Cognitive changes after cerebrospinal fluid shunting in young adults with spina bifida and assumed arrested hydrocephalus

Maria Mataró, Maria Antonia Poca, Juan Sahuquillo, Ampar Cuxart, Jordi Iborra, Maria Dolores de la Calzada, Carme Junqué

Abstract

Objectives—To establish whether surgery can improve the neuropsychological functioning of young adult patients with spina bifida and apparent clinically arrested hydrocephalus showing abnormal intracranial pressure.

Methods—Twenty three young adults with spina bifida and assumed arrested hydrocephalus (diagnosed as active or compensated by continuous intracranial pressure monitoring) underwent surgery. All patients received neuropsychological examination before surgery and 6 months later. Neuropsychological assessment included tests of verbal and visual memory, visuospatial functions, speed of mental processing, and frontal lobe functions.

Results—Shunt placement in this subgroup of patients improves neuropsychological functioning, especially in verbal and visual memory and attention and cognitive flexibility.

Conclusions—Young adults with spina bifida and suspected non-functioning shunt or non-shunted ventriculomegaly should be carefully monitored to identify those who could benefit from shunting.

Keywords: spina bifida; hydrocephalus; neuropsychology; surgery

Early hydrocephalus is associated with various cognitive deficits. Persistent neuropsychological difficulties affecting visuospatial and motor functions, and difficulties in other non-verbal domains have been consistently found in hydrocephalic children. The extent to which these problems are related to hydrocephalus and its treatment or to other brain abnormalities remains unclear. Although a range of factors such as raised intracranial pressure (ICP), size of ventricles, and other neuroanatomical structures, as well as shunt complications have been shown to influence cognition, the precise nature and course of the neuropsychological deficits are not fully understood.

Today, due to recent medical advances, older patients with congenital hydrocephalus are now available for study. In these patients, both those with prior shunt and those without, moderate or severe stabilised ventriculomegaly is often found. Some authors have indicated that although the hydrocephalus is apparently arrested, the disorder may in fact progress insidiously in certain patients. In addition to the abnormal CSF dynamics found in such patients, continuous ICP monitoring has demonstrated an increase in pressure and abnormal ICP waves. In a previous study of 19 patients with spina bifida and assumed arrested hydrocephalus, continuous ICP monitoring showed that hydrocephalus was active in 58% of the patients and compensated in 32%, and in only 10% was the diagnosis of arrested hydrocephalus confirmed. Because abnormal ICP can cause further neurological impairment, monitoring of ICP and serial neuropsychological assessments are considered valuable tools in the assessment of assumed arrested hydrocephalus.

Few studies to date have assessed the effectiveness of shunt treatment in these patients with apparent arrested hydrocephalus. Several have noted that some patients present cognitive improvement. However, many of these studies are case reports or are based on small samples; others include hydrocephalus of different aetiologies, or fail to monitor ICP consistently. In view of our previous experience with this population of patients and the repeated subjective reports from parents of increased attentiveness and mental ability after surgery, we sought to evaluate and document the neuropsychological effects of this treatment. A second purpose of this study was to investigate the effect of a range of hydrocephalus related factors on cognition and surgery outcome. We hypothesised that shunt treatment would improve the cognitive functioning of young adult patients with an apparent arrested hydrocephalus in whom continuous ICP monitoring showed non-arrested hydrocephalus.

Method

SAMPLE

The institutional ethics committee on human research of Vall d’Hebron University Hospitals approved the study, and informed consent was obtained from each patient or an authorised family member. The study included 23 consecutive patients with spina bifida meningomyelocele and Chiari malformation with increased but stable ventriculomegaly. None of the patients had overt clinical signs or symptoms of increased ICP. They were either asymptomatic or had only minor symptoms (sporadic headache, attention and memory difficulties, psychomotor slowness, etc). Mean
age was 22.5 (range 14–42). Twelve were male and 11 female. A shunt had been implanted in 12 patients during childhood and, at present, was non-functioning. Median age at the time of first shunt in these patients was 1.6 months (range 1–5), with a shunt revision rate of 1.8/patient. The other 11 patients had never been treated for hydrocephalus. Inferior intellectual performance (full scale intelligence quotient <70) was present in three patients (two of them shunted, one non-shunted (table 1)).

The presurgical investigation of each patient included a standard neurological examination, continuous extradural ICP monitoring, neuroradiographic studies (CT or MR) and a comprehensive neuropsychological battery. In all cases the diagnosis of active or compensated hydrocephalus was established by ICP monitoring, for which the therapeutic intervention was judged to be appropriate. All patients underwent shunt surgery and were re-evaluated 6 months after operation (table 2). The control sample consisted of 23 subjects who were age and sex matched with the patient group, and who volunteered for the neuropsychological evaluation. None of the control group had a history of psychiatric, neurological, or metabolic disease.

### Table 1 Demographic characteristics of patients and control group

<table>
<thead>
<tr>
<th>Spina bifida patients</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>23</td>
</tr>
<tr>
<td>Sex (males/females)</td>
<td>12/11</td>
</tr>
<tr>
<td>Age</td>
<td>22.52 (SD=6.52)</td>
</tr>
<tr>
<td>Education (y)</td>
<td>10.87 (SD=3.45)</td>
</tr>
<tr>
<td>WAIS/WISC:</td>
<td></td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>85.14 (SD 14.64)</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>86.14 (SD 18.79)</td>
</tr>
<tr>
<td>Full scale IQ</td>
<td>84.38 (SD 16.81)</td>
</tr>
</tbody>
</table>

WAIS=Wechsler intelligence scale for adults; WISC=Wechsler intelligence scale for children; IQ=intelligence quotient.

### Table 2 Presurgical clinical characteristics of the patient group (n=23)

<table>
<thead>
<tr>
<th>Shunt status:</th>
<th>Non-shunted</th>
<th>Shunted previously</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of previous shunt revisions:</td>
<td>None</td>
<td>3 (25.0%)</td>
</tr>
<tr>
<td>1 revision</td>
<td>3 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>2 revisions</td>
<td>3 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>4 revisions</td>
<td>3 (25.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Causes of previous shunt revisions:

- Growth development: 12 (60.0%)
- Infection: 1 (5.0%)
- Malfunction: 7 (35.0%)

Epilepsy:
- Absence: 21 (91.3%)
- Presence: 2 (8.7%)

Present clinical symptoms:
- Asymptomatic: 7 (25.0%)
- Minor symptoms: 16 (57.1%)
- Hydrocephalus category:
  - Active hydrocephalus: 5 (21.7%)
  - Compensated hydrocephalus: 18 (78.3%)

Level of lesion:
- Thoracic: 2 (8.7%)
- Lumbar (L1–3): 6 (26.1%)
- Lumbar (L4–5): 10 (43.4%)
- Sacral: 5 (21.7%)

TC or MR abnormalities:
- Partial callosal agenesis: 5 (21.7%)
- Thinning of corpus callosum: 9 (39.1%)
- Heterotopias: 3 (13.0%)
- Aqueductal stenosis: 16 (69.6%)
- Interdigitation: 10 (43.5%)
- Impingement: 12 (52.2%)
- Siringomielia: 3 (13.0%)
- Chiari I malformation: 1 (4.3%)
- Chiari II malformation: 1 (4.3%)

ICP waves:
- Presence of A waves: 2 (8.7%)*
- Presence of B waves: 23 (100.0%)

*One patient presented nocturnal A waves between 20 and 40 mm Hg. The other patient presented both diurnal and nocturnal A waves between 20 and 40 mm Hg.

Percentage of B waves during the total monitoring time:
- < 25%: 8 (34.8%)
- 25–49%: 8 (34.8%)
- 50–74%: 4 (17.4%)
- ≥75%: 2 (8.7%)

ICP mean (active group): 16.00 (SD 3.16)

ICP mean (compensated group): 9.47 (SD 2.96)

Evans index: 0.39 (SD 0.08)

Ventricular score: 108.10 (SD 24.9)

Cella media index: 0.34 (SD 0.08)

Third ventricle index: 0.10 (SD 0.05)

ANATOMICAL MEASUREMENTS

From the CT several measurements and ratios were obtained and considered (fig 1)—namely, Evans index, third ventricle index, ventricular score, and cella media index.

**NEUROPSYCHOLOGICAL ASSESSMENT**

Patients underwent neuropsychological examination before surgery and were re-assessed 6 months after shunting. The tests were administered in the same order. Neuropsychological assessment before and after operation was repeated in the same order. Neuropsychological assessment before surgery and were re-assessed 6 months after operation (table 2). The control sample consisted of 23 subjects who were age and sex matched with the patient group, and who volunteered for the neuropsychological evaluation. None of the control group had a history of psychiatric, neurological, or metabolic disease.

Patients underwent neuropsychological examination before surgery and were re-assessed 6 months after shunting. The tests were administered in the same order. Neuropsychological assessment before and after operation was always performed by the same examiner. Neuropsychological assessment included tests of verbal and visual memory, visuoconstructive functions, speed of information processing, and frontal lobe functions. The selective reminding test was used to assess verbal learning and memory. The version used consists of 12 words presented over six selective reminding trials. A cued recall is presented according to a key provided at the top of the figure. The copy trial of the complex figure was used as a measure of both visual scanning and motor speed and attention and mental flexibility. Word fluency evaluated the spontaneous production of words beginning with a given letter for 1 minute. C, B, and V were used in preoperational assessment and F, A, and S in postoperative assessment; in Spanish these letters do not differ in terms of vocabulary choices. The Lafayette grooved pegboard test was used as a measure of both speed and fine motor coordination. In this test, subjects insert grooved keys in keyholes as rapidly as possible. In the symbol digit modalities test, subjects place numbers below the mark according to a key provided at the top of the page for 90 seconds. It is used to assess visual scanning, tracking, and motor speed.

The percentage of change between basal and postoperative conditions was determined for each neuropsychological measure using the following calculation: ((postoperative-preoperative)/preoperative×100).

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INTRACRANIAL PRESSURE MONITORING AND CEREBROSPINAL FLUID SHUNTING

Continuous intracranial pressure was monitored using a fibroptic extradural device (LADD Research Industries, Inc, USA). Hard copies of the ICP were obtained through a single channel recorder with a paper speed of 20 or 60 cm/hour. In all patients, ICP monitoring was performed for at least 72 hours. The quantitative analysis of the ICP records was made using a computerised system. The presence of A waves (ICP increases at least 20 mm Hg above the resting line, with abrupt onset and end, and lasting for at least 10 minutes) and high or low amplitude B waves (0.5–2 ICP waves/minute, lasting for at least 10 minutes) was evaluated and expressed as the percentage of the total monitoring time.

Depending on the ICP recording, each patient was included in one of the following categories, previously defined and published by our group:

1. **Active hydrocephalus**—mean ICP above 12 mm Hg; or
2. **compensated hydrocephalus**—mean ICP < 12 mm Hg, but with the presence of A or B waves. None of the patients in this study had an arrested hydrocephalus—mean ICP below or equal to 12 mm Hg but without any pathological waves during recording time.

SURGICAL METHOD

A ventriculoperitoneal shunt was inserted in all patients. Previous shunts were removed when possible. Strongly calcified shunts or old devices encrusted in the cranial bone were left in place. In two patients, a non-programmable Hakim-Medos valve of 70 mm H2O (Johnson and Johnson Company, Switzerland) was implanted. In the other patients we used a diaphragm valve with antisiphon (Delta valve with a performance level of 0.5 in 17 patients and a performance level of 1 in four patients) (Medtronic PS Medical, USA). Ventricular size and ICP recording were used to decide the most appropriate valve.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (Version 6.0) was used for data analysis. For group comparisons we used Mann-Whitney U procedures. Preoperative and postoperative differences were analysed by the Wilcoxon matched pairs signed ranks test. Spearman’s rank correlation test was performed to study the relation between morphological data and neuropsychological functioning. Statistical significance was established at p < 0.01%.

Results

NEUROPSYCHOLOGICAL FUNCTIONING OF YOUNG ADULT PATIENTS WITH SPINA BIFIDA AND ASSUMED ARRESTED HYDROCEPHALUS

Table 3 summarises the results of the neuropsychological testing in hydrocephalic patients and controls. Patients presented poorer performance on most neuropsychological measures than controls. Statistically significant differences
were found in visual memory, visuoconstructive and frontal functions, and fine motor speed.

NEUROPSYCHOLOGICAL CHANGES AFTER SHUNTING

At 6 months after surgery, patients showed improvement in all neuropsychological functions. Improvement was statistically significant on verbal and visual memory, unilateral motor coordination, and speed, as well as on a test of attention and mental flexibility (table 3 and fig 2).

Using a cut off score of 2 SD below the control mean in each test, we found that in 11 patients (47.8%) two or more tests which were impaired in the presurgical assessment achieved normal scores after treatment. In two patients (8.7%) two or more tests previously within the normal range became impaired, and in 10 patients (43.5%) there was no change according to this arbitrary criterion.

EFFECTS OF HYDROCEPHALUS RELATED FACTORS

To assess the effect of several clinical variables on cognition and shunt improvement, patients were divided into groups based on type of hydrocephalus, presence of prior shunt, and symptomatology. There were no significant

Figure 2 Preoperative and postoperative neuropsychological measurements versus control subjects. *Time measures.

Figure 3 Box and whisker plot of measurements in ventricular size before and after shunting.
di

Verences between patients with active and compensated hydrocephalus, patients with previously shunted hydrocephalus and those without, or between asymptomatic patients and those with minor symptoms. Patients with an active hydrocephalus tended to perform worse preoperatively than those with compensated hydrocephalus. Patients with minor symptoms also tended to perform worse than the asymptomatic group.

RELATION BETWEEN MORPHOLOGICAL DATA AND NEUROPSYCHOLOGICAL MEASURES

In preoperational assessment, the third ventricle correlated significantly with the score in delayed free recall ($r_s=-0.52$, $p=0.010$) and Rey’s complex figure 30 minutes recall ($r_s=-0.52$, $p=0.012$). Both Evans index and ventricular score correlated significantly with long term retrieval ($r_s=-0.56$, $p=0.005$; $r_s=-0.51$, $p=0.013$). Larger ventricles were associated with worse performance on these verbal and visual memory tests.

Correlational analysis yielded only one significant relation between morphological data and postoperative percentage of change in neuropsychological testing. A larger cella media index was associated with a worse percentage of change on cued recall ($r_s=-0.61$, $p=0.002$).

SURGICAL OUTCOME

Ventricular size was significantly reduced in all patients in our sample (figs 3 and 4). There were no shunt related complications in 19 patients. Four patients had some type of surgical complication without any associated clinical repercussion. One of these patients developed a small parenchymal haemorrhage during shunt implantation which meant that surgery had to be postponed for 1 week. Two other patients had a small asymptomatic subdural hygroma which remitted spontaneously. In the fourth patient a proximal catheter had to be changed due to incorrect positioning.

Discussion

Our study included 23 young adult patients with spina bifida and ventriculomegalia who, despite the absence of overt clinical signs of increased ICP, had an active or compensated hydrocephalus according to ICP monitoring criteria. In all patients continuous ICP monitoring showed a mean ICP above 12 mm Hg or the presence of abnormal ICP waves. Neuropsychological assessment in these patients demonstrated poor performance on visual memory, visuoconstructive and frontal functions, and fine motor speed. Shunt surgery in this group of patients improved neuropsychological functioning. Significant improvements were obtained in verbal and visual memory, motor coordination, and attention and cognitive flexibility. The most significant gains were attained in a measure of frontal lobe functioning (trail making test part B) which assesses attention and cognitive flexibility (the ability to modify an ongoing activity or maintain two trains of thought at the same time). This test has been found to be very sensitive to brain damage and predictive of the functional outcome in terms of independent living in patients with head injury.

The neuropsychological improvement found after shunting was confirmed by the family members. In 11 patients (47.8%) two or more tests that were impaired in the presurgical assessment achieved normal scores after treatment. Although in two patients (8.7%) two or more tests previously in the normal range were impaired after surgery, there was no evidence of a general cognitive worsening in either
patient. Individual analysis of these two patients did not disclose any reason for this result.

It is well known that early hydrocephalus produces neuropsychological deficits which are most evident in the visuospatial and motor domains. Our patients presented marked impairment in these areas, which were improved after shunt surgery. This finding highlights the need to distinguish between the chronic residual features of an arrested hydrocephalus and the cognitive deficits produced by persistent alterations in ICP. At present, the understanding of the mechanisms by which abnormal ICP affects cognition is very limited. Several studies have reported impaired cerebral metabolism, reduced concentration of neurotransmitters and peptide neuromodulators, and parenchymal cellular damage related to raised ICP. These alterations, which seem to result from mechanical stresses and impaired cerebral blood flow, reflect neuronal dysfunction and may explain part of the cognitive deficits presented by these patients and their recovery after normalization of ICP. In our sample, comparison of patients with active versus compensated hydrocephalus was not significant, although the active hydrocephalus group showed a trend towards poorer performance in neuropsychological tests. More studies are required to understand the pathophysiology of hydrocephalus and resolve many important questions regarding the diagnosis and management of these patients. On the other hand, an interesting finding was the association between the magnitude of the ventricular dilation and verbal and visual memory. Larger ventricles were associated with worse performance on certain verbal and visual memory tests and less improvement after surgery in a cued recall task.

Diagnosis of an arrested hydrocephalus is often difficult and can be regarded doubtful without an objective testing of CSF dynamics or ICP monitoring. Hydrocephalus is considered arrested when CSF production equals absorption, intraventricular pressure has returned to normal, and there is no abnormal increase in head circumference or progressive neurological dysfunction. As patients with raised ICP may be asymptomatic or may present variable, unusual, and unreliable clinical symptoms, it is potentially difficult to distinguish a covert disorder of the ICP from an arrested hydrocephalus. We agree with the authors who have indicated that non-progressive neurological symptoms cannot be regarded as sufficient criteria for the diagnosis of an arrested state of hydrocephalus, and that direct measurement of ICP and a comprehensive baseline neuropsychological assessment with longitudinal evaluation are the only ways to establish its presence.

To our knowledge this is the first study of the cognitive effects of shunt surgery in a group of young adult patients with congenital ventriculomegaly and assumed arrested hydrocephalus. The decision to implant a shunt or to change a non-functioning valve is often difficult because it may lead to complications and is sometimes based on subjective criteria. None of our patients exhibited significant surgical complications, probably due to the improvements in valve design and to our procedure for avoiding shunt complications, which includes individual selection of the appropriate valve in each case. Many complications of shunts are a consequence of negative intraventricular pressures which lead to overdrafting complications (postural hypotension and subdural hematomas among others). The antisiphon device has been reported to reduce the risk of these complications, and so in the last period of the study we used a valve with this device. With this surgical management, the decision to shunt patients with abnormal ICP is probably the treatment of choice to improve cognitive status and quality of life, even in the absence of overt clinical signs of increased ICP. Shunt surgery in this group of patients will probably halt or delay the progression of the disorder, prevent long standing cognitive deficits which are more difficult to reverse with time, or prevent potential late decompensations.

Today, neither clinical nor radiological examinations can conclusively diagnose an arrested hydrocephalus. In the absence of a less invasive technique, epidural ICP monitoring is at present considered the gold standard of the hydrocephalic condition. In the light of these positive results in a group of young adult patients, this report is particularly relevant for children with hydrocephalus. The greater plasticity of the young brain and the importance of infancy and childhood periods with regard to brain maturation and intellectual development are well known. Therefore, patients with hydrocephalus and suspected non-functioning shunt or non-shunted ventriculomegaly should always be carefully monitored to identify those who could benefit from shunting. Improved cognitive functions will probably lead to clinical, educational, and social benefits. In terms of day to day functioning, better alertness, memory capabilities, cognitive flexibility, and psychomotor speed may help to achieve better educational and vocational opportunities, improve their personal relations and gain greater personal independence. All this may lead to higher levels of self confidence and wellbeing. Taken together, it may constitute a dramatic improvement in their present and future quality of life.

This study was supported in part by Grants number 97/0923 and 99/0968 from the Fondo de Investigaciones Sanitarias de la Seguridad Social (FISS).

Cognitive improvement after shunting in assumed arrested hydrocephalus

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