Effect of endoscopic third ventriculostomy on neuropsychological outcome in late onset idiopathic aqueduct stenosis: a prospective study

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J Neurol Neurosurg Psychiatry 2003;**74**:222–225

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Received 8 March 2002
In revised form 17 July
2002
Accepted
11 November 2002

Objective: To undertake a prospective study of the long term neuropsychological outcome in patients with late onset idiopathic aqueduct stenosis (LIAS) after endoscopic third ventriculostomy.

Methods: Six patients with LIAS were evaluated pre- and postoperatively using magnetic resonance imaging (MRI) and standardised psychometric testing procedures. Endoscopic third ventriculostomy was done using standard surgical techniques. The mean long term follow up was 81.2 weeks.

Results: Preoperatively, all patients had cognitive impairment, four of them showing deficits in several cognitive domains. After endoscopic third ventriculostomy, all patients improved clinically and had ventricular size reduction on MRI. Postoperative neuropsychological testing showed that five patients achieved normal or near normal cognitive functions, and one improved moderately.

Conclusions: Endoscopic third ventriculostomy caused a substantial improvement in the neuropsychological deficit of LIAS patients. This was also true for patients with enlarged ventricles that might be diagnosed radiologically as "arrested hydrocephalus."

Aqueduct stenosis is a well recognised cause of hydrocephalus.^{1–7} In the adult, the idiopathic variant with a late onset has recently been termed LIAS (late onset idiopathic aqueductal stenosis).^{8–11} With the reinvention of cerebral endoscopy during the latter decades, the treatment of LIAS has been changed from shunt implantation to endoscopic third ventriculostomy. Mixer undertook the first successful endoscopic third ventriculostomy in 1923.¹² Today, based on the development of modern neuroimaging^{13–15} and endoscope technologies,^{16–23} endoscopic third ventriculostomy has become the procedure of choice for the treatment of non-communicating forms of hydrocephalus in many centres.^{24–26} Hopf *et al* reported a success rate of 83% in patients with aqueduct stenosis, without mortality or permanent morbidity, in a series of 100 consecutive endoscopic third ventriculostomies.²⁷ However, although the clinical features, magnetic resonance imaging (MRI) findings, and clinical response to endoscopic treatment have been reported recently,²⁸ little is known about the cognitive state of LIAS patients.²⁹ Our primary aim in this study was thus to evaluate neuropsychological function in LIAS patients before and after endoscopic third ventriculostomy.

METHODS

Between July 1997 and April 2000, 14 patients were diagnosed as having aqueduct stenosis at the Neurosurgery Clinic,

University of Innsbruck, Austria. From this group, six subjects (table 1) fulfilled the inclusion criteria for this study, which were as follows:

- no other intracranial pathology apart from hydrocephalus;
- lateral and third ventricles enlarged, with a comparatively small fourth ventricle;
- decreased or absent flow in the aqueductal canal on cross sectional phase contrast MRI for CSF flow, together with morphological signs of obstruction of the aqueduct on sagittal, high resolution gradient echo imaging (3D-MPRAGE, CISS-3D).

None of the patients had had previous surgical treatment for hydrocephalus, and none had a history of meningitis, stroke, epilepsy, or substance abuse. Endoscopic third ventriculostomy was done as described by Hopf *et al*.²⁷ The operation was carried out with rod lens ventriculoscopes (Wolf, Knittlingen, Germany). The outer diameters of the ventriculoscopes (elliptical ventriculoscope-shaft configuration) were 6 mm and 5.8 × 4.8 mm, respectively. They were equipped with a 2.3 mm optical probe and three or four channels for irrigation, suction, and instrument insertion.

Abbreviations: LIAS, late onset idiopathic aqueduct stenosis; MGT, Münchner Gedächtnistest

Table 1 Patient data, preoperative clinical, and magnetic resonance imaging findings

Patient	Sex	Age (years)	Headache	Gait disturbance	Endocrinological dysfunction	Average duration of symptoms before diagnosis	Papilloedema on fundoscopy	Preoperative TFA
WA	M	25	No	No	No	1 month	Yes	No
HE	M	28	Yes	No	No	3 months	No	No
NE	F	37	Yes	No	Yes	3 months	No	No
SB	F	34	Yes	Yes	Yes	6 months	No	No
GR	M	58	Yes	Yes	No	12 months	No	Yes
MM	F	60	Yes	Yes	No	9 months	No	Yes

F, female; M, male; TFA, preoperative transependymal fluid absorption as found on magnetic resonance imaging.

Table 2 Preoperative and postoperative neuropsychological findings

Cognitive function	HE pre	HE post 1	HE post 2	WA pre	WA post 1	WA post 2	SB pre	SB post 1	SB post 2	NE pre	NE post 1	MM pre	MM post 1	MM post 2	GR pre	GR post 1	GR post 2	Maximum possible score
Time postoperative (weeks)	-1	+1	+100	-1	+22	+60	-1	+1	+72	-1	+1	-1	+4	+122	-1	+16	+52	
MMSE orientation	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Digit span forward	NA	NA	7	5	5	6	NA	NA	5	NA	NA	6	8	7	4	5	5	
Digit span backward	NA	NA	5	4	3	4	NA	NA	5	NA	NA	3	6	4	3	3	3	
<i>Münchener Gedächtnistest</i>																		
Encoding trial 1	6	5	8	5	3*	7	6	6	9	9	4*	4*	5	7	2**	3*	5	16
Encoding trial 2	11	9	12	8	9	9	7*	10	12	10	7*	9	12	11	3**	4**	7*	16
Encoding trial 3	11	11	13	10	10	10	9*	9*	14	10	11	8*	14	13	5**	9*	8*	16
Encoding trial 4	7**	11	14	9*	14	14	10*	10*	11	13	11	9*	13	11	3**	10*	10*	16
Encoding trial 5	10*	12	13	9*	15	15	11	13	13	12	13	12	13	15	5**	13	11	16
Short delay free recall	11	10	10	5**	13	10	5**	9*	12	15	14	5**	12	13	1**	8**	6**	16
Short delay cued recall	8*	8*	12	9*	14	12	7**	11	10	15	15	7**	12	16	4**	8*	8*	16
Long delay free recall	8*	10	11	6**	14	12	9*	9*	11	16	13	13	12	15	2**	9*	6**	16
Long delay cued recall	8*	8*	11	8*	15	10	9*	9*	12	16	13	7**	13	15	6**	10	9*	16
Recognition correct	16	16	16	15	16	13*	16	16	15	16	16	15	15	16	12*	16	14*	16
False positive	1*	0	0	0	0	1*	0	0	1*	0	0	7**	0	0	1*	2**	3**	16
Confabulations	0	0	0	0	1	2**	2**	2**	0	0	0	3**	2**	0	6**	2**	2**	
Intrusions	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	
Perseverations	9**	7**	5**	0	1	1	6**	3**	15**	0	0	3**	1	0	3**	3**	3**	
<i>Rey-Osterrieth C figure</i>																		
Copy	35	35	36	35	34	34	36	35	36	21**	33*	30	31	34	36	36	35	36
Short delay free recall	24	25	33	13.5**	26	23	14**	22.5	23	13.5**	22	6**	8**	14.5	16.5	16	22.5	36
Long delay free recall	20	26	33	12**	27	20	21	22.5	23	13.5**	21	6**	8**	15	17.5	16	19.5	36
Category word fluency	28	37	25	12*	20	25	19*	21	25	28	NA	13*	24	35	11*	21	18	
Trail making test A (s)	25	31	27	34	20	20	49*	40	36	27	26	105**	35	33	70**	42	64*	
Trail making test B (s)	72	48	55	68	50	57	116*	102	75	59	46	314**	82	116	300**	147*	212**	
<i>Stroop test</i>																		
Reading of colour words (s)	25	22	23	26	27	26	40*	32	35	28	NA	NA	56*	37	29	44	40	
Naming of colours (s)	39	36	36	42	39	31	58	52	42	45	NA	NA	55	55	42	52	50	
Interference (s)	56	54	54	60	58	53	90	78	75	82	NA	NA	94	100	77	82	76	

*1 SD below group mean (normal subjects), or below 16th centile, or below T value 40.

**2 SD below group mean (normal subjects), or below 3rd centile, or below T value 31.

NA, not administered; post 1, first postoperative examination; post 2, second postoperative examination; pre, preoperative examination.

In all patients, MRI was undertaken before endoscopic third ventriculostomy, and postoperatively within the first week and then at six, 12, and 24 months. Preoperative and postoperative MRI was done on a 1.5 T scanner (Magnetom Vision, Siemens, Erlangen, Germany) using a standard CP head coil. The examination protocol included standard spin echo sequences, cardiac gated cross sectional phase contrast studies and a three dimensional flash sequence (3D-MPRAGE; time of echo (TE) = 4 ms, time of repetition (TR) = 9.7 ms, flip angle (FA) = 40°, slice thickness (SL) = 1 mm) after intravenous administration of contrast agent (Gd-BMA, Nycomed, Vienna, Austria). High resolution CISS-3D imaging was not routinely done. A comparison of preoperative and postoperative MRI was undertaken by an independent neuroradiologist. The preoperative and postoperative clinical status of the patients was assessed by a surgeon who was not involved in the operation (KT). Successful endoscopic third ventriculostomy was defined as:

- evidence for a clear improvement of preoperatively assessed clinical deficits;
- follow up MRI showing flow through the stoma at the third ventricular floor on cross sectional phase contrast studies and diminished ventricular size.

Neuropsychological assessment was done one week preoperatively and on two follow up examinations (mean (SD), 7.5 (9.2) weeks and 81.2 (9.2) weeks after the operation) using standardised psychometric testing procedures for various aspects of memory, attention, visuoconstructive abilities, and executive function (table 2). Testing and evaluation were undertaken by an experienced neuropsychologist. Orientation was tested with the orientation

section of the mini-mental state examination.³⁰ Auditory working memory was evaluated by the digits forward and backward subtest of the Wechsler memory scale.³¹ Verbal memory functions were evaluated with the Münchener Gedächtnistest (MGT),³² a German equivalent of the California verbal learning test.³³ This test taps learning, short term and long term verbal memory, and word recognition, and records confabulations, intrusions, perseverations, and errors of commission during memory performance. To minimise practice effects resulting from repeated use of the MGT, alternate test forms were used. The ability to copy and spontaneously recall a complex figure was assessed with the Rey-Osterrieth complex figure test³⁴; visuo-perceptual, constructive, and mnemonic abilities are involved in the performance of this test. Category word fluency was measured by counting the correctly produced items of a semantic category (animals) within 60 seconds after subtraction of repetitions. Psychomotor speed, attention, and cognitive flexibility were evaluated with the trail making test.³⁵ Focused attention, set shifting, and suppression of distraction were evaluated using the Stroop colour word test.³⁶

Because of the small sample size, a subject by subject analysis of neuropsychological data rather than a group comparison was undertaken.

RESULTS

Clinical and MRI findings

Patient data and relevant clinical findings are summarised in table 1.

Table 3 Neuropsychological findings

Cognitive function	Preoperative		Postoperative 1		Postoperative 2	
	Mean	SD	Mean	SD	Mean	SD
MMSE orientation	10	0.0	10	0.0	10	0.0
Digit span forward	5.0	1.0	6.0	1.7	6.0	1.0
Digit span backward	3.3	0.6	4.0	1.7	4.2	0.8
<i>Münchener Gedächtnistest</i>						
Encoding trial 1	5.3	2.3	4.3	1.2	7.2	1.5
Encoding trial 5	9.8	2.6	13.2	1.0	13.4	1.7
Short delay free recall	7.0	5.1	11.0	2.4	10.2	2.7
Short delay cued recall	8.3	3.7	11.3	2.9	11.4	3.1
Long delay free recall	9.0	5.0	11.2	2.1	11.0	3.2
Long delay cued recall	9.0	3.6	11.3	2.7	11.2	2.3
Recognition correct	15.0	1.5	15.8	0.4	14.6	1.3
False positive	1.5	2.7	0.3	0.8	1.0	1.2
Confabulations	1.8	2.4	1.2	0.9	1.6	1.7
Intrusions	0.0	0.0	0.2	0.4	0.2	0.4
Perseverations	3.5	3.5	2.5	2.5	2.2	1.9
<i>Rey Osterrieth C figure</i>						
Copy	32.2	5.9	34.0	1.8	34.6	0.9
Short delay free recall	14.6	5.8	19.9	6.8	24.2	6.9
Long delay free recall	15.0	5.6	20.1	7.1	22.7	7.0
Category word fluency	18.5	7.9	24.6	7.1	25.2	6.2
Trail making test A (s)	51.7	31.0	32.3	8.4	34.8	17.0
Trail making test B (s)	154.8	119.6	79.2	40.1	103.4	65.5
<i>Stroop test</i>						
Reading of colour words (s)	29.6	6.0	36.2	13.8	31.8	7.2
Naming of colours (s)	45.2	7.4	46.8	8.6	44.0	10.1
Interference (s)	14.5	2.3	73.2	16.8	71.8	19.4

Postoperative 1 and 2, first and second postoperative examination.

Frequent preoperative abnormalities were chronic headache (five patients) and gait disturbance (three patients). No patient complained of urinary incontinence. Only two patients (GR and MM) reported problems at work and during everyday activities related to headache, poor memory, or fluctuating attention. Papilloedema was found in one patient, and endocrinological dysfunction in two female patients.

Endoscopic third ventriculostomy was undertaken in all patients without complication. On postoperative MRI, ventricular size diminished in all cases but did not reach normal size, and transependymal cerebrospinal fluid absorption disappeared where previously present. All patients recovered from their preoperative neurological deficits (table 1). After the third ventriculostomy, the two patients who had suffered from amenorrhoea-dysmenorrhoea syndrome showed normal endocrinological function, resulting in pregnancy six months after surgery in one (NE) and a regular menstrual cycle in the other (SB). With the exception of GR, who continued to experience stress induced headaches, all subjects recovered from chronic headache. Hypersomnia, psychiatric complications, eating disorders, and personality disorders were not observed after the intervention. From MRI and clinical criteria, the endoscopic third ventriculostomy was rated successful in all six subjects.

Neuropsychological findings

Neuropsychological findings are summarised in table 2.

Preoperatively, all patients had normal orientation and auditory working memory. An isolated memory impairment was found in two (HE, NE), and a combination of neuropsychological impairments in four. Impairment of memory, as determined from the MGT, was found in five patients. Common findings were decreased and inconsistent list learning, below average spontaneous short and long delay recall, and perseverations, confabulations, and intrusions during test performance. Recognition was impaired in two

patients (MM, GR). Figural memory was flawed in four patients (WA, SB, NE, MM). Impaired frontal-executive functions, as evidenced by defective verbal fluency, cognitive flexibility, or focused attention, were found in three patients (WA, MM, GR). One patient (NE) presented with poor visuoconstruction. In sum, preoperative screening showed that none of the LIAS patients had completely intact cognitive function, most showing combined deficits of memory and frontal-executive functions.

After endoscopic third ventriculostomy, all patients had improvement in their preoperative LIAS related deficits. A single subject analysis (table 2) shows that two patients (HE and MM) returned entirely to normal. Three patients (WA, SB, NE) showed good recovery but occasional errors. One patient (GR) had persistent chronic verbal memory impairment and frontal-executive deficits, though figural memory, psychomotor speed, and verbal fluency improved. Most subjects were already showing improvement by the time of their first postoperative follow up and there was little change at the second follow up (table 3).

DISCUSSION

Previous studies of LIAS have investigated the long term clinical outcome of patients given shunts during childhood,^{29 37 38} or the MRI characteristics before and after surgical intervention.²⁸ Endoscopic third ventriculostomy has become a standard treatment for LIAS.²⁷ However, the assessment of neuropsychological function as an indicator of outcome after endoscopic surgery has not been reported previously. In this study we evaluated the clinical, radiological, and cognitive outcome of the endoscopic third ventriculostomy procedure in a small but carefully selected sample of LIAS patients. Endoscopic third ventriculostomy was undertaken following the standard, minimally invasive procedure, from a coronary burr hole (Kocher's point) through the foramen of Monro,²⁷ without surgical complications. According to the chosen outcome criteria,

the procedure was considered effective in all the patients. Clinical recovery correlated well with the reduction in ventricular size and the flow through the stoma. Thus postoperative neuropsychological assessment was based on a highly homogeneous group in relation to neurosurgical outcome.

There is a lack of systematic studies of the cognitive impairments found in LIAS patients treated by endoscopic third ventriculostomy. In this study, all LIAS patients showed a preoperative cognitive impairment on standard neuropsychological tests, some of them ranging into the lowest centile scores. The most common problem was an impairment of anterograde memory in combination with frontal-executive and other minor cognitive deficits. As far as can be judged from a relatively small patient group, our investigation suggests that neuropsychological deficits appear to be common in LIAS patients. The deficit pattern is similar to that found in other hydrocephalic disorders,^{39,40} but is very dissimilar to hydrocephalic dementia, which commonly presents with severe cognitive alterations such as apathy, decreased speed of information processing, severe memory impairment, and impaired ability to manipulate acquired knowledge.^{41,42} Follow up examination after endoscopic third ventriculostomy showed a good recovery of memory and other impairments in five patients, and moderate recovery in one. Because the target sample size was too small to have satisfactory statistical power, this conclusion is based on a subject by subject analysis and a comparison of descriptive statistics. Although care was taken to minimise the impact of practice effects in, for example, the MGT, by using alternate test forms, and despite the fact that follow up intervals were long, test-retest effects cannot be ruled out. However, on the basis of the available information we conclude that endoscopic third ventriculostomy may result in substantial and stable neuropsychological recovery in LIAS patients. This finding needs further confirmation in studies with larger numbers of patients and in case-control studies.

Interestingly, three patients (SB, HE, NE) reported no symptoms apart from headache, and they were unaware of any cognitive deterioration. Preoperative MRI did not show signs of transependymal CSF absorption in these subjects. Thus one could have falsely diagnosed their enlarged ventricles as "arrested hydrocephalus," a diagnosis for which a surgical intervention may not be considered necessary. However, all three patients were found to have significant improvement in their test scores after surgery. We can therefore conclude that a subgroup of LIAS patients is unaware of any cognitive deficit, and that patients with MRI findings typical for LIAS (although without signs of transependymal CSF absorption) should be routinely screened for memory and executive functions. Overall, endoscopic third ventriculostomy has proved to be an effective, safe, and minimally invasive surgical procedure for the treatment of LIAS patients.

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Competing interests: none declared

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