Medical Xpress

New technology to speed up research into Huntington's Disease

October 6 2006

A new tool developed at Cambridge University represents a breakthrough in the race to find treatments to help sufferers with Huntington's disease.

Researchers have developed an effective new method of testing cognitive decline in mice with the disease, using an automated touch screen. It is hoped the screen will also allow researchers to study more effectively the cognitive difficulties in other neurodegenerative disorders such as in Alzheimer's and CJD.

Huntington's disease is a genetic disease affecting around 8 in 100,000 people. It is characterised by a progressive decline in cognitive functioning (including memory loss, intellectual decline and disorientation) together with the appearance of abnormal movements and impaired motor skills (such as unsteady gait and poor coordination).

There is currently no cure and whilst some symptoms can be alleviated, no treatments have been developed that help with cognitive deficits, a distressing aspect of the disease. Whilst useful mouse models mimicking this disorder have been developed, it has been difficult to test cognitive skills such as learning, because most traditional experiments demand a level of physical performance that the mice cannot deliver due to the effect of the disease on their motor abilities.

The automated screen developed by Cambridge scientists provides a simple means of assessing cognition, in a way that requires minimal

movement on the part of the mouse. The mouse makes its response by touching its nose to the touch-sensitive screen. This means that the HD mice can complete the task, despite motor problems.

Other benefits are that it is less labour intensive, less time consuming and less stressful for mice, compared to traditional testing methods. Given the difficulties associated with these traditional methods, progress to date in trialling new treatments for cognitive deficits has been slow with contract research organisations understandably reluctant to engage with such research. Given the ease of use of the touch screen system, it is hoped this will change.

Dr Jenny Morton, Dr Lisa Saksida and Dr Tim Bussey from the Departments of Pharmacology and Experimental Psychology at the University of Cambridge, who led the research, tested normal mice and mice carrying the HD gene mutation. The task set was a choice between two visual stimuli on a touch-sensitive computer screen. If a mouse touched the correct stimulus, it was rewarded with food pellets; if it touched the incorrect stimulus, the lights went out and the mouse did not get a reward.

Both normal and HD mice learnt to touch the correct stimulus with their noses and were able to learn the correct stimulus to obtain a reward by day 10.

The researchers also demonstrated that when the stimuli were reversed (so the stimulus that had previously been correct was now incorrect), HD mice struggled with the task although younger HD mice, who had not progressed as far in the disease, eventually learned it. When the mice were then presented with a new pair of stimuli, this proved too difficult even for the younger HD mice.

Importantly, and where the screen is so valuable, all the HD mice were

physically able to complete the task (i.e. they were able physically to touch the screen and obtain rewards, even though their responses were often incorrect). This indicates that their poor cognitive performance was not secondary to motor impairments. It also confirms that mice with HD have cognitive problems that worsen with increasing age.

Dr Morton said, “We are very excited about the results from the touchscreen apparatus. For many HD patients, the cognitive and emotional symptoms are as disabling as the more obvious motor effects of the disease, and much effort is focused on understanding cognitive decline in HD”.

“Useful cognitive testing has been a bottle-neck in developing new treatments for this aspect of HD. The touchscreen system should make it easier to test drugs for treating cognitive decline in HD.”

It is hoped the touchscreen system will also be valuable for testing cognition in animals with other types of neurological dysfunction such as Alzheimer's disease or prion disease, and particularly where motor deficits make cognitive testing difficult or impractical.

Dr Morton said “we are pleased at just how effective the test was and already clinical trial companies are showing an interest in the touch screen system”.

Source: University of Cambridge