THE EFFECT OF PALLIDOTOMY ON MOVEMENT IN SEVERE PARKINSON'S DISEASE

A thesis submitted for the degree of

DOCTOR OF PHILOSOPHY

in

The Department of Medicine

University of Adelaide

Adelaide, South Australia

by

Thomas Kimber MB.,BS (Hons.)

July 2008

TABLE OF CONTENTS

page

page

page

page

page

page

page

ABSTRACT

The effects of ablative and non-ablative pallidal surgery in Parkinson's disease (PD) have been the subject of interest for many years. The techniques used have undergone dramatic change over this time. This study examines the effects of pallidal lesions on the clinical signs and the physiology of motor control in PD.

A method for the kinematic analysis of rapid repetitive finger tapping (an "internally generated" movement) and a two stage sequential arm movement made in response to an auditory stimulus (an "externally generated" movement) was devised and validated in control subjects and in patients with PD. Consecutive patients undergoing pallidotomy for severe PD were studied pre-operatively and at 2-4 weeks, 3 months and 6 months post-operatively. In addition to kinematic assessments, clinical assessments of movement were performed using standardised rating scales. The spontaneous blink rate was measured pre- and post-operatively. In some patients, Bereitschaftspotentials (pre-movement cortical potentials) were recorded pre- and post-operatively, as patients performed a self-paced voluntary arm movement. The location of the pallidotomy lesions was established from post-operative CT head scans.

The most dramatic clinical effect of pallidotomy was on drug-induced dyskinesias. Significant clinical improvements were also seen in limb bradykinesia, particularly on the side contralateral to the lesion. Kinematic analysis showed no improvement in rapid finger tapping after pallidotomy. Nor was there any improvement in the spontaneous blink rate or in the early component of the Bereitschaftspotential. However, both the speed and inter-onset latency of the two stage sequential arm movement improved post-operatively.

It is concluded that the improvement in bradykinesia after pallidotomy is not due to an improvement in function of pallido-thalamo-mesial frontal circuits, which are particularly involved in the performance of internally generated movements. Rather, the abolition of pallidal activity by pallidotomy may allow more laterally placed motor circuits greater use of sensory cues to facilitate movement.

Lesions almost always involved the posteroventral portion of the medial segment of the internal pallidum, the conventional site for pallidotomy in PD. However, many lesions also involved the ansa lenticularis, the lateral segment of the internal pallidum and the external pallidum. The potential relevance of these observations on an understanding of the pathogenesis of bradykinesia and dyskinesia in PD is discussed.

DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

The author acknowledges that copyright of published works contained within this thesis resides with the copyright holders of those works.

Thomas E Kimber

July 2008

ACKNOWLEDGMENTS

I sincerely thank my supervisor, Professor Philip Thompson, for his invaluable support in the performance and analysis of this work. Without his inspiration and academic guidance, this work would not have been possible. Philip first inspired my interest in clinical research and he continues to inspire me as a clinician.

I also thank Professor Brian Brophy, who was the neurosurgeon for all of the patients described in this thesis. He was unfailingly supportive of this work, allowing me access to his patients before, during and after their surgery.

I would also like to acknowledge the patients who participated in this work. I pay tribute to their courage in the face of a debilitating illness. I would also like to acknowledge the kindness of those who acted as control subjects, who also gave generously of their time.

Finally, I would like to thank my wife, Katrina Bochner, who has been unfailingly supportive throughout the long gestation of this thesis.

LIST OF ILLUSTRATIONS

page

page

page

page

LIST OF TABLES