Developmental regulation of the neuromotor circuit: peripheral and central synaptic influences in motoneuron numbers and innervation of muscle

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Neural development is characterized by the formation of complex neural networks such as the neuromotor system. During embryonic development approximately half the number of motoneurons generated undergo cell death. This is at a time when motoneurons are making contact with skeletal muscle, and when contacts onto motoneurons by other neurons are being established. This suggests that both central and peripheral synaptic contacts act to regulate the number of motoneurons during this embryonic period. Recent studies have suggested that glycinergic and GABAergic synaptic activity may be essential for the maturation and refinement of developing neural networks. These transmitters switch from producing excitation to inhibition during late embryonic and early postnatal stages. We and others have shown that functional neuromuscular synaptic outputs regulate motoneuron death. This leaves open the question as to whether central synaptic inputs to the motoneuron might also influence survival or death of the motoneuron during this period of neuron cell death. Morphological and functional evidence indicates that glycinergic and GABAergic synapses control motoneuron development in a region-specific manner during the period of developmental motoneuron death. This evidence is from the physiological and morphological analyses of mice that lack GABA (GAD67 - deficient mice) and from mice lacking post-synaptic Glycine receptors (Gephyrin - deficient mice).