GLOSSARY

ACTIVITIES OF DAILY LIVING (ADLs)

Activities related to personal care such as eating, dressing, bathing, and grooming

INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADLs)

Activities related to independent living such as using a telephone, preparing meals, housework, managing medications and handling money

Greater attention to animal data will improve selection of drugs for clinical trial

Neuroprotectants have shown promise in animal studies, but this promise has not been echoed in the results from clinical trials of acute stroke. In a paper published in *Annals of Neurology*, O'Collins *et al.* have described their investigation into whether results from preclinical trials are a poor indicator of drug efficacy, or whether there is a flaw in the process by which drugs are selected for clinical testing.

A total of 1,026 drugs and treatments tested in experimental or clinical stroke were identified through a detailed search encompassing experimental papers, reference lists, clinical trial databases and reviews. Drugs used in clinical trials ($n=114$) did not appear to be any more effective than those tested only in animal models ($n=912$), indicating that selection of drugs on the basis of preclinical testing results was not being implemented effectively. For instance, agents tested only in focal models of ischemia increased neuroprotection by an average of $24.4 \pm 32.9\%$, compared with $31.3 \pm 16.7\%$ for drugs used clinically ($P>0.05$). Furthermore, the extent of preclinical testing was found to be highly variable for different drugs, and no relationship between mechanism of action and efficacy of drugs was evident.

O'Collins *et al.* conclude that the drugs showing the best results in animal models of stroke might not be those being selected for clinical trial. They urge that drugs are taken into clinical trial only when their efficacy has been proven in animal models of stroke and that, to aid this process, animal trials are conducted, and their data reported, in a more thorough manner.

Pippa Murdie

Original article O'Collins VE *et al.* (2006) 1,026 experimental treatments in acute stroke. *Ann Neurol* 59: 467–477

Brain-derived neurotrophic factor mediates aversion to social contact

Brain-derived neurotrophic factor (BDNF) activity within the brain's reward circuitry might play a pivotal role in the development of disorders characterized by chronic anxiety and social withdrawal, according to research in rodents.

Scientists in Texas induced social withdrawal symptoms in mice by repeatedly exposing them to other, aggressive mice. After 10 days of psychosocial stress, the intimidated animals withdrew even from friendly mice; this aversion to social contact lasted for at least 4 weeks and could be reversed by chronic, but not acute, treatment with antidepressants.

Social defeat was associated with increased levels of BDNF in the nucleus accumbens, where BDNF is a key regulator in the mesolimbic dopamine pathway; this pathway is involved in feelings of reward and pleasure, and also in the development of addiction. When BDNF production in the nucleus accumbens was switched off by a virus-mediated mechanism before intimidation started, exposure to aggressors did not induce social withdrawal. Local removal of BDNF reversed a specific pattern of gene expression changes induced by psychosocial stress, and chronic antidepressant therapy had a similar effect.

Previous research has shown that BDNF activity in the hippocampus has an antidepressant effect, and some antidepressants are thought to boost BDNF activity in this part of the brain. The present findings, however, indicate that increased BDNF activity in the nucleus accumbens mediates the development of experience-dependent social aversion. The findings suggest new directions for the treatment of affective disorders such as depression, social phobia and post-traumatic stress disorder.

Martina Habeck

Original article Berton O *et al.* (2006) Essential role of BDNF in the mesolimbic dopamine pathway in social defeat stress. *Science* 311: 864–868

Comparing patient-reported and performance-based assessment of functional status in PD

Measures of ACTIVITIES OF DAILY LIVING (ADLs) and INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADLs) are often used to make clinical decisions regarding individuals with Parkinson's disease (PD). Shulman *et al.* have investigated whether patient self-rating of their ability to perform these functions differs from their scores in performance-based tests.

This study included 76 individuals with PD. Each participant rated their function from 1 (no difficulty) to 5 (completely unable) on a modified