in the context of a very old question about perception: does paying attention to an object change its appearance? Attention is often likened to a spotlight\(^4\) or zoom lens\(^5\) that brightens or sharpens our perception, but no one has convincingly shown that attention actually changes our phenomenological experience of the world. Many studies have shown that attending to an object amplifies and sharpens neural representations of the object\(^6-8\), leading to an improved ability to detect the object and report its properties\(^9,10\). However, these studies do not show that we actually experience attended objects differently from unattended objects.

The ever-present problem in studies of awareness is that observers’ reports of their experience are very easily biased by a variety of cognitive and affective factors. If observers report that an attended object seems brighter than an ignored object, it is usually impossible to know whether they really experienced it as being visually brighter. It is always possible that attention did not influence their perceptual experience, but rather that preconceptions about attention led them—intentionally or unintentionally—to report it as being brighter. Carrasco and colleagues have developed a new procedure for assessing an observer’s experience that markedly reduces the influence of bias on such reports.

In this procedure (Fig. 1), observers were shown two oriented gratings and asked to report the orientation of the higher-contrast grating (the one with brighter brights and darker darks). Thus, the observers explicitly reported the orientation of a grating, and their decision about which grating was higher in contrast was implicit rather than explicit. Attention was manipulated by preceding one of the two gratings with a small dot that automatically attracted attention.

When the two gratings differed greatly in contrast, the attention-capturing dot had no effect: observers simply reported the orientation of the higher-contrast grating. When the