INTRODUCTION

Several studies have been performed to evaluate the possible effects of carotid endarterectomy (CEA) on cognitive functions, but there is no consensus in the literature (1,2). The methodological problems involved are numerous. In fact, studies that report benefits following CEA lack control groups and fail to eliminate the effects of disease/surgery/anaesthesia and practice, while in those that instead suggest a cognitive impairment, follow-up tests were performed too early. There is also a lack of consensus among the various authors over patient selection criteria (types of cerebrovascular event, time since the last vascular event, degree of recovery), over the types and number of neuropsychological tests and over the timing of assessment. More recently, studies performed using control groups (3,4) and supported by neurophysiological investigations (5) have given rise to the hypothesis that CEA can ameliorate cognitive abilities. Some functions, in particular verbal fluency and visual attention, seem to benefit from CEA; however, this finding needs to be clarified. Some authors have also stressed that CEA can improve both quality of life (evaluated on a functional level) and psychosocial factors.

NEUROPSYCHOLOGICAL CHANGES AFTER CAROTID ENDARTERECTOMY

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Carotid endarterectomy (CEA), performed to prevent stroke, could lead to changes in cognitive functions. Sixty-four patients with severe carotid stenosis undergoing CEA treatment were evaluated by means of a detailed neuropsychological assessment before (baseline), from one to two weeks (1st follow up) after and 3 months (2nd follow up) after surgical operation. A significant post-CEA improvement was found in verbal memory and attention (p<0.05), while other cognitive functions showed no significant changes.

KEY WORDS: Carotid endarterectomy, cognitive functioning, neuropsychological evaluation.

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such as work, leisure and finances (6-8). Heyer et al. (9), finally, have reported both declines and improvements in neuropsychometric performance: the former may be associated with ischaemia due to global hypoperfusion or with embolic phenomena possibly occurring during surgery, while the latter seem to be related to increased cerebral blood flow following removal of the stenosis.

In the light of these observations, we evaluated short- and long-term changes in cognitive performance in a group of patients undergoing CEA.

MATERIALS AND METHODS

Subjects

During 1999 we evaluated 87 patients (63 males and 24 females), who underwent CEA for stroke prevention at the Department of Neurosurgery of the “Circolo” Hospital in Varese, Italy, and at the Department of Vascular Surgery of the S. Matteo Hospital, Pavia, Italy. Only 64 subjects could be included in the complete statistical evaluation.

The main characteristics of the population are reported in Table I. The mean age was 69±7.5 years (range 54-81), and the mean length of schooling was 6.8±3.4 years (range 3-17). Sixty subjects were right-handed, 4 left-handed.

Surgery was indicated in the event of severe stenosis of the internal carotid artery, corresponding to more than 70% of the cross-sectional diameter of the artery, assessed by angiography and/or echodopplersonography. Computed tomography (CT scan) completed the patients’ investigations.

Twenty-three patients received right and 41 left carotid reconstruction.

Before surgery 27 subjects had been asymptomatic, while 28 had experienced one or more transient ischaemic attacks (TIAs) from which they had recovered completely. Eight patients had suffered a stroke (two ipsilateral and the other six contralateral to the operation side); one patient had experienced a retinal infarction. The interval between the last clinical event and the pre-operative investigation was at least one month.

At the baseline evaluation the neurological examination revealed right focal signs in 27 patients and left focal signs in 23 subjects; the findings were negative in the other 14 patients.

Patients with any psychiatric illness, neurological disorder, alcohol or drug abuse problems or any other medical condition liable to interfere with cognitive functions were excluded from the study, as were subjects with severe vascular encephalopathy or vascular dementia.

No patient reported a cerebrovascular event in the post-operative period.

A group of 32 subjects, matched for age, sex, and years of schooling with the patients undergoing CEA, without a history of head trauma or drug abuse, and attending the C. Mondino Institute of Neurology for peripheral nervous problems, were chosen as a control group to eliminate surgery/anaesthesia effects.

Methods

In all patients, CEA was performed under general endotracheal anaesthesia.

Arterial blood pressure and blood gases were monitored through a catheter percutaneously placed in the radial artery.

The carotid bifurcation was exposed through

<table>
<thead>
<tr>
<th>Table I - Population characteristics</th>
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<tbody>
<tr>
<td>Males: 43</td>
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<tr>
<td>Females: 21</td>
</tr>
<tr>
<td>Mean age (yrs): 69±7.5 (range 54-81)</td>
</tr>
<tr>
<td>Years of schooling (mean): 6.8±3.4 (range 3-17)</td>
</tr>
<tr>
<td>Hand preference: right-handed: 60 left-handed: 4</td>
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<tr>
<td>Side of carotid stenosis: right 23; left 41</td>
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a vertical incision along the anterior border of the sternocleidomastoid muscle. The nerve to the carotid artery and sinus was injected with 1% lidocaine to prevent bradycardia.

As soon as the carotid bifurcation had been appropriately prepared, the patient was administered 5,000 units of aqueous heparin sodium intravenously, and vascular clamps were applied to the common, external and internal carotid arteries during a three-minute test occlusion prior to performance of the CEA.

For intraoperative recording, an eight-channel EEG was used. Moderate levels of induced hypertension were maintained along the clamping artery.

Careful surgical technique, with magnification, was employed to reduce the risk of embolisation.

No patient in this series required an intraluminal shunt. The medium clamping time was eleven minutes (range 7-15).

Cognitive evaluation was performed by the same examiner in the week prior to CEA, and two weeks (1st follow up) after and three months (2nd follow up) after surgery. The neuropsychological tests were selected on the basis of their capacity to evaluate the main cognitive domains, while limiting fatigue and loss of attention.

The neuropsychological examination included:

– Trail Making Test parts A and B (TMTA and TMTB): attention and information processing speed (10). In part A the subject is given a worksheet on which to link, with a line, 25 numbered circles. In part B the subject must connect numbered and lettered circles alternately. In each part, the score is based on performance time.
– Digit span: short-term verbal memory (11). Subjects are presented orally with a growing sequence of digits that they are required to repeat correctly. The score corresponds to the highest number of digits correctly repeated.
– Corsi’s span: visuo-spatial short-term memory (12). The subject must reproduce a growing sequence of visual stimuli (cubes arranged in different ways on a board). The score is the highest number of cubes correctly arranged.
– Rey’s 15 words (immediate and delayed recall): short- and long-term memory (13). Subjects are read a list of 15 bisyllabic and trisyllabic words that are neither semantically nor phonologically related and then asked to repeat them. The procedure is repeated five times. After 15 minutes of non-verbal distracting tasks, subjects are asked to repeat the words they remember without another reading of the list. Two separate scores are given: the total number of words remembered during the five trials (immediate recall) and the number of words remembered after 15 minutes (delayed recall).
– Grooved pegboard: manual dexterity (14). The subject has to put pegs into holes on a board as fast as he can, using only one hand, first the right and then the left. The score is the length of time (in seconds) required to perform each trial. A maximum of 5 minutes is allowed for performance of the task.
– Token Test: verbal oral comprehension (15). The examiner arranges on the table 20 tokens having two shapes (circles and squares), two sizes (large and small) and five colours. The test consists of a series of commands delivered in sets of increasing complexity. Items not executed correctly in response to the first command must be repeated. For scoring, tasks executed correctly in response to the first and in response to the second command are counted separately.
– Copy drawing: visuo-constructive abilities (13). The subject is required to copy some geometrical figures.

To minimise the practice effect as far as possible, equivalent versions of the tests were performed at the 1st and 2nd follow ups. All examinations were performed at least 5 hours after the administration of any analgesic or sedative medication.

**Statistical analysis**

Comparisons between and within groups...
were made by analysis of variance (ANOVA), one-way and for repeated measures respectively. The performance scores obtained in cognitive tests by patients and controls were analysed by means of two-way ANOVA with group as the between factor and task as the within factor. The minimum level of statistical significance was set at < 0.05.

RESULTS

The scores in Tables II, III and IV are expressed as raw scores.

Table II shows the results of neuropsychological tests at baseline, 1st follow up and 2nd follow up. A significant improvement in the scores of tests exploring attentive functions (TMTA and TMTB; p<0.01, p<0.001) and learning (Rey’s 15 words, immediate recall; p<0.01) emerged at the 2nd follow up. Comparison of our patients with the control group (Table III) revealed a significant improvement of the same measures, but the significance was weaker (p<0.05) in the controls. Thus, at least the anaesthesia/surgery effect was eliminated, even though the practice effect was not.

The raw test scores were corrected according to age, sex, education and transformed into equivalent scores in accordance with Italian standardised parameters (10,12,13). Equivalent scores of 0 are considered pathological (2.9% of total population), scores of 1 as borderline (10.4% of total population), scores 2, 3, 4 as normal. Table V shows the distribution of equivalent scores both at baseline and at the 2nd follow up in CEA patients. It can be seen that our population was not severely impaired; the functions most impaired were attention and memory.

The data were also analysed to determine whether any variables, such as age, presence or absence of symptoms, and operation side, influenced cognitive performance. No significant correlation with age could be found (younger or older than 70 years) or with the presence/absence of symptoms. We then divided our population according to the side of operation; no direct comparison of the two groups was made because of the difference in their levels of culture (higher in patients undergoing surgery on the

### Table II - Neuropsychological evaluation: baseline vs 1st and 2nd follow up in CEA patients (raw scores)

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>1st follow up</th>
<th>2nd follow up</th>
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<tbody>
<tr>
<td>TMTA</td>
<td>113.7±62.2</td>
<td>87.2±48.4</td>
<td>98.9±62.8***</td>
</tr>
<tr>
<td>TMTB</td>
<td>219.3±87.6</td>
<td>184.8±89.0</td>
<td>194.8±88.0***</td>
</tr>
<tr>
<td>Digit span</td>
<td>5.0±1.3</td>
<td>5.2±1.4</td>
<td>5.0±1.0</td>
</tr>
<tr>
<td>Corsi’s test</td>
<td>4.2±1.1</td>
<td>4.3±0.9</td>
<td>4.2±0.9</td>
</tr>
<tr>
<td>Rey imm</td>
<td>32.1±9.6</td>
<td>32.4±8.8</td>
<td>36.0±11.3**</td>
</tr>
<tr>
<td>Rey del</td>
<td>6.4±3.1</td>
<td>5.8±2.3</td>
<td>6.8±3.4</td>
</tr>
<tr>
<td>GP right</td>
<td>114.5±46.0</td>
<td>100.0±23.4</td>
<td>110.4±34.4</td>
</tr>
<tr>
<td>GP left</td>
<td>128.7±63.6</td>
<td>117.5±53.4</td>
<td>120.6±52.4*</td>
</tr>
<tr>
<td>Token Test</td>
<td>30.9±2.4</td>
<td>31.3±2.7</td>
<td>31.3±2.0*</td>
</tr>
<tr>
<td>Copy drawing</td>
<td>12.7±1.5</td>
<td>13.0±1.1</td>
<td>12.8±1.4</td>
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</tbody>
</table>

Abbreviations: TMTA = Trail Making Test Part A; TMTB = Trail Making Test Part B; Rey imm: Rey’s 15 words (immediate recall); Rey del = Rey’s 15 words (delayed recall); GP = Grooved pegboard. ANOVA for repeated measures: */**/*** p<0.05 / 0.01 / 0.001.
However, all the neuropsychological measures showed a greater degree of impairment in patients with left stenosis than in subjects with right stenosis. At the 2nd follow up, the patients with right stenosis showed a significant improvement in their performance of the Corsi’s and copy drawing tests, which explore visuo-
spatial functions mediated by the right hemisphere (Table IV).

DISCUSSION

The results of this study suggest that CEA may slightly improve cognitive functions (or, at least no significant impairment could be detected following the procedure). In particular, verbal memory and attention significantly improved, a result that is in accordance with reports in the literature (3-5), while no change was detected in the other abilities.

Even though there is no general consensus regarding the effects of CEA on neuropsychological functions, most authors suppose that a worsening in cognition after CEA could be related to intraoperative ischaemia (16,17). For this reason, monitoring of the electrical activity of the brain during surgery is very useful and has become general practice. On the other hand, the mechanisms underlying the improvement of neuropsychological functions are not completely clear. Some authors suggest (9) that improvement could be related to an increase in regional cerebral blood flow following removal of the stenosis. However, other authors have failed to demonstrate improved post-operative cerebral flow, and have instead suggested that the abolition of the source of multiple cerebral embolisation may be a crucial factor (18).

In our patients, we found a relationship between the operated side and the pattern of cognitive improvement. Patients with right stenosis in fact showed a more marked improvement in spatial memory and copy drawing than patients with left stenosis. These patients, on the other hand, presented with a greater level of global cognitive impairment. The significance of these data, at least with regard to the subjects’ demographic and cultural characteristics, is not immediately clear. Although no patients had clinically detectable aphasic disturbances, it might be argued that the possible presence of subtle linguistic abnormalities, of an impairment of verbal reasoning and of a more severe impairment of verbal memory might influence the cognitive status.

It would be of great interest to distinguish subgroups of patients with peculiar cognitive behaviour in particular in relation to the side of

<table>
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<tr>
<th>Equivalent scores</th>
<th>Baseline</th>
<th>2nd follow up</th>
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<tbody>
<tr>
<td>Digit span</td>
<td>14-17</td>
<td>11-2-20</td>
</tr>
<tr>
<td>Rey imm</td>
<td>9-5</td>
<td>9-11-30</td>
</tr>
<tr>
<td>Rey del</td>
<td>4-7</td>
<td>15-10-27</td>
</tr>
<tr>
<td>Copy drawing</td>
<td>1-4</td>
<td>4-8-49</td>
</tr>
</tbody>
</table>

Abbreviations: TMTA = Trail Making Test Part A; TMTB = Trail Making Test Part B; Rey imm: Rey’s 15 words (immediate recall); Rey del = Rey’s 15 words (delayed recall).
lesion. However, in our sample, further investigation was precluded by methodological problems: the small number of subjects in each subgroup, the difficulty in achieving strong statistical significance, and other problems related to the neuropsychological measures employed.

In conclusion, our study supports data in the literature that document improvements in some cognitive functions after CEA and also addresses a number of methodological issues: a control group was included in order to take into account surgery/anaesthesia effects, parallel neuropsychological tests were used to eliminate, as far as possible, practice effects, and definite patient selection criteria were applied. Further investigations, in particular a long-term follow up (one year or more), are needed, as the literature contains very few data in this regard. Improved cognition also brings improvements in various areas contributing to overall quality of life, i.e. work, leisure, social relations. We thus feel that, in a multi-dimensional approach to the treatment of carotid stenosis (surgical versus medical), due consideration should be given to evaluation of cognitive status, an important factor.

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