Editorial

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Taking sides

Corticospinal tract plasticity during development

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Recent studies in many different species have shown that peripheral or CNS damage early in life can affect subsequent brain development and lead to patterns of brain organization and function that differ greatly from normal.[1] Impressive progress is occurring in understanding the nature of these reorganizations, and the mechanisms responsible for them are gradually emerging. At the same time, direct evidence that early lesions have similar effects in humans is limited, and the clinical implications of such effects are largely unknown. In this context, the study of Eyre et al.[2] in this issue of *Neurology* is an important contribution.

Eyre et al.[2] used transcranial magnetic stimulation (TMS) of motor cortex to evoke responses in trunk, arm, and hand muscles in normal subjects from birth to adulthood, in subjects with hemiplegic cerebral palsy, and in subjects with hemiplegia due to stroke at least 6 months earlier. Furthermore, they studied a group of normal neonates within 2 days of birth and then at 3-month intervals until age 2. Their primary goal was to compare contralateral and ipsilateral muscle responses to stimulation and thereby compare contralateral and ipsilateral corticospinal tract projections. In normal neonates, contralateral and ipsilateral responses to TMS were similar in size. Thereafter, ipsilateral responses became steadily smaller and later relative to contralateral responses until adult values were reached by age 16. In subjects who had hemiplegic strokes as adults, this normal pattern of contralateral dominance was still evident when the intact hemisphere was stimulated. In contrast, subjects with hemiplegic cerebral palsy retained the infantile pattern: when the intact hemisphere was stimulated, they displayed low threshold, large amplitude, and short-latency responses in ipsilateral as well as contralateral muscles. These results are consistent with animal studies of the lateralization of corticospinal tract projections during development[3] and provide information on the rate and extent of this process in humans that could not be gained from animals.

The authors propose that perinatal damage to one hemisphere disrupts the normal competition between contralateral and ipsilateral corticospinal projections and thus leads to abnormal preservation of the ipsilateral projections and possibly also to abnormal loss of those contralateral projections that survived the initial insult. A comparable effect occurs with disruption of the normal binocular competition during development in visual cortex (e.g., see reference [4]), and may underlie the gradual development of amblyopia in children with strabismus. The results might also reflect growth of preserved ipsilateral corticospinal projections to contact more spinal cord motoneurons. Such growth after the loss of normal connections can be prominent, even in the mature brain.[1] This possibility could be addressed in future animal studies that use anatomic or physiologic methods to assess the spinal cord terminations of individual corticospinal tract neurons over the course of development.

The early years of life are clearly a busy time for the corticospinal tract. Its activity appears to drive the plasticity that underlies the predominance of the contralateral projection and the well-focused spinal cord reflex patterns evident in normal adults. The data reported in Eyre et al.[2] complement recent insights into the role of the corticospinal tract in shaping spinal cord motor function during development and even later in life.[5] Several research groups, including Eyre et al., have found that perinatal hemispheric damage in humans is associated with abnormal preservation of infantile stretch reflex patterns[6-10]: the short-latency excitation of both agonist and antagonist muscles by muscle stretch that is normally seen only in the infant persists into adulthood. A similar preservation of infantile flexion withdrawal reflex patterns occurs in rats subjected to perinatal spinal cord transection.[11] That normal reflex development depends on the corticospinal tract specifically is also suggested by animal and human data indicating its importance in operant conditioning of spinal reflexes. Humans, monkeys, and rats

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can gradually increase or decrease the amplitude of the spinal stretch reflex (i.e., the tendon jerk) or its electrical analog, the H-reflex, without change in motoneuron background tone when they are rewarded for during so.[12] This ability appears to be abolished by lesions of the corticospinal tract or sensorimotor cortex.[13,14] Throughout life, comparable modifications in spinal reflex function are associated with and contribute to the gradual acquisition of complex motor skills.[5,12]

The study of Eyre et al.[2] has implications for the design of new rehabilitation strategies aimed at reducing the effects of perinatal hemispheric damage. For example, as the authors suggest, techniques that increase the competitive advantage of surviving contralateral projections from the damaged hemisphere might reduce or prevent the gradual development of hemiplegia that often occurs.[15] In addition, methods that provide stereotyped patterns of activity in remaining corticospinal tract projections or peripheral afferents might promote development of more appropriate spinal cord reflex patterns and thereby improve motor function.[5,10]

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