The study of Kendall and colleagues extends preclinical exploration in the rat to a marmoset model of Huntington's disease. The authors define conditions that enable embryonic striatal allografts to survive for up to 12 months, become integrated into the host brain and induce functional alleviation of motor deficits—all in the absence of immunosuppression. Using a staircase task that measures a monkey's motor skills as it reaches and grasps food from two sets of steps, the investigators were able to show that the most functionally effective grafts were always located at a precise site, close to the lateral edge of the globus pallidus. This observation provides new information on the importance of graft placement for functional recovery. In contrast to the findings in rats, the authors did not observe a significant correlation between the percentage of 'P-zone' neurons in the graft and the extent of motor recovery (reflecting the small variability between transplanted animals).

Although the grafts survived well without immunosuppressing the six transplanted animals, the study only reports recovery up to 12 months post-transplantation. Clearly, follow up studies are required to define the importance of graft placement in different areas of the striatum, and the possible need for immunosuppression in longer term grafts. Investigating the outcome of intracerebral allograft transplantation in non-human primates, which have complex brains, well differentiated basal ganglia and sophisticated motor skills, is clearly crucial if this technique is to be successful in treating Huntington's disease patients. Based on results in rat studies, transplantation of human striatal embryonic cells into human patients has already begun. A safety report was published recently by an American team[15], and a French team led by Pierre Cesaro and Marc Peschanski has recently started their own clinical trial (personal communication). Doubtless the Kendall study will spur the launch of clinical trials in Britain as well.

Deciding when to launch a clinical trial always causes deliberations between two ethical positions: (1) has the technique been sufficiently optimized and reproduced in preclinical studies to offer the best chance for patients? (2) is it ethical not to attempt a new therapy if there exists the possibility that it may benefit patients suffering from an incurable disease? It is important to realise that animal models of neurodegenerative disease mimic only some aspects of these disorders. This is precisely why there must be cross-talk between clinical and basic researchers. Discussion based on a wealth of knowledge accumulated both in the clinic and in the laboratory is crucial for successful treatment of patients with neurodegenerative diseases. In the case of Huntington's and Parkinson's diseases cross-talk has already begun with the establishment of NECTAR, the Network of European CNS Transplantation and Restoration.

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à la CART

The latest addition to the menu of brain peptides that regulate feeding is CART, a hypothalamic neuropeptide that inhibits eating. Peter Kristensen and colleagues (Novo Nordisk, Denmark) report that injection of recombinant CART into rat brains blocks feeding behavior, even in starved animals (*Nature* **393**, 72–76, 1998). When they used an antibody that inhibits CART, they found that rats consumed more food during their nightly feeding sessions than did animals treated with control IgG.

What is particularly intriguing, says Kristensen, is that CART is a leptin-dependent molecule—CART mRNA levels in the hypothalamus decrease to zero in the leptin-deficient *ob/ob* mouse and in the leptin receptor-deficient *fa/fa* rat—and its activity antagonizes that of another leptin-regulated brain peptide, neuropeptide Y, a feeding stimulant.

CART was first identified by researchers investigating the effects of amphetamines on brain tissue, hence its name, cocaine- and amphetamine-regulated transcript. It is tempting to speculate that CART may be the molecule responsible for the drastically reduced appetite so common in drug addicts notes Kristensen.

Neurons that secrete CART are found in other areas of the brain such as the nucleus accumbens—a prominent player in the reward pathway (see page 659). Larsen, a co-author on the paper, speculates that CART may somehow be implicated in other behaviors apart from feeding that are also motivated by positive reward.

The next step for the Danish group is to identify the CART receptor, a necessary undertaking in the quest for new anti-obesity drugs. The receptor will be used to screen libraries of small peptide molecules in search of peptide mimetics that stimulate the CART receptor and inhibit eating behavior. Now that food is once more on the shelves of Danish supermarkets (following the end of a general strike), the Novo Nordisk scientists can begin their hunt for the CART receptor in earnest.

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