Pharmacology Biochemistry and Behavior, Vol. 56, No. 4, pp. 781–787, 1997

0091-3057/97 $17.00 + .00

PII S0091-3057(96)00416-9

Uncomplicated Carotid Endarterectomy Is Not Associated with Neuropsychological Impairment

J. L. IDDON,*[1] B. J. SAHAKIAN* AND P. J. KIRKPATRICK†

*Department of Psychiatry and †Department of Neurosurgery, University of Cambridge, Cambridge CB2 2QQ, UK

Received 8 February 1996; Accepted 10 March 1996

IDDON, J. L., B. J. SAHAKIAN AND P. J. KIRKPATRICK. *Uncomplicated carotid endarterectomy is not associated with neuropsychological impairment.* PHARMACOL BIOCHEM BEHAV **56**(4) 781–787, 1997.—Whether neuropsychological changes follow carotid artery surgery is unclear, in part because of complications by multiple perioperative variables. Therefore, we carried out a detailed analysis of patients who underwent carotid artery surgery in which we attempted to control for the most important variables by excluding patients with a preoperative stroke and by adopting a standard operative technique without use of intraoperative carotid shunts. Thirty inpatients with symptomatic carotid artery disease admitted for carotid endarterectomy were assessed with a comprehensive battery of neuropsychological tests administered immediately before and after (48–72 h) surgery. No carotid bypass shunt was inserted during the operation. The battery included dementia and depression screening tests, standardised neuropsychological measures including Verbal Fluency and the National Adult Reading Test, and a battery of contemporary computerised tasks designed to measure different aspects of memory and attention from the Cambridge Neuropsychological Test Automated Battery (CANTAB). No significant difference was found in the cognitive scores postoperatively as compared with the patients' preoperative scores or compared with scores of a control group matched by age and intelligence. © 1997 Elsevier Science Inc.

Neuropsychology Carotid endarterectomy Cognitive deficits Microemboli Transient ischaemic attacks

STROKE continues to be a leading cause of death in the USA and Western Europe. Two large multicentre studies (10,23) have reported on carotid endarterectomy (CE) as a procedure that reduces the incidence of cerebrovascular accidents in patients in good medical condition with symptomatic carotid disease resulting in 70% stenosis or greater. Although the incidence of a perioperative stroke in these studies was approximately 6%, the possibility of subclinical neurological events or cognitive dysfunction was not examined.

There have, however, been other reports in the literature of changes in neuropsychological functioning following CE (3,7,9,12,13,17,18,29). The results are variable, and while some studies claim an initial improvement in cognitive measures immediately after surgery (3,9,13,18), others have reported that performance is impaired (12,29). One study reported an initial decline, but improvement when the patients were retested 3–6 months later (29). Finally, a number of studies have also reported that there is no change in cognitive function either in the short term (3,7,17) or in the longer term (3).

Several explanations for the diversity of reports on cognitive changes after CE are possible. Of particular concern is the spectrum of presenting neurological deficits. Many patients who are considered suitable for CE have experienced a previous stroke affecting various regions of the carotid territory. Others have suffered a transient ischaemic attack (TIA) without loss of neuronal tissue. Surgical procedure also varies (21). Many prefer to use intraoperative shunts that are designed to protect the brain from low cerebral blood flow during carotid cross clamping (16,21). These devices may pose a hazard by causing dissemination of cerebral microemboli from friable atheromatous plaques (1,12). Finally, in some studies, methodological flaws such as test insensitivity have made firm conclusions about cognitive outcome difficult or impossible.

In the present study, we have attempted to assess cognition by using the CANTAB computerised tests in patients both before and after carotid endarterectomy and in age- and intelligence-matched normal controls. Patients were included who

[1]Requests for reprints should be addressed to J. L. Iddon, Department of Psychiatry, University of Cambridge, Level 4, Addenbrooke's Hospital, Cambridge, CB2 2QQ, UK.

TABLE 1
SUBJECT CHARACTERISTICS

Group	Test	*n*	Mean Age	Mean Verbal IQ
Patients	Verbal Fluency	30	64.8 (8.8)	108.4 (8.7)
	Pattern Recognition	30	64.8 (8.8)	108.4 (8.7)
	Spatial Recognition	30	64.8 (8.8)	108.4 (8.7)
	Spatial Span	30	64.8 (8.8)	108.4 (8.7)
	Spatial Working Memory	21	65.5 (8.6)	107.9 (8.8)
	ID/ED Attentional Task	20	63.0 (8.4)	107.6 (7.3)
	Paired Associates Learning	15	62.0 (8.6)	107.8 (7.4)
	Delayed Matching to Sample	11	62.6 (8.1)	110.7 (6.8)
Controls	Pattern Recognition	30	65.2 (8.5)	108.4 (8.6)
	Spatial Recognition	30	65.2 (8.5)	108.4 (8.6)
	Spatial Span	30	65.2 (8.5)	108.4 (8.6)
	Spatial Working Memory	21	64.1 (8.4)	107.7 (7.4)
	ID/ED Attentional Task	20	63.1 (7.9)	106.3 (7.7)
	Paired Associates Learning	15	62.4 (8.4)	106.6 (8.4)
	Delayed Matching to Sample	11	65.2 (6.2)	111.8 (5.1)

Standard deviation is shown in parentheses.

were known to have a history of a TIA, but who had not experienced an irreversible neurological deficit.

During surgery, a standard protocol was followed. No patients received an intraoperative shunt, all patients had careful control of the blood pressure, and all were monitored carefully to identify changes in cerebral oxygenation and middle cerebral artery flow velocity (14). By adopting rigid selection criteria and controlling the intraoperative variables, we have attempted to identify a subclinical end point by closely monitoring the neuropsychological performance of patients before and after CE. Each patient was screened for dementia and depression before surgery, and a battery of tasks assessing a wide range of cognitive function were given before and after CE. These included verbal intelligence and verbal fluency measures as well as tests taken from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (11). In this type of test/retest study, the issue of practice effects is an important one. Many of the CANTAB tests have parallel versions that have been shown to be resilient to the effects of practice in several studies. Coull et al. (6) tested controls within a 1-week period and showed that there were no significant differences in any of these tests from the first to the second session when performing under control ("no drug") conditions. Semple et al. reported findings similar to this in two studies, one assessing normal subjects (34) and another assessing the effects of scopolamine in normal subjects (33). The parallel versions have also been shown to be equivalent (34). These tests have been standardised on an adult population (30) and have been validated in terms of their sensitivity for distinguishing selective patterns of impairment in frontal, temporal, and amygdalo-hippocampal regions following resection (27) as well as for identifying specific patterns of impairment in patients with Alzheimer's disease and Parkinson's disease (8,19,24–26,28,31,32).

METHOD

Patients

Thirty patients with TIAs were admitted to Addenbrooke's Hospital for unilateral carotid endarterectomy due to severe carotid artery stenosis (70% or greater). All patients were screened for dementia using the Mini Mental State Examination (5) and for depression using the Beck Depression Inventory (2). None of the patients were demented or depressed according to these measures (see Table 1).

Controls

Healthy control volunteers drawn from samples in Newcastle and Cambridge were matched to the patient group by age and intelligence level on each test (see Table 1).

Tests

Psychometric assessment. The following psychometric assessments were performed:

National Adult Reading Test (NART) (22): A measure of premorbid verbal intelligence.
Beck Depression Inventory (Beck DI) (2): An assessment of depression.
Mini Mental State Examination (MMSE) (5): A 30-item dementia screening test.
Verbal Fluency (4): A measure of letter and semantic fluency. Stage 1 requires subjects to produce as many words as possible in a minute beginning with each of the letters F, A, and S. Stage 2 requires subjects to generate as many different animals as possible in 90 s.

Computerised Tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (11). The CANTAB computerised tests were presented on a touch-sensitive portable computer screen (comprising a Datalux touch-sensitive screen and a CarryI portable hard disk). The experimenter controlled the computer and gave verbal instructions to the patient for each test.

Pattern Recognition. This is a test of visual recognition memory, and is sensitive to patients with temporal lobe damage and hippocampal lesions (28) and patients with mild dementia of the Alzheimer type (32). Twelve patterns were presented on the centre of the screen in a box, one after another.

The subject was instructed to watch the patterns carefully and to try to remember them. All 12 patterns then reappeared individually and in reverse order, but this time paired with a novel pattern. The subject had to touch the pattern that had appeared before. This procedure was then repeated for a second set of 12 patterns. The maximum score was 24, over two blocks. A parallel version was administered at retest.

Spatial Recognition. This is a test of spatial recognition memory, and is sensitive to frontal lobe damage (28). Five empty white boxes were presented one by one on the screen in different spatial locations. Subjects were instructed to remember the position where each appeared on the screen. After each set, the boxes reappeared individually in reverse order, paired with another box that appeared in a novel location. The subject was asked to touch the box that had appeared in the same location as before. There were four sets with a pause between each one. The maximum score was 20, over two blocks. A parallel version was administered at retest.

Spatial Span. This test assesses short-term memory capacity for spatial information, and has been shown to be relatively insensitive to frontal lobe damage (25). A screen full of boxes appeared and initially two of these changed colour in turn. The subject was required to remember the order in which the boxes changed colour, wait for a tone to sound, and then repeat the exact sequence. Every time the sequence was repeated correctly, a new trial began, showing a new sequence with one more box than the previous level. If the sequence was repeated incorrectly, the same level of boxes that had already been reached was repeated in the next set, but was presented in a different sequence. If the new level was not repeated correctly after three trials, the computer would automatically terminate the task. The final score obtained was the last (highest) level passed (maximum = 9). A parallel version was administered at retest.

Spatial Working Memory Task. This test is highly sensitive to frontal lobe damage (25). Subjects were required to "search through" a number of boxes presented on the screen by touching each one with the result that it "opened up," revealing what was inside. The object of the task was to collect "blue tokens" inside the boxes and, once found, to use them to fill an empty column at the side of the screen. At any one time there would be a single token hidden inside one of the boxes; the subjects were required to search until they found it, at which point the next token would be hidden. The key instruction was that once a blue token had been found within a particular box, then that box would never be used again to hide a token. Returning to a box where a blue token had previously been found would constitute an error.

ID/ED Attentional Set Shifting Paradigm. This test requires the formation and shifting of attentional set, and is sensitive to frontal lobe damage and different forms of frontostriatal dementia (8,27). The task requires the subject to learn in succession a set of discrimination tasks in which one of two stimuli is correct and the other is not, on the basis of feedback provided by the computer following each choice. The main aim is to compare the capacity to make attentional shifts to exemplars within the same stimulus dimension currently attended (intradimensional shift) with shifts to the currently nonattended dimension (extradimensional shift). The test has some similarities to the Wisconsin Card Sorting Test (WCST), but with a tighter control over the experimental contingencies, which enables parcellation of the various components of the WCST in the context of learning theory.

Four boxes are presented on the screen; two of these contain the test stimuli, but the boxes used vary from trial to trial. Subjects are instructed in the following way: "Now you can see two patterns. One of the patterns is correct. You must point to the one that you think is correct. There is a rule you can follow to make sure you make the correct choice each time. The computer will be keeping track of how well you are doing and when it is clear that you know the rule then the computer will change it, although this will not happen very often. To begin with, there is nothing on the screen to tell you which of the two patterns is correct, so your first choice will be a simple guess. However, the computer will give a message after each attempt to tell you whether you are right or wrong. You can start now." If necessary, these instructions were repeated or elaborated to ensure that every subject had a clear idea of what was required of them.

The test then proceeded through a number of stages, each with a different contingency, up to a maximum of nine. For each, continuation to the next trial was dependent on a criterion of six successive correct discriminations being reached. If the criterion was not reached at the 50th trial of a stage, then the test was discontinued. The order of discrimination was fixed so that the extradimensional shift always followed the intradimensional shift.

To begin with, subjects were given a simple simultaneous discrimination in which the stimuli varied along only one of the two dimensions used to derive stimuli. These dimensions were either purple-filled shapes or white lines. A response to one of the two boxes resulted in an auditory tone, together with visual feedback that informed the subjects of the correctness of their responses. This was in the form of the words "correct" or "wrong" presented, respectively, in green or red lettering above the middle two boxes. The same feedback was also used for each of the subsequent phases. After 1.5 s, the screen cleared, and there was an intertrial interval of 1 s before the next trial. Following the simple discrimination (sd), the remaining eight stages were as follows. For the second stage (sdr), the discriminanda remained the same, but the previously incorrect choice became the correct one; that is, the contingencies were reversed. At the third stage (c-d), the second dimension was introduced, with one exemplar of each dimension paired together to give a compound stimulus in each of the two response boxes. To succeed, subjects had to continue responding to the correct exemplar from the previous stage. For this and all other subsequent stages, exemplars of the different dimensions were paired in a pseudorandom fashion with the constraint that runs of no more than three trials with the same pairing were allowed. The stimuli for the fourth stage (cd) and subsequent stages were also compound, but the two exemplars from the different dimensions were superimposed, always with the white line in the foreground. The contingencies again remained unchanged from those for the previous two stages. A reversal then occurred at the fifth stage (cdr). New exemplars for both dimensions were introduced at the sixth stage, the intradimensional shift (IDS), but the relevant dimension was unchanged from the original. This was succeeded by a further reversal at the seventh stage (idr). For the penultimate stage, the extradimensional shift (EDS), new exemplars were again introduced, but success at this point was dependent on the subject shifting the response set to the exemplars of the previously irrelevant dimension. Finally, contingencies were reversed to the previously incorrect exemplar of the new dimension (edr). The number of errors made cumulatively throughout the task was used as the measurement for this study. Failure at any stage automatically incurred 25 errors for each further stage. A parallel version was administered at retest.

Paired Associates Learning Task. This task has been shown to be sensitive to patients with both frontal and temporal lobe damage (28,32). In this test, subjects were required to remember up to eight pattern–location associations. Initially, six white boxes were presented around the screen and subjects were told that they would "open up" in turn, showing them what was inside. This task was to look for coloured patterns in the boxes and to remember which pattern belonged in which box. Each of the boxes opened up and then closed again in a randomized sequence. In the first trial only one of the boxes contained a pattern. Immediately after the last box had opened, this pattern was presented in the centre of the screen and the subject was required to respond by touching the box in which it had appeared. Feedback was *not* provided after each response, although if the choice was correct the words "ALL CORRECT" appeared and the subjects proceeded to the next trial. If the choice was incorrect, the boxes were successively reopened (reminding phase) for 2 s each, and the subject was then given a second attempt to correctly locate the pattern. In each trial the subject was allowed up to nine reminding phases, making 10 attempts in all, before the test was prematurely aborted. After the initial trial with one pattern, there was one more trial with a single pattern, then two trials with two patterns each, two trials with three patterns each, and then one trial with six (one in every box) patterns to locate. Finally, two extra boxes were added to the array on the screen, and the subject was required to correctly locate a total of eight patterns. Performance was assessed by the total number of errors (incorrect placements) summed across the eight trials.

Simultaneous and Delayed Matching to Sample. This test is sensitive to temporal lobe damage (32). At the beginning of each trial, a complex abstract (sample) pattern consisting of four quadrants, each differing in colour and form, appeared in the centre of the screen for a presentation period of 4.5 s. Subjects were told to study the pattern because they would later be required to identify it from among three "distractor" patterns. In the *simultaneous* condition, four choice patterns then appeared, located under the sample pattern. The subject was required to respond by touching the choice pattern that corresponded exactly (in both colour and form) to the sample pattern above. Only one of the choice patterns was identical to the sample. One of the other choice patterns was a novel distractor, differing in both colour and form from the sample. The remaining two choice patterns were "partial distractors" in that one had the colours of the sample but the form of the novel distractor, while the other was the same shape as the sample but had the colours of the novel distractor. In addition, one of the four choice patterns had one (random) quadrant in common with the sample to discourage mnemonic strategies based on remembering the colour and shape of a single quadrant. The subject's response was accompanied by an auditory tone, and visual feedback was provided in the form of green ticks and red crosses. After an incorrect response, the subject had to continue to choose until the correct (target) stimulus had been touched.

The *delay* condition was identical to the simultaneous condition in every way except that after the initial 4.5-s presentation period, the sample stimulus disappeared from the screen. There then followed a 0-s, 4-s, or 12-s delay before the four choice stimuli appeared and the subject was required to make a selection. After three practice trials (one each of simultaneous, 0 s, and 12 s), a total of 10 test trials in each of the four simultaneous and delay conditions were presented sequentially, in pseudorandom order (total test trials = 40). Each subject was scored according to the number of trials correct on the first choice in each condition. A parallel version was administered at retest.

Procedure

Patients were tested individually over two sessions. The first session took place presurgery in Addenbrooke's Hospital. The second test session took place within 72 h postsurgery. A core battery of tests was administered to *all* patients included in the study (NART, Beck DI, MMSE, Verbal Fluency, Pattern Recognition, Spatial Recognition, and Spatial Span), whilst other tests were given if time permitted (Spatial Working Memory, ID/ED Attentional Task, Paired Associates Learning, and Delayed Matching to Sample) (see Table 1 for numbers completing each test). Several recent studies have assessed the possibility of practice effects on the parallel versions of the CANTAB battery and found no significant difference on the repeat test session, even in the case of the ID/ED Attentional Set Shifting paradigm, although it is a rule-learning task (6,33,34). As part of audit in the Department of Neurosurgery, patients were seen as part of their pre- and postoperative clinical assessment. The procedure was explained and verbal consent obtained.

Surgery

All patients underwent surgery (performed by P. J. K.) using a standard protocol. Cerebral monitoring was used to detect evolving cerebral ischaemia (14), and blood pressure was supported if necessary. No intraoperative shunt was required in any patient.

Statistical Analysis

Two-tailed Student's paired *t*-tests were used to compare results on each individual test before and after surgery. Comparisons were also made between preoperative scores on the CANTAB tests and control scores using unmatched *t*-tests. (One main measure is given for each test.)

RESULTS

See Table 2 for a summary of the main results.

Surgical Outcomes

All patients underwent uneventful surgery. No perioperative strokes occurred, and all patients were ambulant on the first postoperative day.

Preoperative Psychometric Assessments

None of the patients included were demented or depressed as measured by the screening tests (MMSE and Beck DI). On the Verbal Fluency task they were in the normal range according to the Benton and Namsher norms (15).

Preoperative CANTAB Assessments

There was no significant difference on any task at test session 1 as compared with age- and intelligence-matched controls: Pattern Recognition (see Fig. 1A), $t(58) = 0.24$; Spatial Recognition (see Fig. 1B), $t(58) = 1.65$; Spatial Span, $t(58) = 1.03$; Spatial Working Memory total errors, $t(40) = 0.54$; ID/ED Attentional Set Shifting Paradigm total errors, $t(38) = 0.22$; Paired Associates Learning total errors over all

TABLE 2
SUMMARY OF MAIN RESULTS

Test	Mean Score			Significance	
	Patient Test 1	Patient Test 2	Controls	Preop. vs. Postop.	Preop. vs. Control
Pattern Recognition	19.53 (0.4)	19.47 (0.4)	19.37 (0.6)	0.85	0.81
Spatial Recognition	15.63 (0.3)	15.13 (0.4)	14.63 (0.5)	0.34	0.11
Spatial Span	4.83 (0.1)	5.00 (0.1)	4.63 (0.1)	0.28	0.31
Spatial Working Memory (errors)	30.10 (3.9)	31.05 (4.4)	30.6 (4.8)	0.60	0.36
ID/ED Attentional Task (total errors)	17.3 (3.7)	18.5 (3.2)	16.2 (3.5)	0.54	0.8
Paired Associates Learning (total errors)	26.0 (3.4)	23.0 (3.8)	20.9 (3.2)	0.26	1.02
Delayed Matching to Sample (total)	33.2 (1.1)	33.9 (1.1)	31.0 (1.2)	0.56	0.2
Verbal Fluency					
FAS	38.5 (1.7)	38.6 (1.6)	Norms	0.9	—
Animals	20.8 (0.7)	20.9 (0.7)	Norms	0.9	—

Standard error is shown in parentheses.

sets, $t(28) = 1.02$; Delayed Matching to Sample total score, $t(20) = 1.35$ (no significant difference at any stage).

Postoperative Psychometric Outcomes

Postoperatively, none of the patients were demented or depressed, as measured by the screening tests (MMSE and Beck DI). On the Verbal Fluency task, scores did not change significantly between test and retest [Letters FAS, $t(29) = 0.07$; Animals, $t(29) = 0.13$].

Postoperative CANTAB Assessments

The patient group showed no significant postoperative change on any CANTAB task as compared with their preoperative scores: Pattern Recognition (see Fig. 1A), $t(29) = 0.18$;

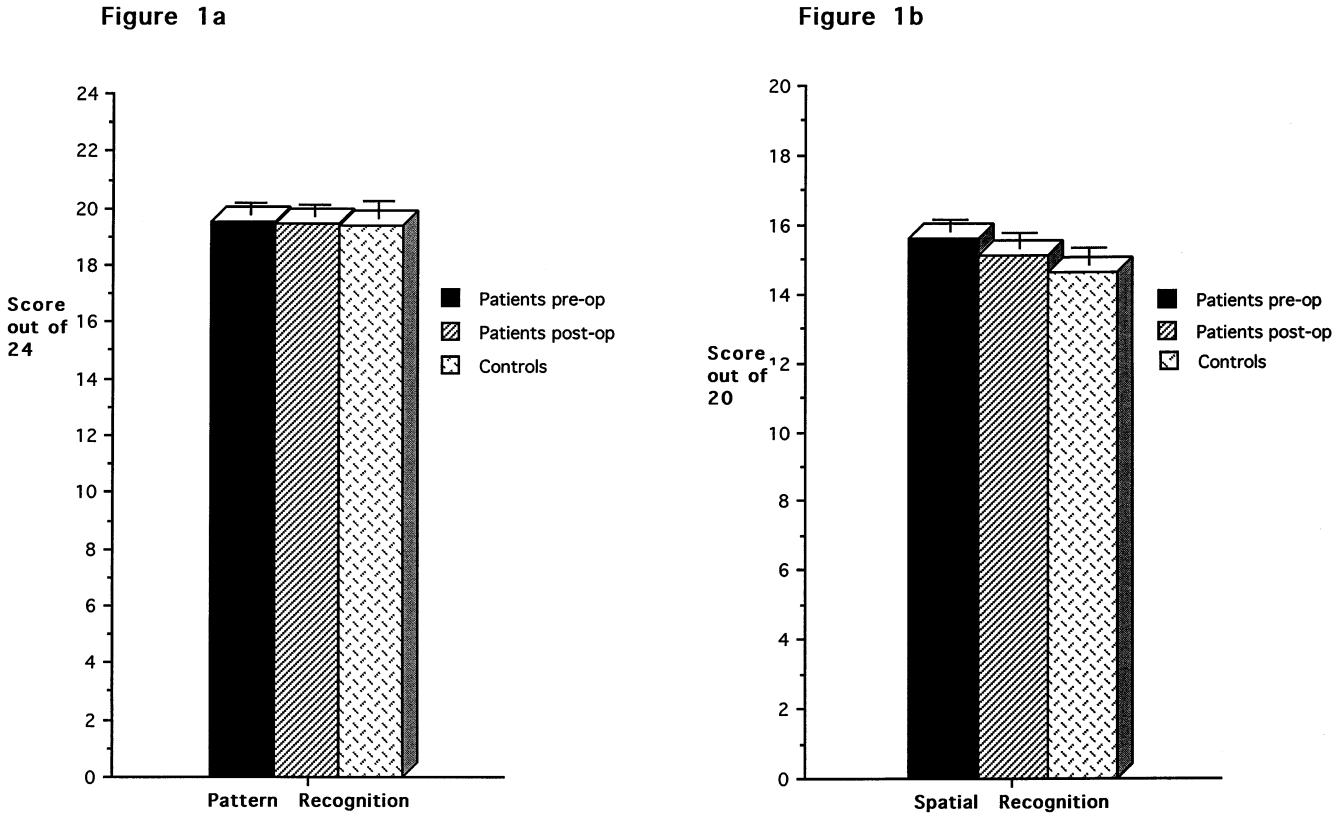

FIG. 1. Pattern Recognition and Spatial Recognition tasks: results pre- and postcarotid endarterectomy and comparison with controls. (a) The Pattern Recognition task is out of a maximum total score of 24. (b) The Spatial Recognition task is out of a maximum total score of 20.

Spatial Recognition (see Fig. 1B), $t(29) = 0.96$; Spatial Span, $t(29) = 1.1$; Spatial Working Memory total errors, $t(20) = 0.54$; ID/ED Attentional Set Shifting Paradigm total errors, $t(6) = 1.33$; Paired Associates Learning total errors over all sets, $t(14) = 1.1$; Delayed Matching to Sample total errors, $t(10) = 0.62$ (no significant difference at any stage).

DISCUSSION

This study addressed the concern that patients undergoing CE may have cognitive deficits despite a good clinical recovery from their surgery. We specifically assessed each patient between 48 and 72 h after surgery because perioperative cerebral ischaemia will have maximal effects on higher functions of cognition within that time. This leaves little opportunity for recovery, and hence provides maximal sensitivity for such tests. By delaying the assessment by 24 h, we avoided conflicting variables such as the after effects of anaesthesia. Despite adopting a vigorous procedure, no change was seen in any neuropsychological measure preoperatively as compared with postoperatively in a population of patients who had undergone uncomplicated unilateral carotid endarterectomy without a shunt. There was also no significant difference on any test prior to surgery as compared with an age- and intelligence-matched normal control population, and there were no individual exceptions to this finding.

The present methods of neuropsychological assessment (CANTAB) are highly sensitive and controlled, and are known to detect cognitive changes in diseased states and in the early stages of neurodegenerative diseases well before structural damage can be seen in high-resolution cerebral images (8,20,24–28,31,32). Thus, we do not consider method artefact a likely cause for these results. We conclude that, provided the selection of patients is restricted to those presenting with TIAs and without a clinically relevant stroke, CE under a highly controlled surgical setting is not complicated by impairment in cognitive function. Thus, use of detailed cognitive assessments does not provide an investigational end point in these patients. Our study is in keeping with the results of studies that found no change postoperatively (3,7,17).

Of those studies in which cognitive deficits were identified following surgery, specific differences in methods appear. Gaunt et al. (12) showed that changes on neuropsychological measures were likely to be seen where there was a significant number of intraoperative microemboli detected with ultrasonography. The use of an intraoperative shunt may, in part, explain these findings. The present study used sensitive tests designed to measure different aspects of mental function. Many had parallel versions, thus removing the possibility of practice effects, and the patients were unimpaired on the tasks. Some studies have claimed an initial improvement on tests immediately after surgery (3,9,13,18,29), but few reported the possibility of practice effects. It may be that an initial postoperative improvement could be due to familiarity with the testing methods the experimenter, and the relief of a successful operation. In the present study, the research neuropsychologist (J. L. I.) made every attempt to relax each patient at both test sessions by administering simple tasks first in a quiet room before moving on to more challenging ones. The tests from the CANTAB battery are novel and enjoyable, being administered on a touch sensitive computer screen. It is important to acknowledge that the present study was designed to assess specific cognitive functions such as visual memory and learning, attention, and planning, and was not concerned with assessing temporary states such as anxiety or stress. In four of the six studies that reported initial improvement after CE (3,8,18,29), the authors administered measures that are likely to improve following the relief of a successful operation.

To conclude, the present study indicates that in patients suffering TIAs from carotid artery stenosis, carotid endarterectomy under highly controlled operative conditions does not cause significant neuropsychological change. Furthermore, this subgroup of patients was not neuropsychologically impaired when compared with age- and intelligence-matched controls.

ACKNOWLEDGEMENTS

We thank Dr. T. W. Robbins for his helpful comments on the manuscript. J. L. I. is supported by the Wellcome Trust.

REFERENCES

1. Baker, W. H.; Dorner, D. B.; Barnes, R. W.: Carotid endarterectomy: Is an indwelling shunt necessary? Surgery 82:321–326; 1977.
2. Beck, A. T.: Depression: Causes and treatment. Philadelphia: University of Pennsylvania Press; 1970.
3. Bennion, R. S.; Owens, M. L.; Milson, S. E.: The effect of unilateral carotid endarterectomy on neuropsychological test performance in 53 patients. J. Cardiovasc. Surg. 26:21–26; 1985.
4. Benton, A. L.; Hamshire, K. de S.: Multilingual aphasia examination. Iowa City, IA: University of Iowa; 1976.
5. Cockrell, J. R.; Folstein, M. F.: Mini-mental state examination (MMSE). Psychopharmacol. Bull. 24:689–692; 1988.
6. Coull, J. T.; Middleton, H. C.; Robbins, T. W.; Sahakian, B. J.: Contrasting effects of clonidine and diazepam on tests of working memory and planning. Psychopharmacology 120:311–321; 1995.
7. Cushman, L.; Brinkman, S. D.; Ganji, S.; Jacobs, L. A.: Neuropsychological impairment after carotid endarterectomy correlates with intraoperative ischemia. Cortex 20:403–412; 1984.
8. Downes, J. J.; Roberts, A. C.; Sahakian, B. J.; Evenden, J. L.; Morris, R. G.; Robbins, T. W.: Impaired extra-dimensional shift performance in medicated and unmedicated Parkinson's disease: Evidence for a specific attentional dysfunction. Neuropsychologia 27:1329–1343; 1989.
9. Doyle Haynes, C.; Gideon, D. A.; King, G. D.; Dempsey, R. L.: The improvement of cognition and personality after carotid endarterectomy. Surgery 80(6):699–704; 1976.
10. European Carotid Surgery Trialist's Collaborative Group: MRC European surgery trial: Interim results for symptomatic patients with severe (70–99%) or mild (0–29%) carotid stenosis. Lancet 337:1235–1243; 1991.
11. Fray, P. J.; Robbins, T. W.; Sahakian, B. J.: Neuropsychiatric applications of CANTAB. Int. J. Geriatr. Psychiatry 11:329–336; 1996.
12. Gaunt, M. E.; Martin, P. J.; Smith, J. L.; Rimmer, T.; Cherryman, G.; Ratliff, D. A.; Bell, P. R. F.; Naylor, A. R.: Clinical relevance of intraoperative embolization detected by transcranial Doppler ultrasonography during carotid endarterectomy: A prospective study of 100 patients. Br. J. Surg. 81:1435–1439; 1994.
13. Kelly, M. P.; Garron, D. C.; Javid, H.: Carotid artery disease, carotid endarterectomy, and behaviour. Arch. Neurol. 37:743–748; 1990.
14. Kirkpatrick, P. J.; Smielewski, P.; Whitfield, P. C.; Czosnyka, M.; Menon, D. K.; Pickard, J. D.: An observational study of near-infrared spectroscopy during carotid endarterectomy. J. Neurosurg. 8:756–763; 1995.

15. Lezac, M. D.: Neuropsychological assessment, 3rd ed. New York, Oxford Univ. Press; 1995: 544–546.
16. Littooy, F. N.; Halstuk, K. S.; Mamdani, M.: Factors influencing morbidity of carotid endarterectomy without a shunt. Am. Surg. 50:350–353; 1984.
17. Mazzucchi, A.; Scoditti, U.; Uttini, G.; Parma, M.; Banchini, E.; Villani, L. G.; Botta, G. C.: Valutazione comparative delle funzioni cognitive in pazienti affetti da patologia carotidea sintomatica trattati o non con tromboendoarteriectomia. Giorn. Chir. 7(3):439–443; 1994.
18. Mononen, H.; Lepojarvi, M.; Kallanranta, T.: Early neuropsychological outcome after carotid endarterectomy. Eur. Neurol. 30: 328–333; 1990.
19. Morris, R. G.; Downes, J. J.; Sahakian, B. J.; Evenden, J. L.; Heald, A.; Robbins, T. W.: Planning and spatial working memory in Parkinson's disease. J. Neurol. Neurosurg. Psychiatry 51:757–766; 1988.
20. Morris, R. G.; Evenden, J. L.; Sahakian, B. J.; Robbins, T. W.: Computer aided assessment in dementia: Comparative studies of Alzheimer-type dementia and Parkinson's disease. In: Stahl, S.; Iverson, S. D.; Goodman, E., eds. Cognitive neurochemistry. Oxford, UK: Oxford University Press; 1987:21–36.
21. Murie, J. A.; John, T. G.; Morris, P. J.: Carotid endarterectomy in Great Britain and Ireland: Practice between 1984 and 1992. Br. J. Surg. 81:827–831; 1994.
22. Nelson, H. E.: National adult reading test. Test manual. Windsor: NFER-NELSON; 1982.
23. North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effects of carotid endarterectomy in symptomatic patients with high grade stenosis. N. Engl. J. Med. 325:445–453; 1991.
24. Owen, A. M.; Beksinka, M.; James, M.; Leigh, P. N.; Summers, B. A.; Quinn, N. P.; Sahakian, B. J.; Robbins, T. W.: Visuospatial memory deficits at different stages of Parkinson's disease. Neuropsychologia 31:627–644; 1993.
25. Owen, A. M.; Downes, J. D.; Sahakian, B. J.; Polkey, C. E.; Robbins, T. W.: Planning and spatial working memory following frontal lobe lesions in man. Neuropsychologia 28:1021–1034; 1990.
26. Owen, A. M.; James, M.; Leigh, P. N.; Summers, B. A.; Marsden, C. D.; Quinn, N. P.; Lange, K. W.; Robbins, T. W.: Fronto-striatal cognitive deficits at different stages of Parkinson's disease. Brain 115:1727–1751; 1992.
27. Owen, A. M.; Roberts, A. C.; Polkey, C. E.; Sahakian, B. J.; Robbins, T. W.: Extra-dimensional versus intra-dimensional set shifting performance following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 29:993–1006; 1991.
28. Owen, A. M.; Sahakian, B. J.; Semple, J.; Polkey, C. E.; Robbins, T. W.: Visuo-spatial short-term recognition memory and learning after temporal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 33(1):1–24; 1995.
29. Owens, M. O.; Pressman, M.; Edwards, A. E.; Tourtellotte, W.; Rose, J. D.; Stern, D.; Peters, G.; Stabile, B. E.; Wilson, S. E.: The effect of small infarcts and carotid endarterectomy on postoperative psychologic test performance. J. Surg. Res. 28:209–216; 1980.
30. Robbins, T. W.; James, M.; Owen, A. M.; Sahakian, B. J.; McInnes, L.; Rabbitt, P. M.: Cambridge Neuropsychological Test Automated Battery (CANTAB): A factor analytic study of a large sample of normal elderly volunteers. Dementia 5:266–281; 1994.
31. Sahakian, B. J.; Downes, J. J.; Eagger, S.; Evenden, J. L.; Levy, R.; Philpot, M. P.: Sparing of attentional relative to mnemonic function in a subgroup of patients with dementia of the Alzheimer type. Neuropsychologia 28:1197–1213; 1990.
32. Sahakian, B. J.; Morris, R. G.; Evenden, J. L.; Heald, A.; Levy, R.; Philpot, M.; Robbins, T. W.: A comparative study of visuospatial memory and learning in Alzheimer type dementia and Parkinson's disease. Brain 111:695–718; 1988.
33. Semple, J.; Kamur, R.; Truman, M. I.; Shorter, J.: The effects of scopolamine hydrobromide upon perfomance of the CANTAB battery. J. Psychopharmacol. [BAP and EBPS Joint Meeting Abstr. Book] A23: 90; 1992.
34. Semple, J.; Link, C. G. G.: CANTAB parallel battery: A suitable tool for investigating drug effects on cognition. Soc. Neurosci. Abstracts. [Abstr. 273.10] p. 17; 1991.