

Becky Hales

From: Tyrer, Bob [bob.tyrer@sunday-times.co.uk]
Sent: 01 June 2010 18:08
To: Becky Hales
Subject: Complaint 100832

Dear Rebecca,

The attached document sets out the history of research using macaque monkeys in the development of deep brain stimulation as a treatment for Parkinson's disease. It was written at the request of Sir Mark Walport, director of the Wellcome Trust and former Professor of Medicine and Head of the Division of Medicine at Imperial College, by Craig Brierley, senior media officer at the Wellcome Trust.

In preparing it, Mr Brierley consulted Roger Lemon, Sobell Professor of Neurophysiology at UCL, and Tipu Aziz, Professor of Physiology at Oxford University and consultant neurosurgeon at the Radcliffe Infirmary.

It makes clear that monkeys were crucial to the development of the DBS technique.

With best wishes,

Bob

Deep brain stimulation

Research using macaque monkeys has been instrumental to the development of deep brain stimulation (DBS) as a treatment for Parkinson's disease, both in terms of providing animal models (simulations) of Parkinson's and in directly testing the technique.

In the early 1980s, a designer drug known as MPTP was found to be causing Parkinson-like symptoms in young addicts. This chance finding led scientists to develop a primate model of Parkinson's by injecting MPTP into monkeys to induce a Parkinson-like state¹ allowing them to explore the mechanisms behind Parkinson's disease and test potential therapies in a way which would not have been possible or ethical in humans.

Further studies in macaques throughout the 1980s showed that the damage caused by MPTP (and hence Parkinson's) meant that an area of the brain known as the sub-thalamic nucleus became over-active. By creating lesions in this area, researchers were able to completely and permanently reverse the effects of MPTP^{2,3}.

Lesions are not an ideal treatment as their effects - including any negative side effects - are permanent. However, their effects can be mimicked by inserting electrodes into the relevant area of the brain and stimulating it with a gentle electric current. Techniques for delivery of current via electrodes accurately placed in the brain were developed over a long period in animal models including monkeys.

In 1995, the journal *The Lancet* published a study detailing how a team led Professor Alim Benabid and colleagues used DBS in humans⁴. The paper acknowledged the pioneering monkey work reported by Bergman et al and Aziz et al previously. Professor Benabid and colleagues implanted electrodes in the sub-thalamic nucleus on both sides of the brain and effectively managed to control the severe tremors symptomatic of Parkinson's disease. Although DBS had been used previously to target other sites in the brains of Parkinson's patients (1991-1995), the sub-thalamic nucleus as the optimal target for treating Parkinson's disease was identified in monkeys, not in humans.

References

1. Burns RS et al. 1983. A primate model of parkinsonism: selective destruction of dopaminergic neurons in the pars compacta of the substantia nigra. PNAS 80:4546.
2. Bergman H et al. 1990. Reversal of experimental parkinsonism by lesions of the subthalamic nucleus. Science 249: 1436.
3. Aziz TZ et al. 1991. Lesion of the subthalamic nucleus for the alleviation of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced parkinsonism in the primate. Mov Disord; 6: 288-92.
4. Limousin P et al. 1995. Effect on parkinsonian signs and symptoms of bilateral subthalamic nucleus stimulation. Lancet 343: 91.