

and memory. These aspects of brain function are more appropriately assessed in the Morris water maze. In this model, a rodent's ability to remember the spatial relationships of object within a previously encountered environment is measured. The model itself consists of a pool of water in which the animal must swim. A single platform is placed in the pool below the water surface, but high enough that the rodent can stand on the platform rather than swim in the water. Rodents are initially trained in the pool with clear water so that they can see the platform below the surface of the water. Once the rodents are trained, which generally requires several days, the pool water is made opaque with a coloring agent. When the rodents are placed in the pool, the time required to find the hidden platform is measured, providing an assessment of their ability to form spatial memories regarding the location of the platform. Alternatively, the platform can be removed from the opaque pool, and the amount of time the rodent spends in the quadrant that previously contained the platform can be measured. Rodents suffering from cognitive decline, such as transgenic mice designed to model Alzheimer's disease, will require longer periods of time to find the hidden platform. If the platform has been removed, impaired rodent will spend less time in the appropriate quadrant of the pool as compared to normal rodents. The ability of a test compound to prevent cognitive decline, restore, or enhance memory can be tested in this model. Compounds that either protect or restore cognitive function would be expected to decrease the time required for a rodent to locate the hidden platform or increase the time spent in the proper quadrant of the pool if the platform has been removed as compared to control animals (Figure 7.5).

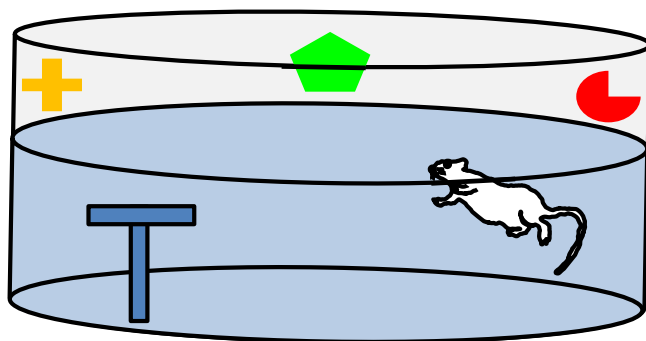


FIGURE 7.5 The Morris water maze provides an assessment of a candidate compound's impact on learning and memory. Rodents are trained to locate a submerged platform in a clear pool. Their ability to remember the location of the raised platform is then challenged by replacing the clear water with an opaque solution that hides the submerged platform. Candidate compounds that impact learning and memory will affect the rodent's ability to locate the submerged platform when the liquid is opaque.