Animal Models of Neurodegeneration

Although memory loss and cognitive decline are important aspects of human health, there are other diseases of the central nervous system that do not impact effect memory and learning. Neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, and Huntington's disease are linked to death or dysfunction of nerve cells associated with movement. Models that recapitulate the symptoms of movement-associated neurodegenerative diseases have been developed using both pharmacological intervention and transgenic science. It is worth noting, however, that these models are generally isomorphic in nature, as the cause of the human conditions are unknown. The loss of motor control associated with Parkinson's disease, for example, is the result of the death of dopamine-generating cells in the substantia nigra region of the brain, but the cause of the cell death remains a mystery. These models have face validity, making them useful for exploring pathophysiology and possible treatments for the associated conditions.

The SOD1-G93A Mouse of Amyotrophic Lateral Sclerosis[6,22]

Amyotrophic lateral sclerosis is a debilitating neurodegenerative disease characterized by the death of both upper and lower motor neurons in the motor cortex of the brain, the brain stem, and the spinal cord. The progressive denervation of muscle tissue causes muscular weakness, paralysis, and atrophy that become more extensive through the course of the disease. Although the exact cause of ALS is unknown, the SOD1-G93A mouse model suffers from the same progressive motor neuron death. These transgenic mice overexpress mutated human copper–zinc superoxide dismutase (SOD1) in which the glycine in the 93rd position is replaced with an alanine residue. The pathology created in this transgenic mouse model correlates well with the human condition, as symptoms such as paralysis begin to occur at approximately 90 days old, and in the absence of therapeutic intervention, the mice die in approximately 135 days.

Novel compounds that are capable of slowing or stopping the progression of this neurodegenerative disease can be studied in this animal model by observing physical capabilities and changes in compound-treated animals as compared to untreated control animals. Grip strength, body weight, righting reflex (the ability of an animal to right itself after being placed on its back), and rotarod performance (Figure 7.6) can all be observed as the treated and untreated animals age. Compounds capable of slowing motor neuron degeneration will demonstrate improved responses in these measures for treated animals. Overall mortality will also improve with compounds that are efficacious.

An important aspect of this model is the length of time and resources required to complete an experiment. Unlike the previously described