

Measuring recovery of forelimb function after CNS injury in rodents and primates, with notes on man

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The development of reliable, valid, and quantifiable measurement of neurological function is important for the testing and translation of strategies aimed at improving function after CNS injury or disease. Tests of neurological function in spinal cord and brain injury range from descriptive locomotor measures to high speed kinematics. In this section of our symposium, we will describe a variety of tests aimed at determining loss and recovery of forelimb function in rats and monkeys, and will refer to techniques used to measure function and functional recovery after stroke and brain injury in man. The goal for the future is to determine common tests or common features of recovery that can then be used to integrate animal models with planning for outcome measures in human clinical trials of treatments for CNS injury.

A number of laboratories study recovery of function after unilateral cervical injuries in the rat, usually after partial or complete hemisections at high cervical levels. We and others have also devised unilateral and bilateral contusion lesion of the cervical cord in rats (Gensel et al, 2006). The unilateral lesions allow for contralateral comparisons in function, and also provide a useful model that has much less disability than either a bilateral cervical or thoracic contusion lesions. A variety of forelimb tasks have been adapted to this model (see Gensel et al, 2006), including the use cylinder test for limb use, a grooming test that engages a stereotyped forelimb motor pattern and can be scored, and locomotor analyses on the CatWalk apparatus (Hamers et al, 2006) such as the area occupied by the forepaw. These will be described and demonstrated in rats with unilateral cervical contusion injuries. A new test developed in the laboratory will also be described and demonstrated: rats are videotaped while eating various shaped pieces of cereal using both forepaws. They exhibit considerable dexterity in this task, and after injury, lose function of the ipsilateral paw. Forepaw dexterity recovers in a predictable pattern over time, and plateaus at different levels of function depending upon the severity of the contusion injury. This can be scored on a 10 point scale, Recovery curves are comparable to those seen in the Gensel et al (2006) study for the cylinder tests and the grooming test.

Additional tests of skilled limb movements will be described in the presentation by Dr. Metz.

In collaboration with the California Primate Spinal Cord Consortium, led by Drs. Mark Tuszynski and Reggie Edgerton, our laboratory has been involved in developing relatively simple and repeatable tests of forelimb function in rhesus macaques that have focal, unilateral, spinal cord lesions. These tests include a reach-grasp-and pull task, a food retrieval task, and a drawer-pull task that requires thumb-finger apposition for success. These tasks are also compatible with electromyographic (EMG) measurements that can demonstrate the degree of flexor-extensor co-activation. Parallels between these tasks and those used for the rats will be discussed.

Finally, a brief discussion of current literature describing the ways in which human stroke and traumatic brain injury patients are tested for arm and hand function and recovery will be given, with parallels and potential applications to the animal model techniques also discussed.

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References

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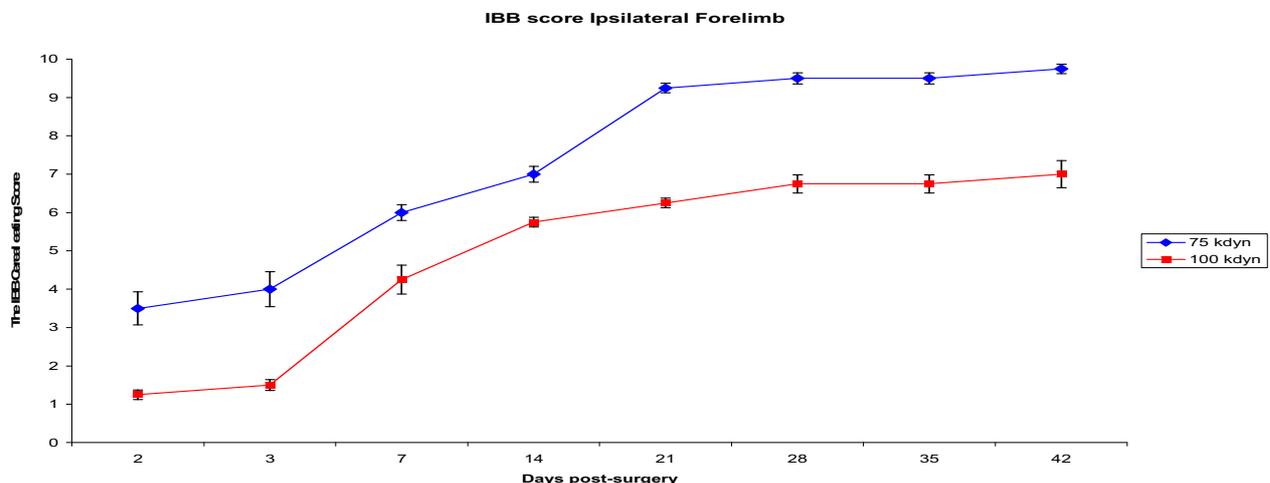


Figure 1. Recovery of forelimb use during a cereal eating task as scored on the new rating scale after a 100 Kdyne (red) and 75 Kdyne (blue) contusion injury with the IH device. Weeks post-injury are shown across the bottom.