Neuropsychological Changes Following Carotid Endarterectomy

ROBERT A. BORNSTEIN, BRIEN G. BENOIT and RONALD L. TRITES

SUMMARY: *Fifty-five subjects undergoing carotid endarterectomy were grouped according to side of operation, i.e. right, left and bilateral. These subjects were administered a comprehensive neuropsychological battery prior to and six months following surgery. The performance of these subjects was compared with a control group undergoing surgical procedures that did not involve the brain or cerebral vasculature, and a second control group composed of patients with cerebrovascular symptoms who were not operated. It was found that as a group the endarterectomy subjects improved on a greater percentage of measures. When various subgroups were examined, it was found that the right operated stroke patients improved on significantly more measures than any other group. The difference between right and left stroke patients was significant, but there was no difference between right and left TIA patients in the extent of improvement. These findings were discussed in terms of possible underlying mechanisms.*

RÉSUMÉ: *Nous avons étudié 55 sujets ayant subi une endartérectomie carotidienne, groupés selon le côté de l'opération (droit, gauche ou bilatéral). Chaque sujet a reçu une évaluation neuropsychologique complète avant l'opération, et six mois après. La performance de ces sujets fut comparée à celle d'un groupe contrôle subissant des procédures chirurgicales n'impliquant ni le cerveau ni la vasculature cérébrale, et également à un second groupe contrôle de patients éprouvant des symptomes cérébrovasculaires, mais non opérés. Il fut montré que le groups de sujets endartérectomisés s'améliorait, en tant que groupe, sur un plus grand nombre d'items que les groupes contrôles. Parmi les sous-groupes, it fut montré que les patients vasculaires cérébraux opérés à droites s'amélioraient sur plus d'items que les autres. La différence entre les sous-groupes droits et gauches était significative, alors qu'il n'existait aucune différence droite-gauche dans l'amélioration spontanée des sujets vasculaires (schémie transitoire). Nous discutons des mécanismes sous-jacents possibles.*

From the Neuropsychology Service, University of Alberta Hospital, the Department of Neurosurgery, Ottawa Civic Hospital, and the Neuropsychology Laboratory, Royal Ottawa Hospital.

Reprint requests to: R.A. Bornstein, Neuropsychology Service, Department of Psychiatry, 1-115 Clinical Sciences Building, University of Alberta, Edmonton, Alberta, Canada T6G 2G3.

INTRODUCTION

Since the introduction of carotid endarterectomy (Eastcott et al., 1954), there have been several anecdotal and experimental reports of post-operative improvements in various aspects of mental function. These reports have been overshadowed by investigations which emphasize the prophylactic aspects of endarterectomy, a view which is consistent with prevailing neurosurgical opinion.

Williams and McGee (1964) presented the first study of patients undergoing endarterectomy which employed objective psychological tests. Their patients were tested over a one month pre to post surgery interval. There was no statistical analysis of the data and minimal improvement in mental function was thought to occur, however, considerable reduction of symptoms was noted.

Duke et al., (1968) found improvements on an intelligence test but not on two motor tasks. The gains on the intelligence test were largely attributed to practice effects and hence these results were viewed as support of the prophylactic role.

Goldstein et al., (1970) studied six patients with the Halstead-Reitan Neuropsychological Test Battery over a 3 month pre to post surgery interval. The improvements observed on some measures that were relatively insensitive to practice effects were regarded as support for the conclusion of an improvement in the general condition of the brain.

Perry et al., (1974) administered the Halstead-Reitan Neuropsychological Test Battery and also obtained intra-operative carotid artery blood flow measurements. There was a significant improvement in the overall measure of impairment obtained from the neuropsychological test battery (Impair-

https://doi.org/10.1017/S031716710004302X Published online by Cambridge University Press

ment Index) over the three month intertest interval. A significant increase in carotid artery blood flow was also achieved, but there was no relation between increased flow and improved test performance. The authors did not address the possibility of practice effects, although this may have influenced the results. It was shown that tests on which improvement occurred were also those particularly sensitive to practice effects.

Several other studies have examined the changes following endarterectomy (Horne and Royle, 1974; King et al., 1977; Kelly et al., 1979; Shatz et al., 1979; Matarrazo et al., 1980; and Owens et al., 1980). These papers were inconclusive in resolving the prophylactic versus restorative roles of carotid endarterectomy.

Asken and Hobson (1977) reviewed the psychological studies of endarterectomy and outlined the numerous weaknesses which undoubtedly have contributed to the failure to arrive at meaningful conclusions regarding the possible restorative role of endarterectomy. Among the methodological flaws discussed by them were the lack of appropriate control groups, and the failure to consider various medical and surgical variables. The present investigation was designed to resolve the debate surrounding the restorative role of endarterectomy by controlling for a large number of medical and surgical variables.

METHOD

Subjects

The sample included 55 subjects undergoing endarterectomy who were grouped on the basis of the side of operation left (n=20), right (n=23) and bilateral (n=12). In addition to the endarterectomy patients, two control groups were employed. Two control groups were utilized because the ideal control group was ethically unavailable. An operated control group (n=13) was composed of patients undergoing some other surgical procedure (of approximately the same duration as endarterectomy) which entailed a general anesthetic but did not involve the brain or cerebral vasculature. This group was employed not only to observe the effects of a general anesthetic, but primarily to control for the effects of pre operative depression and anxiety relief following major surgery. The second control group (n=14) was composed of patients with symptoms of cerebrovascular disease who did not undergo endarterectomy. This group included patients with arterial stenosis judged insufficient to warrant surgical intervention, patients with unilateral carotid occlusion without contralateral stenosis, and patients who met all the criteria and were offered surgery, but refused for personal reasons. This cerebrovascular control group (V.C.) was included to control for the effects of spontaneous recovery from vascular symptoms. As can be seen in Table 1, the endarterectomy and vascular control groups were similar in regard to age, sex and education.

PROCEDURE

Subjects undergoing carotid endarterectomy were referred for neuropsychological examination after angiography had demonstrated the presence of a surgically accessible stenotic lesion. Surgical controls were studied after other diagnostic procedures (e.g. myelography). The neuropsychological assessment was performed 1—2 days prior to surgery and again following a six month interval. All but four patients were reassessed within two weeks of the six month anniversary of the initial assessment. Twelve endarterectomy patients and two operated controls were unavailable for reassessment. There was one death in the immediate post operative period, and two other endarterectomy patients died of causes not directly related to surgery. No deaths occurred among the control subjects.

The neuropsychological assessment consisted of the Halstead-Reitan Neuropsychological Test Battery, the Wechsler Adult Intelligence Scale, the Wechsler Memory Scale, an extensive battery of motor and sensory-perceptual measures and the Minnesota Multiphasic Personality Inventory. This battery of tests has been extensively described elsewhere (Reitan and Davison, 1974), and has been well validated as sensitive to the presence of cerebral dysfunction (Klove, 1974; Stuss and Trites, 1977). In some cases the complete battery could not be administered due to time constraints or the patient's neurological condition (e.g. aphasia or hemiparesis). In those cases, the post operative assessment consisted of the same measures that had been obtained preoperatively.

In addition to the neuropsychological measures, a large number of medical and surgical data were gathered. This included angiographic and pathological estimates of the degree of stenosis, duration of arterial clamping during endarterectomy, duration and severity of symptoms and a number of variables which have been identified as being related to an increased incidence of stroke. These included blood levels of cholesterol,

TABLE 1

Group Composition in Regard to Age, Years of Education, Sex, and Clinical Diagnosis

	LCE*	RCE*	BCE*	VC*	NC*
Age	63.6	63.3	57.8	50.7	43.5
Males	13	17	8	10	6
Females	7	6	4	4	7
Education	9.9	11.2	8.2	10.3	12.7
T.I.A.	12	8	5	7	-
C.V.A.	8	15	7	7	-

* LCE = left carotid endarterectomy
RCE = right carotid endarterectomy
BCE = bilateral carotid endarterectomy
VC = cerebrovascular controls
NC = surgical controls

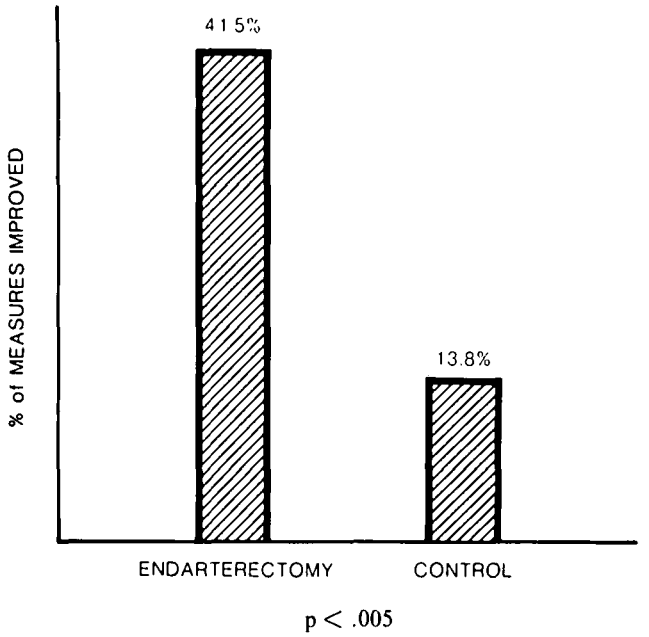

Figure 1 — Percentage of measures improved for combined endarterectomy and control groups.

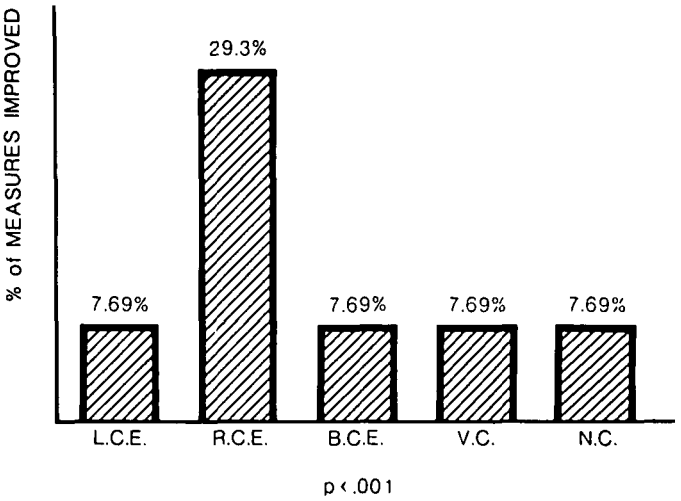

Figure 2 — Percentage of measures improved for three endarterectomy and two control groups.

LCE = Left Carotid Endarterectomy
RCE = Right Carotid Endarterectomy
BCE = Bilateral Carotid Endarterectomy
VC = Cerebrovascular Control
NC = Operated "normal" control

p indicates significance of difference in percentage of measures improved

hemoglobin, hematocrit and glucose; systolic and diastolic blood pressure and cigarette smoking (amount and duration).

RESULTS

The preoperative neuropsychological test scores were grouped according to logical considerations and subjected to a series of six separate factor analyses to reduce the data to more manageable proportions. Factor score coefficients were computed for the 21 factors that were derived and these coefficients were employed to generate factor scores. These coefficients were also applied to the post operative data to obtain a second set of factor scores which were then subtracted from the initial factor scores. These discrepancy scores were entered into a multiple discriminant function analysis which suggested that there were differences in the extent of post operative improvement (Wilks λ=.013, $p<.02$).

A group of 65 measures which had been employed in the initial factor analyses were selected for further examination. The subjects were formed into two groups (endarterectomy patients vs. control patients) and for each group paired t-tests were used to determine whether significant change had occurred on the selected variables. The results of this analysis are presented in Figure 1 which demonstrates that as a group the endarterectomy patients improved on significantly more measures than the control patients (x^2=10.43, df=1, $p<.005$). The combined endarterectomy and control groups were then broken down and the individual groups were compared on the extent of improvement on the selected test scores. The results of this analysis are presented in Figure 2 which demonstrates that the left and bilateral endarterectomy groups and both control groups improved on approximately 8% of the measures while the right operated patients improved on nearly 30% (x^2=21.67, df=4, $p<.001$). As can be seen in Table 1 the right and left endarterectomy groups differed somewhat in the relative number of patients with stroke vs. TIA (although this difference did not reach statistical significance).

It was considered that the relatively greater number of stroke patients in the right operated group may have accounted for the differential improvement. Therefore, it was decided to examine the relative performance of patients with TIA as compared to those with completed stroke. The conventional criterion of no neurological deficit after 24 hours was used as an operational definition of TIA. The subjects were grouped according to the severity of presenting symptoms (TIA vs. stroke) regardless of the side of operation, and were then compared with the cerebrovascular control group on the extent of improvement on the selected group of neuropsychological measures. The results of this comparison are presented in Figure 3 which reveals that the stroke patients undergoing endarterectomy improved on a significantly greater percentage of measures than either the operated TIA patients or the cerebrovascular controls (x^2= 13.69, df=2, $p<.01$). The fact that the operated stroke patients showed greater improvement than the cerebrovascular controls suggested that the improvement in the operated group could not be completely attributed to spontaneous recovery from vascular symptoms.

In view of the differences related to side of operation and severity of presenting symptoms, the TIA and stroke patients in the right and left endarterectomy groups were compared as to the extent of improvement. These results are presented in Figure 4 which demonstrates that the stroke subjects in the right operated group improved

https://doi.org/10.1017/S031716710004302X Published online by Cambridge University Press

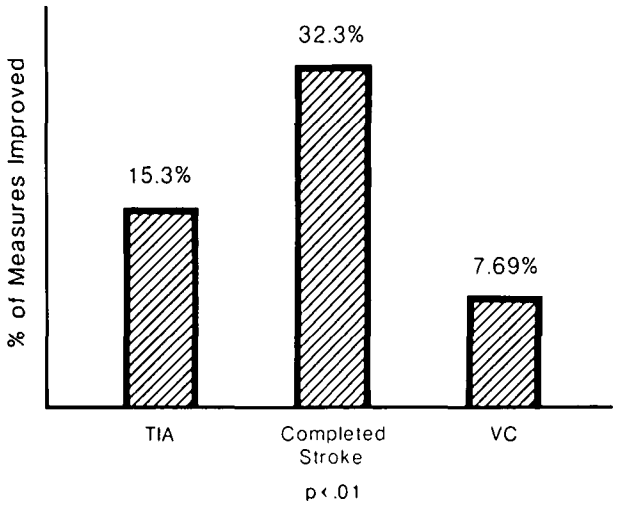

Figure 3 — Percentage of measures improved for operated TIA and stroke patients and vascular controls.

TIA = Transient Ischemic Attack patients who underwent endarterectomy
VC = Cerebrovascular Controls

p indicates significance of difference in percentage of measures improved

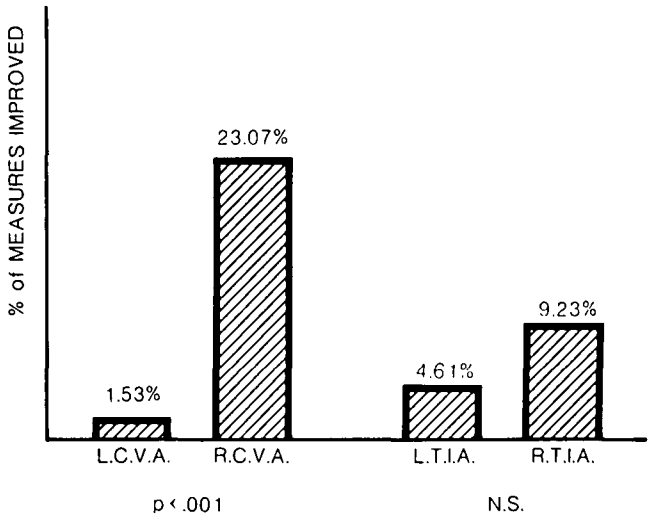

Figure 4 — Percentage of measures improved for stroke and TIA patients from right and left endarterectomy groups.

LCVA = Left Completed Stroke
RCVA = Right Completed Stroke
LTIA = Left Transient Ischemic Attack
RTIA = Right Transient Ischemic Attack

p indicates significance of difference in percentage of measures improved

to a greater extent than the left operated stroke patients (x^2=13.97, df=1, p<.001). Furthermore, it was obseved that the left operated stroke patients were virtually unchanged over the intertest interval. These subjects improved on only one measure (Performance I.Q.) which is susceptible to practice effects. This pattern however was not observed among the TIA patients. There was no difference in the extent of improvement between the left and right operated TIA patients (x^2=.89, df=1, p>.30).

An attempt was made to determine if a pattern of improvement could be discerned. This was accomplished by rating the neuropsychological measures as reflecting the function of one or both cerebral hemispheres. In this manner, tests of motor and sensory functions and some cognitive measures (e.g. V.I.Q. and P.I.Q.) were regarded as primarily measuring the activity in one hemisphere, while the other tests (e.g. category test) were regarded as bihemispheric. The right and left operated groups were then examined to determine any differences in the pattern of tests which improved.

There were no differences between the groups in regard to improvement in measures of the hemisphere ipsilateral to endarterectomy (e.g. right hemisphere tests in RCE vs. left hemisphere tests in LCE) x^2=.698, df=1, ns. However, there were differences in regard to the improvement of measures contralateral to operation. It was found that the right operated patients improved on a greater number of measures of the contralateral hemisphere than the left operated patients (x^2=4.79, df=1, p<.05). This suggests that the differences between the right and left operated patients was related to improvements of contralateral hemisphere function in the right operated patients.

There was no evidence of change on any of the personality measures examined. The Minnesota Multiphasic Personality Inventory includes scales which measure depression, anxiety, social withdrawal and concern over somatic function. Among the endarterectomy patients there was no improvement of any of the personality scales of the MMPI. The only significant change which occurred suggested greater concern over somatic function in the vascular control group.

DISCUSSION

There has been considerable debate surrounding the question of a restorative role for carotid endarterectomy. The conventional neurosurgical opinion maintains that there are only prophylactic effects, but there have been several reports of improvements in various aspects of mental function following surgery. These previous investigations have suffered from numerous methodological flaws including lack of appropriate controls, and failure to consider such potentially important variables as side of operation and severity of neurological symptoms.

The present investigation has found that these are important considerations in resolving the debate regarding the restorative effects of endarterectomy. As expected, it was found that stroke patients improve more than TIA patients undergoing endarterectomy (because, by definition there is no detectable deficit between attacks in patients with TIA). The fact that the operated stroke patients improved more than the cerebrovascular controls suggests that the operative procedure influenced the extent of recovery following endarterectomy. It was an unexpected finding that right operated stroke patients would improve more than left operated stroke patients. The difference between these groups appeared to be related to greater

https://doi.org/10.1017/S031716710004302X Published online by Cambridge University Press

improvement in functions subserved by the hemisphere contralateral to operation in the right operated subjects.

The mechanism for this contralateral improvement could not be definitely established from the available data, but several possibilities may be considered. Abnormalities of cerebral blood flow in the hemisphere contralateral to an infarction (diaschisis) have been reported by several authors (Meyer et al., 1970; Slater et al., 1977; Lavy et al., 1975). There have been no reports of differences between the hemispheres in regard to the potential for diaschisis, but the reports of Meyer et al. and Slater et al. both had a greater percentage of patients with right hemisphere lesions. Slater et al. reported that eight of the twelve patients showing diaschisis had right hemisphere lesions while all three of the patients not showing diaschisis had left hemisphere lesions. Unfortunately, this possibility could not be examined in the present study because blood flow measurements were unavailable.

A second possibility was that there may have been some factor which prevented the left operated stroke patients from improving to the same extent as the right operated stroke patients. This is supported by the fact that on the preoperative assessment, the differences between the right and left operated stroke patients were generally indicative of greater impairment among the left operated patients. Thus it is possible that the left operated stroke patients may have exceeded some critical level of impairment beyond which the beneficial results of carotid endarterectomy could not be realized.

Asken and Hobson (1977) have suggested the possibility that anxiety relief may explain the improvement following endarterectomy. Ostensibly, patients' anxiety prior to surgery could detract from performance and the relief derived from surviving the surgery could be related to increased ability to perform psychological tests. King et al., (1977) have reported improvement in personality function following endarterectomy. In the present study however, there was no indication of anxiety reduction (or any pattern of personality improvement) among either endarterectomy or operated control patients. The only significant change in the MMPI indicated increased concern over somatic function in the cerebrovascular control group. Therefore anxiety reduction clearly does not account for the improvement in neuropsychological performance in the present sample.

Finally, it was considered that perhaps the cerebral hemispheres differed in a way that could influence the potential for benefitting from endarterectomy. A recent study by Gur et al. (1980) using cerebral blood flow measurement has presented evidence that the composition of the hemispheres are different. These authors have found that the left hemisphere has a greater ratio of grey to white matter than the right hemisphere. This was interpreted by Gur et al. as suggesting that the left hemisphere is characterized by an organization emphasizing transfer within regions while the right hemisphere is characterized by an organization emphasizing transfer across regions. This hemispheric difference in neural organization might account for the benefits noted following carotid endarterectomy.

It may be that permanent damage to the left hemisphere may prevent the restorative potential of endarterectomy. This would be consistent with the finding that differences were noted in the extent of improvement which occurred between the right and left stroke patients but not the TIA patients. This would also explain why the bilateral endarterectomy patients (with bilateral arterial stenoses) failed to obtain the restorative effects since it was observed that six of the seven stroke patients in this group were symptomatic in the left hemisphere. The presence of left hemisphere symptoms among those patients may have been an overriding factor.

Although the mechanism underlying the improvements is not apparent, it seems clear that endarterectomy does influence the extent of postoperative improvement. The changes observed could not be attributed completely to practice effects, spontaneous recovery from vascular symptoms or anxiety relief. In spite of the improvements obtained by the operated subjects, their performance in general continued to be below normal. Therefore these findings can be interpreted as evidence for a partial restorative role for endarterectomy in addition to the well accepted prophylactic role of preventing stroke.

REFERENCES

ASKEN, M.J., and HOBSON, R.W. (1977). Intellectual change and carotid endarterectomy, subjective speculation or objective reality: a review. J. Surg. Res. 23: 367-375.

DUKE, R.B., BLOOR, B.M., NUGENT, G.R. et al. (1968). Changes in performance on WAIS, trail making test and finger tapping test associated with carotid artery surgery. Percept. Mot. Skills 26: 399-404.

EASTCOTT, H.H.G., PICKERING, G.W.J. and ROB, G.C. (1954). Reconstruction of internal carotid artery in a patient with intermittent attacks of hemiplegia. Lancet 2: 994-996.

GOLDSTEIN, S.G., KLEINKNECHT, R.A. and GALLO, A.E. (1970). Neuropsychological changes associated with carotid endarterectomy. Cortex 6: 308-322.

GUR, R.C., PACKER, I.K., HUNGERBUHLER, J.P. et al. (1980). Differences in the distribution of gray and white matter in human cerebral hemispheres. Science 207: 1226-1228.

HORNE, D.J. and ROYLE, J.P.(1974). Cognitive changes after carotid endarterectomy. Med. J. Aust. 1: 316-317.

KELLY, M.P., GARRON, D.C. and JAVID, H. (1979). Carotid artery disease: carotid endarterectomy and behavior. Paper presented at Int. Neuropsych. Soc., New York.

KING, G.D. GIDEON, D.A., HAYNES, C.D. et al. (1977). Intellectual and personality changes associated with carotid endarterectomy. J. Clin. Psychol. 33: 215-220.

KLOVE, H. (1974). Validation studies in adult clinical neuropsychology. in R. Reitan and L. Davison (eds.) Clinical Neuropsychology: Current Status and Applications, John Wiley and Sons, New York.

LAVY, S., MELAMED, E. and PORTNOY, Z. (1975). The effect of cerebral infarction on the regional cerebral blood flow of the contralateral hemisphere. Stroke 6: 160-163.

MATARAZZO, R.G., MATARAZZO, J.D., GALLO, A.E. et al. (1979). IQ and neuropsychological changes following carotid endarterectomy. J. Clin. Neuropsychol. 1: 97-116.

MEYER, J.S., SHINOHARA, Y., KANDA, T. et al. (1970). Diaschisis resulting from acute unilateral cerebral infarction. Arch. Neurol. 23: 241-247.

OWENS, M., PRESSMAN, M., EDWARDS, A.E. et al. (1980). The effect of small infarcts and carotid endarterectomy on postoperative pyschological test performance. J. Surg. Res. 28: 209-216.

PERRY, P.M., DRINKWATER, J.E. and TAYLOR, G.W. (1975). Cerebral function before and after carotid endarterectomy. Brit. Med. J. 4: 215-216.

REITAN, R.M. and DAVISON, L.A. (1974). Clinical Neuropsychology: Current Status and Applications. John Wiley & Sons, New York.

SHATZ, M., SCHWARTZ, M., ROBBINS, R. et al. (1979). Carotid endarterectomy: changes in higher cortical functions at one and one half year postoperative follow up. Paper presented at Int. Neuropsychol. Soc., New York.

SLATER, R., REIVICH, M., GOLDBERG, H. et al. (1977). Diaschisis with cerebral infarction. Stroke 8: 684-690.

STUSS, D. and TRITE, R. (1977). Classification of neuropsychological status using multiple discriminant function analysis of neuropsychological test scores. J. Cons. Clin. Psychol. 45: 145.

WILLIAMS, M. and McGEE, T.F. (1964). Psychological study of carotid occlusion and endarterectomy. Arch. Neurol. 10: 293-297.