Cognitive impairments after surgical repair of ruptured and unruptured aneurysms

Argye E Hillis, Nancy Anderson, Prakesh Sampath, Daniele Rigamonti

Abstract

Objectives—To determine the frequency and severity of neuropsychological impairments associated with aneurysmal subarachnoid haemorrhage, and associated with repair of intracerebral aneurysms.

Methods—Two groups of patients who underwent repair of intracerebral aneurysms were studied: patients with unruptured aneurysms (n=20) and patients with ruptured aneurysms (n=27). All patients were administered a battery of standardised neuropsychological tests about 3 months after surgery. A subset of 12 patients with unruptured aneurysms were administered the battery before and after elective repair of the aneurysm(s). A subset of six patients with ruptured aneurysms were given the test at both 3 months and 1 year after surgery.

Results—As previously reported for patients with ruptured aneurysms, patients with both ruptured and unruptured aneurysms performed, as a group, significantly below published norms on many of the neuropsychological tests after surgery. However, there were significant differences between preoperative and postoperative performance in the unruptured aneurysm group only on a few tests: measures of word fluency, verbal recall, and frontal lobe function. Performance of patients with ruptured aneurysms was significantly below that of patients with unruptured aneurysms only on a few tests of verbal and visual memory. In addition, group differences compared with published norms reflected severely impaired performance by a minority of patients, rather than moderately impaired performance in a majority of patients.

Conclusions—Although patients who undergo repair of ruptured aneurysms perform, as a group, below published norms on many neuropsychological tests, significant impairments are seen in a minority of patients. Some of the impairments are associated with subarachnoid haemorrhage, whereas others (found in patients who underwent repair of unruptured aneurysms) are due to general effects of neurosurgery and perioperative management. Finally, some of the postoperative deficits are merely a reflection of premorbid weaknesses.

Keywords: subarachnoid haemorrhage; intracerebral aneurysm; cognitive outcome

Long lasting cognitive deficits after aneurysmal subarachnoid haemorrhage (SAH) and subsequent repair of the aneurysm have been well documented. In fact, it has been found that 30%-55% of patients have “severe” or “marked” deficits in one or more cognitive domains 1–7 years after surgery. However, the evidence for these estimations of the long term effects of SAH and its management has come from studies of postoperative performance of patients on neuropsychological tests or questionnaires, or both, compared with published norms or with a matched control group of normal subjects. In a few cases, there was no clear control group. The drawback of the established approach is twofold. Firstly, performance of a large group of people on a large set of tests compared with published norms for each individual test will always, by virtue of individual variation in abilities, show relatively poor performance on one or more tests in a substantial number of the people tested. Secondly, differences between postoperative patients and normal controls may reflect general effects of stay in hospital, illness, bed rest, and general anaesthesia in addition to the specific effects of the SAH and aneurysm surgery. Only Richardson compared patients who underwent aneurysm surgery with a control group of patients who underwent laminctomy, thereby eliminating possible contributions of debility and general anaesthesia to long term cognitive sequelae.

Furthermore, in most of these studies, the documented cognitive impairments have been attributed to the SAH itself, rather than to complications of SAH or to neurosurgery. However, this hypothesis has not been directly tested. The only evidence that has been cited for this view is that patients who have non-aneurysmal SAH may be as likely as patients who undergo aneurysm repair after SAH to have long term mild to moderate cognitive deficits. However, other authors have found that patients with spontaneous SAH in whom no aneurysm is found have less marked long term neuropsychological impairments than those reported for patients with SAH who undergo aneurysm repair. Therefore, although Desantis et al found that neuropsychological deficits were more severe in patients with delayed, relative to early, surgery, it remains likely that aneurysm clipping with craniotomy, or surgical complications, or both, account for at least some of the associated cognitive sequelae of aneurysmal SAH. Documentation of the risk of temporary or permanent cognitive deficits associated with unruptured aneurysm repair, or its complica-
Cognitive impairments after surgical repair of ruptured and unruptured aneurysms

Table 1  Mean (SD) characteristics of the three groups used for analyses

<table>
<thead>
<tr>
<th></th>
<th>Patients with unruptured aneurysm</th>
<th>Patients with ruptured aneurysm (postop data)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With preop and postop data</td>
<td>(n=12)</td>
</tr>
<tr>
<td>Age</td>
<td>49.6 (7.89)</td>
<td>50.4 (8.46)</td>
</tr>
<tr>
<td>Education</td>
<td>12.5 (1.77)</td>
<td>11.6 (2.42)</td>
</tr>
<tr>
<td>Sex</td>
<td>17% Male</td>
<td>15% Male</td>
</tr>
<tr>
<td>Estimated IQ*</td>
<td>102.8 (7.42)</td>
<td>103.5 (8.67)</td>
</tr>
</tbody>
</table>

*Based on scores from the national adult reading test (NART).

In this paper we report the incidence and range of cognitive deficits consequent to unruptured aneurysm repair must be established to provide adequate counselling on the risks and benefits of surgery, and to evaluate variations in management of unruptured aneurysms.

In this paper we report the incidence and range of cognitive deficits consequent to unruptured and ruptured cerebral aneurysms. Neuropsychological testing was performed about 3 months postoperatively in patients who underwent repair of ruptured aneurysms (n=27) and unruptured aneurysms (n=20), and was compared with preoperative performance on the same tests in the unruptured aneurysm group.

METHODS

POPULATION

All patients who were scheduled for clipping of one or more intracranial aneurysms by the senior author during the period of February 1993 to July 1996 were invited to participate in the study. Additional inclusion criteria were: at least one intracranial aneurysm; able and willing to provide informed consent to participate; native speaker of English; and age of at least 21 years. Exclusion criteria included previous neurosurgery or pre-existing neurological disease other than aneurysm. Patients were not excluded from testing if they had incurred perioperative complications, such as vasospasm or hydrocephalus. There were 20 patients who had never had an aneurysmal haemorrhage and underwent clipping of at least one unruptured aneurysm. There were 27 patients who, after SAH, underwent clipping of at least the ruptured aneurysm (and in some cases, clipping of additional unruptured aneurysms in the same operation). The distribution of aneurysms by site was as follows: 42% internal carotid artery (ICA); 39% anterior cerebral artery (ACA); 13% middle cerebral artery (MCA); and 7% in the posterior circulation (includes aneurysms of the basilar artery, the superior cerebellar artery, and the posterior inferior cerebellar artery). In the patients with ruptured aneurysms, the Hunt-Hess scale score at admission ranged from 1 to 4, with a mean of 2.0 (1.1). Aneurysm diameter ranged from 4 mm to 53 mm, with a mean of 15 mm and a median of 10 mm. The age ranged from 30 to 77 years, with a mean of 51.1 and median of 52. Education ranged from 4 to 18 years, with a mean of 11.8 and a median of 12. Fifteen per cent (7/47) of patients were left handed. Seventy four per cent (35/47) were women. There were no significant differences between the ruptured and unruptured aneurysm groups for site of aneurysm, age, education, estimated IQ, or sex, or handedness (Table 1). Some patients were not administered one or more of the neuropsychological tests due to premorbid impairments. For example, one patient with a broken finger on the dominant hand was not administered the grooved peg board test, which requires fine motor function of the hand. Patients with poor corrected vision due to premorbid eye disease were not administered tests with visual stimuli.

All patients who had an SAH due to ruptured aneurysms were treated with nimodipine (60 mg orally every 4 hours), hyper- volaemia, and mild hypertension induced with hypertonic saline for prevention/treatment of vasospasm, and phenytoin for seizure prophylaxis, beginning at admission and throughout postoperative management. Surgical intervention was scheduled as soon as possible after admission in patients with ruptured aneurysms. Patients who underwent temporary clipping during surgery were administered propofol until burst suppression on EEG, and mean arterial pressure was raised by 10 mm Hg over baseline during this part of the procedure.

PROCEDURES

All patients were administered a battery of neuropsychological tests about 3 months after surgery (median surgery-test interval=81 days). A subset of 12 of the 20 patients with unruptured aneurysm were administered the same battery before surgery to clip the aneurysm(s). Additionally, six patients in the ruptured aneurysm group were administered the same battery at about 1 year after surgery (median surgery-test interval=361 days). Although it would have been ideal to study all of the patients with unruptured aneurysms before surgery, and all of the patients in both groups at 1 year, we were not able to do so. Because the surgery was done at a tertiary referral centre, where many of the patients come from distant countries as well as distant regions of the United States, many patients were unavailable for testing before the surgery or at 1 year. The neuropsychological battery included the following tests: (1) the Wechsler adult intelligence scale-revised (WAIS-R)33 digits forward and backward, block design, and digit-symbol sub-tests; (2) the Wechsler memory scale-revised34; (3) the Boston naming test35-split half version; (4) the Warrington recognition memory test36 for faces and words; (5) the Rey auditory verbal learning test37; (6) the Rey-Osterreith complex figure test38; (7) the Stroop test39; (8) the controlled oral word association test30 (naming words beginning with F, A, and S); (9) the grooved peg board test40; and (10) the Zung depression scale.31 These tests were included to assess a broad range of cognitive skills thought...
Table 2  Mean (SD) scores on standardised tests for patients with unruptured v ruptured aneurysms given in mean Z scores unless otherwise stated

<table>
<thead>
<tr>
<th>Cognitive domains and tests</th>
<th>Unruptured aneurysm</th>
<th>Ruptured aneurysm</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention (digit span)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digits forward</td>
<td>6.13 (1.36)</td>
<td>6.31 (1.46)</td>
<td>NS</td>
</tr>
<tr>
<td>Digits backward</td>
<td>5.06 (1.24)</td>
<td>4.65 (1.98)</td>
<td>NS</td>
</tr>
<tr>
<td>WMS-R attention/concentration sum</td>
<td>95.9 (12)</td>
<td>98.9 (19)</td>
<td>NS</td>
</tr>
<tr>
<td>Memory:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAVLT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>−0.26 (1.7)</td>
<td>−0.70 (2.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Delayed</td>
<td>−0.82 (1.6)*</td>
<td>−1.53 (2.1)**</td>
<td>NS</td>
</tr>
<tr>
<td>Recognition memory test</td>
<td>−0.12 (0.13)</td>
<td>−0.50 (0.56)*</td>
<td>NS</td>
</tr>
<tr>
<td>Faces</td>
<td>−0.11 (0.12)</td>
<td>−0.61 (0.55)**</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Words</td>
<td>−0.11 (0.12)</td>
<td>−0.61 (0.55)**</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>WMS-R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal summary</td>
<td>111 (15)†</td>
<td>87.5 (17)</td>
<td>p&lt;0.003</td>
</tr>
<tr>
<td>Visual Summary</td>
<td>106 (16)</td>
<td>82.8 (15)*</td>
<td>P&lt;0.04</td>
</tr>
<tr>
<td>Language:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boston naming test mean score</td>
<td>48 (11)**</td>
<td>44.5 (14)*</td>
<td>NS</td>
</tr>
<tr>
<td>Partial lobe function:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WAIS block design (scaled score; norm=10)</td>
<td>6.22 (2.6)***</td>
<td>7.5 (2.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Frontal lobe function:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop (interference)</td>
<td>−0.99 (1.4)**</td>
<td>−1.70 (2.8)*</td>
<td>NS</td>
</tr>
<tr>
<td>Verbal fluency (F-A-S)</td>
<td>−3.08 (1.5)**</td>
<td>−4.24 (1.6)**</td>
<td>NS</td>
</tr>
<tr>
<td>Motor psychomotor function:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grooved pegboard</td>
<td>−0.73 (1.9)</td>
<td>−2.17 (4.0)*</td>
<td>NS</td>
</tr>
<tr>
<td>Dominant hand</td>
<td>−0.60 (1.4)</td>
<td>−0.96 (1.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Non-dominant</td>
<td>−1.26 (1.2)***</td>
<td>−1.48 (1.2)**</td>
<td>NS</td>
</tr>
<tr>
<td>WAIS symbol-digit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zung depression inventory</td>
<td>39.5 (8.7)</td>
<td>41.3 (9.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values in parentheses are SD of the Z scores or scaled scores. Superscripts indicate significantly different from published norms. *p<0.05; **p<0.01; ***p<0.001, lower than the norm. †p<0.03, above the norm. For tests with published norms and scoring in percentile ranges rather than Z scores, a standard conversion table was used to convert percentile scores to Z scores (obtained above the norm). For tests with published norms (performance for non-brain damaged adults of matched age and education), at different time points, were analysed with Student’s t tests. In addition, preoperative and 3 month postoperative performance were compared, for the patients who had testing before and after repair of unruptured aneurysm (n=12) using paired t tests, to identify the effects of surgery and perioperative care. Performance of the ruptured aneurysm group (n=27) was compared with that of the unruptured aneurysm group (n=20) at 3 months after surgery using one way analysis of variance (ANOVA), to identify the effects of SAH. Results of testing at 3 months and 1 year postsurgery were compared in the six patients with ruptured aneurysms who returned for 1 year follow up, to identify effects of recovery over time. Due to the multiple comparisons (multiple tests at each time period), we evaluated the possibility that the significant differences found for each of these effects were not due to chance alone. It should be noted that the group comparisons employed statistical analyses that assume a normal distribution of data. We point out comparisons where this assumption is violated, showing that some apparently significant differences between the studied population and published norms were due to a highly skewed distribution of results among the patients with aneurysms.

Throughout, different degrees of freedom reflect missing values caused by individual patients who could not perform one or more tests (for example, one patient had a broken finger and could not perform the grooved pegboard or block design test). Summary scores have the lowest degrees of freedom because a missing value on any subtest precludes calculating a summary score for that patient.

Results

EFFECTS OF SURGERY

Preoperative versus postoperative performance in patients with unruptured aneurysms

As a group, patients who underwent repair of unruptured aneurysms showed poorer postoperative performance, compared with preoperative performance, on the following tests: (1) word fluency (the COWT; r=−4.62; df=11, p<0.003); immediate verbal recall (RAVLT; r=−2.76; df=11; p<0.02); delayed verbal recall (RAVLT, delayed; r=−3.87; df=11; p<0.005); and “frontal lobe” function (the Stroop test; r=2.36; df=10; p<0.05 (the fewer degrees of freedom for this test reflect the fact that one person could not perform the Stroop test due to premorbid colour blindness)). These differences are shown in fig 1. The probability of identifying a significant (p<0.05) decline between preoperative and postoperative performance on more than three out of 16 tests by chance alone is <0.01. Of note, however, is that only 33% of patients showed a deterioration in any or all of these scores from the preoperative to the postoperative scores. Only one patient deteriorated on all three tests. There was no difference between preoperative and postoperative performance on tests of attention (digits), confrontation naming (the Boston naming test), non-verbal memory (repetition memory test for faces, Rey-Osterreith complex figure test), visuoconstructional skills (the block design subtest of the WAIS-R) or psychomotor speed (grooved pegboard, symbol-digit subtest of the WAIS-R). However, when the data from the same subset of patients who were studied both preoperatively and postoperatively were analysed in the more traditional method for such studies, patients who underwent clipping of unruptured aneurysms performed at least 2 SD below the published mean for normal controls, postoperatively, on tests of psychomotor speed (symbol digit subtest of the WAIS-R; r=13.87; df =11; p<0.01), visuo-constructional skills (the Block...
Design subtest of the WAIS-R; df=11; \( t = -5.89; p < 0.0001 \), as well as "frontal lobe" function (the Stroop test; \( t = -3.04, \text{df}=10; p < 0.02 \)). The probability of this finding (more than two of the 16 tests being significantly below normal) by chance alone is 0.04—that is, there was a marginally significant impairment on the set of tests compared with normal controls. Moreover, as there was not a significant decrease in scores from their preoperative performance on the WAIS-R subtests, it is unlikely that the significantly "impaired" scores were a result of the aneurysm surgery or associated factors.

Postoperative performance in patients with unruptured aneurysms compared with published norms

For the entire group of patients with unruptured aneurysms (including those who were not tested preoperatively), mean performance was significantly below published norms on: word fluency (the COWT; \( t = -3.08, \text{df}=19; p < 0.01 \)); delayed verbal recall (RAVLT; \( t = -2.23; \text{df}=19; p < 0.05 \)); "frontal lobe" function (the Stroop test; \( t = -3.07; \text{df}=17; p < 0.01 \)); psychomotor speed (WAIS digit-symbol; \( t = -4.47, \text{df}=18; p < 0.0001 \)) and block design (\( t = -6.11; \text{df}=17; p < 0.0001 \)). The probability of this result (more than four of the 16 tests being significantly lower than normal) by chance alone is <0.001. Mean performance of this group was significantly above the published norms on the Wechsler memory scale-revised verbal summary score (\( t = 2.81; \text{df}=16; p < 0.03 \); table 2). However, the finding of at least one of 16 tests being significantly higher than normal by chance alone is 0.56; in other words, this finding is likely due to chance.

EFFECTS OF SAH PLUS SURGERY

Postoperative performance in patients with ruptured aneurysms compared with published norms

As a group, patients who underwent clipping of ruptured aneurysms showed postoperative performance significantly below the mean for normal controls on nearly all tests: verbal fluency (COWT; \( t = -7.78; \text{df}=18; p < 0.0001 \)); delayed verbal recall (RAVLT; \( t = -3.38; \text{df}=20; p < 0.002 \)); non-verbal recognition memory (recognition memory test for faces; \( t = -2.96; \text{df}=17, p < 0.01 \)); psychomotor speed (grooved pegboard; \( t = -2.53; \text{df}=21; p < 0.03 \)); visuocon-
EFFECTS OF SAH
Performance of patients with ruptured aneurysms versus unruptured aneurysms 3 months after aneurysm clipping
Performance of the patients who underwent clipping of ruptured aneurysms was significantly below that of patients who underwent clipping of unruptured aneurysms on a subset of the memory tests, but no other tests. There were significant group differences on the Wechsler memory scale-visual memory summary score ($F=12.8; df=1, 23; p<0.003$) and verbal memory summary score ($F=17.4; df=1, 23; p<0.001$), and the Warrington recognition memory test for words ($F=4.46; df=1, 36; p<0.05$), as shown in Table 2. The probability of group differences on more than two of the 16 tests by chance alone is 0.04; thus, the documented differences between groups was marginally significant ($p<0.05$). On most tests, patients with ruptured aneurysm repair performed no worse postoperatively than did the patients after unruptured aneurysm repair. As most patients with unruptured aneurysm repair performed no worse postoperatively than preoperatively, it is likely that neither surgery nor SAH leads to diffuse deterioration in cognitive skills at 3 months, in the absence of complications such as hydrocephalus. Nevertheless, these results indicate that SAH itself may be associated with some circumscribed memory deficits.

There was also no significant difference between the unruptured and the ruptured aneurysm groups on the Zung depression inventory ($F=0.44; df=1,40$; NS). Altogether, 36% of patients rated themselves as not depressed, 36% as minimally to moderately depressed, 23% as moderately to markedly depressed, and 5% as severely depressed.

THE EFFECTS OF RECOVERY OVER TIME
Three month versus 12 month postoperative performance in patients with ruptured aneurysm
Regrettably, only a subset of six patients with ruptured aneurysms returned for long term follow up testing (mean 361 days postoperatively). These patients, as a group, showed significant improvement only in confrontation naming (the Boston naming test; $r=3.05; df=5; p<0.03$), a finding that could be due to chance alone in making multiple comparisons (16 tests at two time periods). There may have been inadequate power to detect additional group improvements, particularly as most patients performed in the normal range at 3 months. That is, there was a ceiling effect for most patients. Also, it is not clear that this subset is representative of the entire ruptured aneurysm group. Nevertheless, this significantly improved test performance is consistent with the well known finding that patients with residual cognitive deficits at 3 months (who were few in this study) often show further recovery over the first year.

Discussion
There are several important results of this investigation that have not been previously reported. Firstly, although the patients with ruptured aneurysm as a group had significant impairments compared with published norms on nearly all of the neuropsychological tests administered (as reported in previous studies), the impairments were found in a minority of individual patients. That is, we found a bimodal distribution of cognitive function in patients at 3 month follow up after aneurysm clipping. For example, on the Warrington recognition test for words, a large percentage (44%) of patients scored below the 10th percentile, and an equally large percentage (44%) scored above the 60th percentile for normal controls. Although the median percentile score was 10 and the mode was <5, almost half of the patients scored above average. Furthermore, the mean percentile score for this group was 45.5%, but none of the patients scored between the 20th and 60th percentile, indicating that the mean score was virtually meaningless. Although few authors have brought attention to this aspect of results, inspection of individual data reported in several investigations indicates similar findings. Ogden et al reported (their Table 3) that 10 week follow up testing of patients with SAH disclosed “severe” impairments on the recognition memory test for words in 10.4% of patients and an impairment in 83.1%; only 6.5% of patients scored in the moderate range of impairment. Furthermore, in the study by Barbarotto et al, their Table 2 shows that on the verbal fluency test with phonological cue (similar to our word fluency test, the COWT, and their most sensitive measure), 30% of patients after left MCA aneurysm repair scored below the lowest 5% of normal controls, but 40% of patients obtained an average score or higher than normal controls. Similarly, the tables in the study by Romner et al indicate that 30% of patients who had weighted impairment indices (based on Z scores) above 20, indicating widespread, marked deviations from normal performance, but 60% had impairment indices of <10, indicating a range in performance across tests from normal to moderate impairment. Only 10% had an impairment index in the middle range from 10–20. These results are comparable with those of Stenhouse et al, who reported that 23% of their patients 12 to 84 months after aneurysm repair had “pervasive global impairment”, with inability to perform (or very poor scores on) the Wisconsin card sorting test, and below average performance on the Wechsler memory scale, whereas 42% of patients showed no deficits on follow up neuropsychological testing. The other 30% of patients had only focal deficits on neuropsychological testing. Other authors have reported only group means1,3 or the percentage of patients who were impaired versus unimpaired on each test,5 which may have obscured a bimodal distribution of performance. Our data indicate that, even when the group mean performance is statistically significant from normal, only a minority of patients in the group have what is likely to be a clinically significant impairment.

Secondly, although many of the neuropsychological tests showed differences between
groups (ruptured and unruptured) relative to published norms, only a few tests documented a change from preoperative testing even in the subset of patients with unruptured aneurysm with significant postoperative impairments. This result indicates that previous studies comparing mean performance in patients to published norms may overestimate the effects of SAH or aneurysm repair. Preoperative data from the patients with unruptured aneurysm represent their premorbid, baseline performance. Preoperative to postoperative decline in performance occurred on a few tests, by a subset of patients. Patients in the unruptured aneurysm group showed significant declines from preoperative performance on tests of word fluency (COWT—naming words beginning with F, A, and S), verbal recall (the Rey auditory-verbal learning test), and so-called "frontal lobe functions" (the Stroop test). Notably, these are the very cognitive functions that are most often found to be impaired in follow up after aneurysm repair after SAH. This finding indicates that a large proportion of the long term cognitive sequelae reported in earlier studies — impairments in verbal fluency, immediate and delayed verbal and non-verbal recall, and "frontal lobe" function — may have resulted from effects of brain surgery, such as prolonged anaesthesia, temporary regional cessation of blood flow, brain retraction, use of antiepileptic medications, or even more general effects of bed rest and debility, rather than SAH alone. Other cognitive deficits, such as postoperative psychomotor slowing and visual memory impairments were only observed postoperatively in patients with ruptured aneurysms in our study, indicating that some cognitive deficits can be attributed to the SAH itself. In addition, performance on verbal and non-verbal recall was significantly more impaired in the ruptured aneurysm group relative to the unruptured aneurysm group, indicating that SAH itself may exacerbate or cause impairment in recall beyond the impairment attributable to stay in hospital and surgical management, at least in some patients. Thus, testing of both patients with both ruptured aneurysms (with SAH) and patients with unruptured aneurysms, who underwent comparable surgical management and perioperative care, is a unique aspect of this investigation that allowed us to separate the neuropsychological deficits resulting specifically from SAH from those resulting from general effects of neurosurgical intervention, perioperative complications, general anaesthesia, depression, or debility.

It has been proposed that the mechanism by which SAH negatively affects memory and "frontal lobe function" is focially decreased perfusion and/or depressed metabolism of brain regions critical to these skills, secondary to focal vasospasm or the clipping itself. In this case, the site of aneurysm should be crucial to the effects on subsequent cognitive functions. However, in this study, site alone was not clearly a predictor of significant impairment. Of the seven patients who showed the most marked deficits in memory and "frontal lobe function" (with percentile scores <5 on the recognition memory test; see fig 1) after ruptured aneurysm, the distribution of aneurysm sites was as follows: two right posterior communicating artery; two right MCA; one left MCA, one right ACA, and one basilar artery. There was an overrepresentation of MCA aneurysms in this subset of patients with poor cognitive outcome relative to the entire group of patients with ruptured aneurysms (43% of patients with poor outcome versus 13% of all patients, had MCA aneurysms; $\chi^2=3.4; df=1; p=0.06; $Fisher’s exact: $p=0.10$), but this difference did not reach significance perhaps due to the few patients with poor cognitive outcome. There was also no difference in the mean Hunt-Hess scale score on admission between those with marked cognitive impairment at follow up (mean 1.8 (SD 1.3)) versus those without such impairments (mean 2.0 (SD 1.3)). However, all of the patients with marked deficits in memory and frontal lobe function at 3 month follow up had either documented basal ganglia or frontal lobe ischaemic changes on postoperative CT (n=3) or had postoperative hydrocephalus requiring shunt (n=4). These complications were significantly more common in the subset of patients with severe cognitive impairments than in those without such significant impairments (100% vs 20%; $\chi^2=11.8; df=1; p<0.001; $Fisher’s exact: $p<0.001$).

By contrast with the deleterious effects of some postoperative complications, clinical vasospasm did not clearly predict impaired performance in the ruptured aneurysm group at 3 month follow up. Most patients with ruptured aneurysms, with or without lasting cognitive deficits, had at least moderate vasospasm by transcranial Doppler (TCD) criteria (for example, velocity of 140–200 cm/s in M1 or M2 segments of the MCA, or C1 segment of the internal carotid). However, only one of the seven patients with the most severe cognitive impairments had documented clinically significant vasospasm (in this case, associated with contralateral hemiparesis). Nevertheless, the frequent occurrence of vasospasm defined by TCD in the ruptured aneurysm group, compared with the absence of vasospasm, clinically or by TCD, in the unruptured aneurysm group, may account for at least some of the difference between ruptured and unruptured aneurysm groups found on three memory tests. We will report details of the relation between the degree and duration of vasospasm by TCD and performance on various neuropsychological tests at 3 months in the ruptured aneurysm group in a separate paper.

Previous studies have reported conflicting results regarding the effects of postoperative vasospasm on cognitive function after SAH. Whereas Adams et al., Hori and Suzuki, Fortuny et al., and Stenhouse et al. have all reported that postoperative vasospasm was a significant predictor of residual cognitive impairment at variable periods of follow up, Ogden et al. and Gilsbach failed to find any association between vasospasm and cognitive function. The predictive value of postoperative lesions on imaging
for lasting cognitive impairments has also been controversial. Ogden et al. found that ischaemic changes on neuroimaging postoperatively were predictive of more significant cognitive impairments at 1 year; and Hardemark et al. found that ventriculomegaly on CT was related to deficits on neuropsychological testing at 1 year. By contrast, Romner et al. reported no correlation between tissue loss on late postoperative MRI and cognitive deficits at long term follow up (13–32 months after surgery). Contrast results may reflect differences in the definitions or methods for identifying postoperative vasospasm and ischaemic changes. For example, early MRI may show reversible lesions due to retraction injury or vasospasm that will not be seen on later MRI. The recent availability of technology to measure vasospasm, blood flow, and other aspects of regional metabolism, and new MRI techniques to distinguish cerebral hypoperfusion from infarction, may be helpful in evaluating the aetiology of neuropsychological impairments after surgery in future studies.

The few previous studies that have evaluated cognitive changes after surgery in patients with unruptured aneurysms used very limited measures of cognition. The International Study of Unruptured Intracranial Aneurysms reported that 5.5% of patients with unruptured aneurysms and no history of SAH, and 9.6% of patients with unruptured aneurysms but history of SAH from a different aneurysm, had cognitive impairment (defined as <24 on the mini mental state examination or a score of less than 27 on the telephone interview for cognitive status) at 3 months after intervention (>80% surgical; the remainder endovascular). Similar results were found at 1 year. No preintervention data are available to determine whether or not the cognitive impairment was due to the intervention (or perioperative management), or reflected premorbid variability among the study population. It seems likely from these results that the difference between groups reflected cognitive impairments associated with previous SAH. This study has been widely and severely criticised along methodological lines, and with respect to the interpretation of the findings and will not be further discussed here. In a separate study, Fukunaga et al. administered the mini mental state examination, in addition to a letter search test and a maze test, to 30 patients before and after surgery for unruptured aneurysms. They reported that 10 patients showed a deterioration in score on the mini mental state examination from the preoperative test to the 1 month postoperative test, but failed to make note of the result (data in their table 3) that a larger number of patients (12) actually showed an increase in the mini mental state examination score at 1 month after surgery. No statistical comparisons between preoperative and postoperative scores were reported.

In the present study, we documented deficits in verbal fluency, recall, and frontal lobe functions in a subset of patients after unruptured aneurysm repair. Decline from the preoperative period to the postoperative 3 month follow up period was largely limited to four patients, who had either large left MCA (n=2) or large ophthalmic artery aneurysms (n=2). In this group the size of aneurysm may well have been the crucial variable associated with the documented deficits, although the numbers are too small to detect a significant relation. That is, it is plausible that impairments in verbal fluency, verbal recall, and the Stroop test (also a verbal test) in the two patients with left MCA aneurysms were due to focal retraction injury involving the language cortex, and that impairments on the same tests (which also depend on frontal lobe function) in the two patients with ophthalmic artery aneurysms was due to focal retraction injury involving the frontal lobes. Notably, one of the patients with MCA had small intraparenchymal haemorrhages in the deep frontal and temporal regions on CT, consistent with localised contusion. By contrast with our findings of marked impairments only in patients with MCA or ophthalmic aneurysms, Gade et al. suggested that patients who undergo repair of ACA aneurysms are particularly vulnerable to amnesia. However, no data from cognitive testing were reported in that study.

One potential application of the findings of the present study is in evaluating modifications of surgical or perioperative management of patients with intracerebral aneurysms. As repair of unruptured aneurysm now carries a very low risk of mortality (1%) or major physical morbidity (4%), mortality and morbidity rates are not sufficiently sensitive measures of outcome to identify possible differences in outcome due to variations in operative techniques or perioperative care. By contrast, we have documented that cognitive dysfunction after (even unruptured) aneurysm repair is more common. The frequency or severity of cognitive deficits may be associated with particular aspects of surgical management, and might be reduced by changes in protocol to provide neural protection (for example, hypothermia) or aimed at avoiding hypoperfusion, hypoxia, or damage to an eloquent brain region (for example, using temporary clipping). Thus, evaluation of cognitive function is likely to provide a sensitive measure of outcome, with which variations in operative or perioperative procedures can be evaluated in future investigations.

In summary, this investigation documented performance on neuropsychological tests by patients undergoing clipping of intracerebral aneurysms. The crucial aspects of the study that distinguish it from previous studies of this type are: (1) the inclusion of patients with unruptured aneurysms as well as those with ruptured aneurysms; and (2) the analysis of preoperative versus postoperative performance on the neuropsychological battery in patients with unruptured aneurysms. Comparison of patients with ruptured and unruptured aneurysms allowed us to differentiate deficits due to SAH (and possibly associated complications such as vasospasm) versus deficits due to more general effects of neurosurgical intervention, anaesthesia, and debility. Measuring preopera-
tive performance permitted us to determine which differences from published norms in this group were due to operative and peroperative management, and which differences were due to premorbid variability. Although our study was small by comparison with some previous studies, the numbers were adequate to identify significant differences between patients who underwent repair of ruptured versus unruptured aneurysms, and significant differences between preoperative and postoperative performance. Finally, analysis of individual data provided reason to doubt the prevailing view that moderate or “marked” cognitive impairments after cerebral aneurysm repair are common. Rather, the moderate differences in group means, on a subset of tests in this study, reflected uncommon severe deficits. That is, very deviant scores by a few patients substantially lowered the group means. Unfortunately, the design of the study and the relatively few patients did not allow us to determine the cause of the marked cognitive impairments experienced by a few patients. Future studies (in progress) not only aim to recruit a greater number of subjects, but also to prospectively evaluate independent variables that might influence cognitive outcome, using serial TCD, magnetic resonance perfusion and diffusion imaging, CT perfusion scans, and other advanced imaging techniques.

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