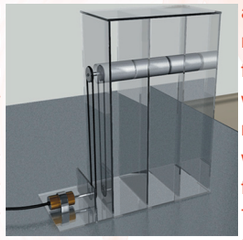
# NeuroInvestigations

NeuroInvestigations Inc. offers a wide range of services for investigating therapeutic modalities for stroke. We have a scientific advisory committee that includes several world renowned behavioural neuroscientists who are at your service to help you design the most thorough and cost effective experimental design to meet your research needs. We have developed a state-of-the-art functional recovery assessment that can be repeated many times over an extended period following stroke damage. This battery of tests allows us to accurately quantify functional recovery over time, and to provide a composite recovery index that is comprehensive and easy to communicate. Our functional battery includes the following.



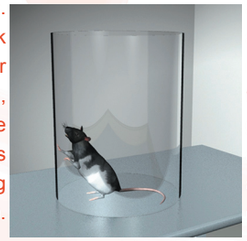
Rotorod

• Tray Reaching: Recovery of forepaw motor coordination is measured by analysis of successful versus non successful reaching, grasping and consuming of tasty food pellets. Performance in tray reaching is greatly affected following stroke involving the motor cortex. Recovery of this function can be followed for months following stroke.

• Gridwalk: Forelimb and hindlimb motor coordination is measured using an elevated bridge of unevenly spaced rungs. Motor incoordination is measured as the number of placement errors (i.e., limb falls between the rungs). Rats with cortical damage due to stroke show a large number of paw placement errors while traversing the bridge. Recovery of paw coordination can be assessed for many months following stroke using the gridwalk.

• Forepaw Asymmetry: Asymmetry of forelimb use is assessed by analyzing the use of left and right forepaws for bracing against a cylinder wall during rearing. Normally rats use each forepaw equally often for bracing while rearing. A rat with stroke to motor cortex and related structures will show a large asymmetry in forepaw bracing during rearing. This test can be used to assess functional recovery for an extended assessment following stroke.

• Sunflower seed test: Forepaw motor coordination is assessed by analyzing the efficiency (speed and number of shell breaks to reach and consume inner seed) in eating sunflower seeds. Normally rats will break into and consume the inner seed with great efficiency (i.e., only 1 or 2 breaks to get to the seed, and only a few seconds will pass between obtaining and consuming of the seed).

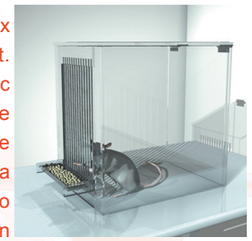


Forepaw Assymetry

• Forelimb Inhibition: Normally rats swim with their forelimbs tucked (unmoving) under the chin. Rats with motor cortical damage tend to stroke with the forelimbs during swimming. We assess the degree of disinhibiting of forelimb stroking while swimming in rats following stroke damage.

• Rotorod: Balance and motor coordination are assessed using the rotorod. Ability to walk on a rotating drum at various speeds is assessed.

• Tail hang: The tail hang reflex will be assessed in this test. Normal rats show a characteristic position of forelimbs during the hang, that is, tucked up under the chin and close to the body, with a fist made of the digits. They also show anticipatory digit extension when lowered toward the test table. They do not show a turn bias. Turn direction, position of, and digit extension can be assessed repeated following stroke.



Tray Reaching

• Single pellet reaching: Qualitative assessment of posture, motor coordination, and grasp strength are all assessed in the single pellet reaching test. Single reaches through an elongated window to grasp a sweet pellet are filmed and analyzed frame-by-frame according to ten components of each reach: 1) limb lift, 2) digits close, 3) aim, 4) advance, 5) digits open, 6) pronation, 7) grasp, 8) supination I, 9) supination II, and 10) release. This is an extremely thorough and sensitive measure of limb function following stroke, and can be repeated as necessary.

Histology: At the conclusion of testing we have available a very wide range of techniques for evaluating cellular changes and stroke volumes. Tissue can be cut using microtome, cryostat, or vibratome techniques and prepared for light, fluorescence, electron, or confocal microscopic examination or measurement. We have a variety of digital imaging techniques for histochemical, immunocytochemical, and stains/markers available for quantifying tissue effects.

NeuroInvestigations routinely employs 2 animal models of human stroke (pial stripping and Middle cerebral artery occlusion (MCAO)). Please note that we are not limited to these models and have the expertise to serve your particular requirements.

Pial stripping involves localized devascularization of neocortical tissue. The technique was developed by one of our three scientific advisors, Dr. Bryan Kolb. Typically, the pia mater overlying the cortex is removed. This results in a permanent interruption of blood flow to the underlying brain tissue and subsequent damage to neuronal circuitry. Because only a very circumscribed brain area is damaged, this model lends itself to the study of functional loss and recovery of sensory or motor functions. We have a battery of behavioural and physiological tests available that is sensitive to damage to the primary motor cortex. The test battery can be repeated many times, both prior to the stroke, as well as for extended times following surgery. Changes in performance on these tests allow us to carefully quantify the extent of functional loss caused by the stroke, and to carefully measure the recovery of functions over many months following the stroke. This model is very useful in testing therapeutic compounds which are thought to have neuroprotective effects during a stroke, as well as therapeutic compounds which are thought to accelerate recovery.

Middle cerebral artery (MCA) occlusion is our second animal model of human stroke. We disrupt blood supply to the frontal cortical region and the striatum. This interruption can be temporary or permanent. In a temporary occlusion the artery is either clipped or plugged for 60 minutes. Following 60 minutes the clip or plug is removed from the artery and the blood flow is allowed to resume. In the permanent occlusion the middle cerebral artery is electrocauterized thereby blocking blood flow. A battery of tests that includes both motor and cognitive assessments is employed to measure the magnitude of the initial deficit caused by the stroke, as well as to track the functional recovery following the insult. This model is particularly useful if one wishes to assess neuroprotection during the trauma with reperfusion of the tissue following the stroke.