Skilled Limb Use in Rat Models of Human Neurological Disease

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Introduction

Skilled movements are voluntary movements requiring irregular motor patterns. Skilled movements are characterized by a complex sequence of movement components, which can be observed in rats eating specialty food items, such as sunflower seeds or crickets, or when navigating across difficult territory [5]. Tests of skilled movement are of increasing importance as sensitive assessment tools for rat models in pre-clinical studies of neurological disease.

A number of formal tests for skilled movements have been developed in order to allow objective and reproducible evaluation of limb function. Tests of skilled movement have the advantage to produce a variety of different parameters, such as end point measures and qualitative measures. The majority of skilled movement tests focus on the analysis of forelimb use, such as grasping and retrieving food items, or applying force to retrieve an object. More recently, a task for skilled walking has been developed, which allows assessment of hind limb functions as well as forelimb functions.

Skilled Reaching as a Tool to Assess Recovery and Compensation

One of the most sensitive tests for motor control and postural adjustments in rat models of neurological disease is the single pellet reaching task. The task is designed in a way to allow for measuring reaching success while at the same time performance can be filmed and scored frame-by-frame [1,4]. In this task, rats are trained to extend their preferred forelimb through an opening to grasp and retrieve small food pellets. Once the rat has obtained the food pellet, it withdraws the paw through the opening and sits back on its haunches to consume the food.

The sequence of components comprising the rat's skilled reaching movement is relatively fixed [1]. Thus, rats possess limited ability to modify movement components to adapt to a changing context. Consequently, even a subtle brain damage will permanently compromise reaching movement performance. Reaching movements are differentially affected by discrete lesions of motor cortex and corticospinal tract, basal ganglia, dorsal columns and red nucleus. This makes skilled reaching a useful tool for the study of disease conditions such as spinal cord injury, stroke, and Parkinson's disease. In addition, physiological conditions such as stress, strain, sex and aging affect both reaching success and qualitative movement performance.

Recent studies have shown that skilled reaching movements are useful tools for distinguishing between genuine functional recovery and compensation. Through practice animals with brain damage might show considerable improvement in reaching success [4], however, qualitative analysis of reaching movements might still reveal permanent deficits. This indicates that rats are able to develop successful alternative movement strategies to overcome primary motor deficits. Thus, descriptive movement analysis represents an important supplementary technique to determine compensatory behavior and permanent motor deficits.

The relevance of skilled reaching tasks for rodent models of neurological disease has been established. The study of skilled reaching in rats is especially useful because reaching movements in rats and humans are homologous [6]. Comparisons have shown that the essential components of skilled reaching movements are similar in both rodent and humans. Moreover, reaching movement abnormalities detected in rodent models of human neurodegenerative disease show similarities to human patients. Thus, skilled reaching tasks are a useful model for pre-clinical studies in rodents and clinical studies in humans.

Rung Walking to Assess Skilled Fore- and Hind Limb Function

Recent investigations showed that rats use skilled hind limb movements to adapt their gait pattern to a difficult territory. The rung walking task is a simple and sensitive test to simultaneously assess skilled fore- and hind limb movements [2]. The rung walking task resembles a horizontal ladder with rungs that can be adjusted individually. A regular pattern of rungs allows animals to anticipate rung location and learn a specific sequence of patterns across repeated test sessions. An irregular pattern prevents animals from learning the rung sequences and patterns can be changed from session to session.

Rung walking performance can be video recorded for further analysis of end point measures, such as number of placement errors, and qualitative analysis of the type of error made. As a result of limb-placement errors occurring in the affected limbs, the number of errors also increases in the intact limbs, thus revealing compensatory adjustments. Animals with lesions to various motor areas, such as motor cortex and its efferent corticospinal tract, and basal ganglia, show chronic impairments in limb placement. Furthermore, the rung walking task also monitors changes in errors in response to physiological variables such as aging and stress [3].

Conclusion

The design of standardized skilled movement tasks provides a reliable and high-resolution test strategy for studies of functional recovery. Repeated testing allows monitoring discrete changes in movement ability over time. The combination of quantitative and qualitative measures in skilled movement tasks elaborates recovery versus compensation, thus providing insights into underlying structural changes of regeneration and plasticity.

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