Reversibility of functionally injured neurotransmitter systems with shunt placement in hydrocephalic rats: implications for intellectual impairment in hydrocephalus

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Intellectual impairment has been related to alteration of neuronal innervation in the following regions: cholinergic basal forebrain nuclei (Ch1–Ch6, learning and memory), dopaminergic ventral tegmental area (emotional control), and noradrenergic locus ceruleus (cognition). Recent studies have implicated neuronal injury in the pathogenesis of hydrocephalus.

**Object.** The authors used immunohistochemical techniques to investigate functional injury in these regions in animals with progressive hydrocephalus, following shunt placement for cerebrospinal fluid (CSF) drainage.

**Methods.** Hydrocephalus was induced in 20 Wistar rats by intracisternal injection of 0.05 ml of 25% kaolin solution. Four control animals (Group 1) received the same volume of saline. Ventriculoperitoneal shunts were inserted in eight rats at 2 and 4 weeks after kaolin injection and the animals were killed at 8 weeks (Group 2). The other 12 hydrocephalic animals were killed at 2, 4, and 8 weeks without undergoing shunt placement (Group 3). Immunoreactive (IR) neurons to choline acetyltransferase (ChAT) in Ch1–Ch6, tyrosine hydroxylase (TH) in the ventral tegmental area, and dopamine B-hydroxylase (DBH) in the locus ceruleus, as well as IR projection fibers in the terminal areas, were compared between groups. The number of ChAT- and TH-IR neurons in rats with and without shunt placement was counted for quantitative analysis. The number of ChAT-IR neurons was progressively reduced during the development of hydrocephalus in Ch1, Ch2, Ch3, and Ch4 (p < 0.05). Tyrosine-hydroxylase-immunoreactive neurons were also reduced in number, and demonstrated decreased projection fibers and terminals. Early shunting (at 2 weeks) restored ChAT and TH immunoreactivity to control levels, but late shunting (at 4 weeks) did not (p < 0.05). The DBH-IR neurons in the locus ceruleus were remarkably compressed by the dilated fourth ventricle, and diminished immunoreactivity was observed in the terminal areas. Shunt placement for CSF also restored the immunoreactivity in this system.

**Conclusions.** These findings indicate that a progressive functional injury occurs in the cholinergic, dopaminergic, and noradrenergic systems as a result of hydrocephalus. This may contribute to intellectual impairment and might be prevented by early treatment with shunt placement.

**Key Words** • acetylcholine • dopamine • noradrenaline • intellectual impairment • kaolin-induced hydrocephalus • cerebrospinal fluid shunting • rat

Although intellectual impairment is a common and important consequence of hydrocephalus, there is little information about its pathogenesis. Various studies have indicated that intellectual impairment is mediated in part by alteration of neuronal innervation: the cholinergic system from the basal forebrain nuclei (Ch1–Ch6) participates in learning and memory, the dopaminergic system from the ventral tegmental area and the medial part of the substantia nigra compacta participates in emotional control, and the noradrenergic system from the locus ceruleus and subceruleus is involved in cognition.

The cholinergic neurons uniquely contain acetylcholine as well as its synthetic enzyme, choline acetyltransferase (ChAT). Using an immunostain to ChAT, Mesulam, et al., designated six sectors (Ch1–Ch6) of cholinergic projection neurons in each innervation field in the rat brain. The Ch1 sector is contained within the medial septal nucleus and, with part of the Ch2 sector, provides major cholinergic projections to the hippocampus. The Ch2 and
Ch3 sectors are located mostly within the nuclei of the diagonal band and both provide major cholinergic innervation to the olfactory bulb. The Ch4 sector, the nucleus basalis magnocellularis in the rat, is considered to be homologous to the nucleus basalis of Meynert in primates and provides principal cholinergic innervation for the neocortex. The Ch5 and Ch6 sectors are situated in the upper brainstem, mostly within the nucleus of pontomesencephalic reticular formation (Ch5) and within the tegmental gray of the periventricular area (Ch6), providing a major cholinergic innervation of the thalamus and minor innervation of the neocortex. Tyrosine hydroxylase (TH), which catalyzes the first step in catecholamine biosynthesis, appears to be a unique constituent of dopaminergic neurons in the midbrain. The ventral tegmental area and medial substantia nigra compacta have been considered to be the main sites of origin of the mesocorticolimbic dopaminergic pathway, projecting to the nucleus accumbens, amygdaloïd complex, lateral septal nucleus, olfactory tubercle, olfactory bulb, and several cortical areas, mostly to the medial aspect of the hemisphere. Dopamine β-hydroxylase (DBH), working in the biosynthetic step from dopamine to noradrenaline, is a specific marker of noradrenergic systems using immunohistochemical techniques and to determine whether this functional injury is reversible with CSF shunt placement.

Materials and Methods

This research was approved by the Animal Care Committee of the University of Toronto.

Induction of Hydrocephalus and Experimental Design

Twenty adult male Wistar rats, each weighing between 200 and 280 g, were anesthetized with intraperitoneally administered chloride hydrate (28 mg/100 g body weight), and 0.05 ml of 25% kaolin solution (Sigma Chemical Co., St. Louis, MO) was manually injected into the cisterna magna with the aid of an operating microscope as described in our previous studies. The same volume of sterile saline was injected in a similar manner into four control rats (Group 1). The kaolin-injected animals were divided into groups with (Group 2, eight animals) and without shunts (Group 3, 12 animals) and these were further divided into five subgroups, each consisting of four animals: three subgroups consisting of rats without shunt placement killed at 2, 4, and 8 weeks; and two subgroups consisting of rats undergoing shunt placement at 2 and 4 weeks and killed at 8 weeks, as shown in Table 1.

Shunt Operation and Cortical Biopsy Sampling

A silicone–rubber catheter (outer diameter 1.65 mm, inner diameter 0.76 mm, 20 cm long without a valve) was used as a ventricular-peritoneal (VP) shunt in the rats. The animals were anesthetized with intraperitoneally administered chloride hydrate (35 mg/100 g body weight) and immobilized in a stereotactic frame with their body axis rotated to expose their upper abdominal wall. A body weight (and provides principal cholinergic innervation for the neocortex. The Ch5 and Ch6 sectors are situated in the upper brainstem, mostly within the nucleus of pontomesencephalic reticular formation (Ch5) and within the tegmental gray of the periventricular area (Ch6), providing a major cholinergic innervation of the thalamus and minor innervation of the neocortex. Tyrosine hydroxylase (TH), which catalyzes the first step in catecholamine biosynthesis, appears to be a unique constituent of dopaminergic neurons in the midbrain. The ventral tegmental area and medial substantia nigra compacta have been considered to be the main sites of origin of the mesocorticolimbic dopaminergic pathway, projecting to the nucleus accumbens, amygdaloïd complex, lateral septal nucleus, olfactory tubercle, olfactory bulb, and several cortical areas, mostly to the medial aspect of the hemisphere. Dopamine β-hydroxylase (DBH), working in the biosynthetic step from dopamine to noradrenaline, is a specific marker of noradrenergic neurons. Those neurons in the locus ceruleus provide the innervation of the neocortex, hippocampus, amygdaloïd complex, and cerebellum.

Our purpose was to evaluate carefully the effect of progressive hydrocephalus on the cholinergic, dopaminergic, and noradrenergic systems using immunohistochemical techniques and to determine whether this functional injury is reversible with CSF shunt placement.

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<table>
<thead>
<tr>
<th>Subgroup</th>
<th>W/O or Preshunt</th>
<th>Postshunt</th>
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<tbody>
<tr>
<td>control</td>
<td>3.000 ± 0.041</td>
<td>NA</td>
</tr>
<tr>
<td>killed at 2 wks</td>
<td>1.788 ± 0.033</td>
<td>NA</td>
</tr>
<tr>
<td>killed at 4 wks</td>
<td>1.413 ± 0.156</td>
<td>NA</td>
</tr>
<tr>
<td>killed at 8 wks</td>
<td>1.125 ± 0.060</td>
<td>NA</td>
</tr>
<tr>
<td>VP shunt at 2 wks &amp; killed at 8 wks</td>
<td>2.025 ± 0.085</td>
<td>2.525 ± 0.095</td>
</tr>
<tr>
<td>VP shunt at 4 wks &amp; killed at 8 wks</td>
<td>1.725 ± 0.155</td>
<td>2.175 ± 0.085</td>
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* Values are expressed as the mean ± standard deviation. Abbreviation: NA = not applicable.
† Statistically different from control value (p < 0.05).
‡ Statistically different from the value in animals killed at 8 weeks without undergoing shunt placement (p < 0.05).

lateral ventricle. The distal end was passed beneath the subcutaneous space of the neck, shoulder, axilla, and abdomen to be inserted 5 to 7 cm into the peritoneal cavity. The VP shunt was fastened at the upper and lower ends by suturing it to the subcutaneous tissue.

Immunohistochemical Staining

The experimental (including the animals killed at 2 and 4 weeks) and control animals were deeply anesthetized with intraperitoneally administered chloride hydrate (42 mg/100 g body weight), and then they were killed by transcardial perfusion in which 0.9% saline (50 ml/100 g body weight) followed by 7% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4, 100 ml/100 g body weight) was used. Their brains were removed and immersed overnight in phosphate-buffered solution containing 20% sucrose. Serial sections were cut coronally at a thickness of 60 μm on a freezing microtome and delivered in sequence into four vials. Three of the divided sections were immunostained for ChAT (polyclonal/rabbit AB-143, diluted 1:5000; Chemicon International, Inc., Temecula, CA), TH (monoclonal/mouse 22941, diluted 1:5000; Incastar Corp., Stillwater, MN), and DBH (polyclonal/rabbit AB-145, diluted 1:5000; Chemicon International) according to the avidin–biotin complex method as described previously.

Confirmation of Shunt Effect

The core of the frontal cortex, which had been removed during the shunt placement, was cut into vertical sections at a thickness of 60 μm. These sections and those from the opposite side of the cortex taken at the same level of section after shunt placement were immunostained for calbindin D28K (CaBP) (monoclonal/mouse 300, diluted 1:5000; Swant, Bellinzona, Switzerland) to compare immunoreactivity before and after shunt placement in the same rat. The thickness of these bilateral cortices was also measured from the cortical surface to the outer ventricular wall to verify the shunt effect morphologically.

Nissl Staining and Quantitative Analysis

The serial sections were taken from another vial and consecutively mounted on gelatin-coated slides, then stained with cresyl violet for a counterstain against immunostaining.

With the aid of microscopy, the numbers of ChAT-immunoreactive (IR) neurons in the Ch1–Ch6 sectors of the treated and control animals were counted on the representative sections, which contained the sectors and landmarks shown in Fig. 1. The numbers of TH-IR neurons in the ventral tegmental area and the medial part of the substantia nigra compacta (demarcated at the lateral end of the medial lemniscus) were similarly counted at the level of a section containing the fasciculus retroflexus and accessory optic tract.
Counts in the different regions were subjected to analysis of variance with Bonferroni correction for multiple comparisons.

**Results**

**Animal Model of Hydrocephalus With and Without VP Shunts**

After kaolin injection, the animals showed neurological impairment for the first several days; poor activity with sluggish movement and abnormal limb positioning. Behavioral effects including indifference and delayed response to external stimuli persisted longer, but generally had resolved by the end of the 2nd week. The animals in Group 3 showed transient loss of appetite, which resulted in significant weight loss (14%) at 2 weeks after kaolin injection, and at 4 weeks (8.7%), compared with Group 1 (p < 0.05). However, at 8 weeks there were no significant differences in body weight among the three groups (p > 0.05). The animals in Group 3 developed variable but progressive ventricular enlargement.

Those in Group 2 were restored to normal activity and weight development a few days after shunt placement.

** Confirmation of Shunt Effect**

The animals in Group 3 demonstrated a progressive reduction in the CaBP immunoreactivity of the frontal cortex relative to the ventricular enlargement, as reported in our previous study. All animals that underwent shunt placement exhibited dramatic recovery of the CaBP immunoreactivity of the cortex posttreatment except for one in which a shunt was inserted at 4 weeks. The reduction of ventricular size was more pronounced in the animals undergoing shunt placement at 2 weeks than at 4 weeks, and the caliber of the frontal cortex in the group receiving shunts was significantly greater than in animals without shunt placement that were killed at 8 weeks (p < 0.05) (Table 1).

**Immunohistochemical Changes of Cholinergic Neurons**

In Group 1, the Ch1 sector contained relatively smaller cholinergic neurons that projected many longitudinal fibers to the hippocampus via the fimbria–fornix (Fig. 2A). The Ch2–Ch3 sectors consisted of ChA T-IR neurons that demonstrated considerable variations in their size and density. The Ch4 sector contained a broad group of large and multipolar cholinergic neurons with abundant axonal fibers (Fig. 2D). The Ch5–Ch6 sectors were in partial continuity with each other in the upper brainstem, but the characteristic shapes of constituent neurons could be distinguished; Ch5 contained generally elongated and angular cell bodies, whereas Ch6 neurons were more radial and symmetrical.

With the progression of hydrocephalus, the ChAT-IR neurons in all sectors were flattened by compression, concomitant with the disappearance of their axonal fibers and reduction in their neuronal number. In the case of very large lateral ventricles, the ChAT-IR axonal fibers at the junction of the fimbria–fornix were compressed into a fine tract and ultimately disrupted. Simultaneously, Ch1 and the dorsal part of Ch2 neurons were remarkably reduced in number, becoming pyknotic degenerated neurons (Fig. 2B). In the Ch4 sector, the prominent processes of ChAT-IR multipolar neurons progressively diminished in number at 4 weeks and the large cell bodies diminished in size at 8 weeks (Fig. 2E).
The animals in Group 2 revealed some restoration in the number, size, and axon fibers of ChAT-IR neurons (Fig. 2C and F), which was greater in the animals that underwent shunt placement at 2 weeks than at 4 weeks.

**Immunohistochemical Changes of Dopaminergic Neurons**

In Group 1, the ventral tegmental area contained a wide variety of dopaminergic neurons with abundant axons terminating in the limbic system and cerebral cortex; small neurons in the interfascicular nucleus, small-to-medium fusiform neurons in the parabrachial pigmented nucleus, and medium-to-large trigonal neurons in the paranigral nucleus as well as in the medial substantia nigra compacta (Fig. 3A). Tyrosine hydroxylase immunoreactivity was progressively decreased in the axonal/dendritic field of the ventral tegmental area and medial substantia nigra compacta at 4 weeks (Fig. 3B) with further demonstrable reduction in neuronal size and number at 8 weeks (Fig. 3C). The animals with severe cases of hydrocephalus showed diminished TH immunoreactivity in projection fibers of the terminal areas in the pathway (Fig. 4A and B).

The animals in Group 2 demonstrated restoration of TH immunoreactivity in dopaminergic neurons and the axonal/dendritic field of the ventral tegmental area and medial substantia nigra compacta, and in projection fibers of the terminal areas. The recovery of immunoreactivity in the terminal areas was better in the animals that underwent shunt placement at 2 weeks than at 4 weeks.

**Immunohistochemical Changes of Noradrenergic Neurons**

In the Group 1 animals, relatively large and oval DBH-
IR neurons were clearly observed in the ventral locus ceruleus and subceruleus, whereas DBH-IR fibers covered the dorsal locus ceruleus so densely as to make it impossible to distinguish the neurons for a quantitative analysis. Dense and fine axonal fibers running on the edge of the fourth ventricle were directed dorsally to the cerebellum via the superior peduncle and ventromedially to the forebrain via the dorsal noradrenergic bundle (Fig. 5A).

The enlarged fourth ventricle compressed the locus ceruleus ventrolaterally, in which region deformed DBH-IR neurons revealed some enhancement of immunoreactivity with an increase in density and thickness of axonal fibers. In particular the DBH-IR neurons and fibers in the dorsal locus ceruleus coalesced into an arched strongly stained area (Fig. 5B and C). With the progression of hydrocephalus the aqueduct and fourth ventricle expanded remarkably, eventually disrupting the tegmentum dorsally and compressing the pons ventrally. In the most severe cases of hydrocephalus showing a crescent-shaped strongly stained area coalesced by deformed neurons and stretched fibers (arrowheads) and a small number of shrunken neurons (arrows). Bar = 200 µm.

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The numbers of Ch1 and Ch2 cholinergic neurons were progressively fewer at 4 and 8 weeks (p < 0.05), whereas those of Ch3 and Ch4 neurons were significantly reduced only at 8 weeks (p < 0.05). The numbers of Ch5 and Ch6 neurons were not significantly changed in the process of ventricular enlargement (p > 0.05). The numbers of ChAT-IR neurons were significantly increased in the animals that underwent shunt placement at 2 weeks, but at 4 weeks there was no significant increase of Ch1, Ch3, and Ch4 neurons (Fig. 6A–D). The numbers of TH-IR neurons in the ventral tegmental area and medial substantia nigra compacta were significantly decreased at 8 weeks (p < 0.05) and showed good restoration only in the animals that underwent shunt placement at 2 weeks (Fig. 7A and B).

Nissl Staining

Nissl staining revealed viable neurons with no degenerative changes in the animals that underwent shunt placement at 2 weeks and in those killed at 2 and 4 weeks without undergoing shunt placement, as shown in our previous paper.40 However, the animals with severe hydrocephalus without shunt placement that were killed at 8 weeks demonstrated remarkably flattened neurons with loss of staining and reduction in number (Fig. 8A and B). One rat in the group that underwent shunt placement at 4 weeks displayed some vacuolated neurons in the medial septal nucleus (Ch1 sector) (Fig. 8C).

Discussion

The salient finding of this study is that a progressive functional injury occurs with the development of hydrocephalus in the cholinergic, dopaminergic, and noradren-
There are a few reports of clinical cases although motor disabilities and regrowth of injured cerebral. Similar to Alzheimer's disease, which is characterized by atrophy or degeneration in this area, loss of memory occurs, especially for recent events. It is interesting to speculate that the dementia of normal-pressure hydrocephalus, and possibly the intellectual impairment of infantile hydrocephalus, may be related to pathological changes in this area. The projection from Ch4 accounts for 70 to 80% of cortical cholinergic innervation. Miyajima, et al., reported that ChAT activity of the parietooccipital cortex was significantly decreased, whereas the nerve growth factor concentration of that cortex increased in a compensatory manner in 3-week-old hydrocephalic HTx rats. These results may coincide with our findings of immunohistochemical consequences of loss of ChAT immunoreactivity in the Ch4 sector, with subsequent functional injury of its axonal components.

**Cholinergic System**

The septal–hippocampal pathway consists of the cholinergic projection fibers from the medial septal nucleus and part of the vertical limb nucleus of the diagonal band of Broca to the hippocampus via the fimbria–fornix. Lesions of the medial septal nucleus or fimbria–fornix have been reported to induce learning disability, especially in spatial working memory tasks, because this system is selectively involved in cognitive mapping. The number of neurons in Ch1 and Ch2 sectors is significantly reduced after short-term hydrocephalus (4 weeks). The intraventricular location of the fimbria–fornix and the septum may make this pathway anatomically vulnerable at an early stage. Our results indicate that the functional injury could occur earlier than the structural disruption and might extend toward the original neurons retrogradely, dependent on neuronal vulnerability and probably axonal length.

The Ch4 sector (nucleus basalis magnocellularis) provides cholinergic innervation mainly to the neocortex and additionally to the amygdala complex and thalamus. Admittedly, the behavioral effects of lesions in the nucleus basalis magnocellularis are variable, but in general, rats with lesions in the nucleus basalis magnocellularis have been reported to exhibit selective impairment in acquisition of temporal memory, discrimination, and habituation. Similar to Alzheimer’s disease, which is characterized by atrophy or degeneration in this area, loss of memory occurs, especially for recent events. It is interesting to speculate that the dementia of normal-pressure hydrocephalus, and possibly the intellectual impairment of infantile hydrocephalus, may be related to pathological changes in this area. The projection from Ch4 accounts for 70 to 80% of cortical cholinergic innervation. Miyajima, et al., reported that ChAT activity of the parietooccipital cortex was significantly decreased, whereas the nerve growth factor concentration of that cortex increased in a compensatory manner in 3-week-old hydrocephalic HTx rats. These results may coincide with our findings of immunohistochemical consequences of loss of ChAT immunoreactivity in the Ch4 sector, with subsequent functional injury of its axonal components.

**Dopaminergic System**

The mesocorticolimbic dopaminergic pathway has been implicated in incentive motivational learning, emotional processing, selective attention, sensorimotor integration, and goal-directed behavior. Although motor disabilities may be characterized as an initial and prominent symptom caused by impairment of the dopaminergic system in hydrocephalus, there are a few reports of clinical cases in which these disabilities are combined with akinetic mutism, which is likely caused by impairment of the mesocorticolimbic pathway.

The concentration of dopamine and its metabolites (homovanillic acid and 3,4-dihydroxyphenylacetic acid) in hydrocephalus has been reported to be irregularly increased or decreased in the terminal areas, whereas the TH immunoreactivity of these areas in our study was uniformly decreased considerably with the development of hydrocephalus. We also demonstrated a significant decrease in the number of the dopaminergic neurons at 8 weeks after kaolin injection, whereas Miwa, et al., measured no change of dopamine levels in the midbrain within 4 weeks. It may take longer to affect the change of mesencephalic neurons by retrograde axonal dysfunction through this pathway.

**Noradrenergic System**

The noradrenergic neurons in the locus ceruleus have been implicated in a broad range of brain activities. Among their higher functions, the main role of these neurons is defined as cognition, attentiveness, and behavioral discrimination. The dorsal noradrenergic bundle has been purported to play a role in postnatal development of the cerebral cortex and regrowth of injured cerebral.

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**Fig. 6.** Graphs revealing the change in the number of ChAT-IR neurons in the unilateral Ch1–Ch4 sectors. Values reflect the average of number of ChAT-IR neurons at 0, 2, 4, and 8 weeks and their standard deviations (vertical bars) in Group 3 (nonsunted) and Group 2 (shunted) animals. Asterisks denote values that are statistically different from the control value (p < 0.05).
Functional reversibility in shunt-treated hydrocephalus

Functional injury of this pathway could cause intellectual impairment with reduced attentiveness, or possibly maldevelopment during the neonatal period. Decreased noradrenaline levels in the neocortex in experimental hydrocephalus and recovery after shunting have been reported. Increased noradrenaline levels in the brainstem and the appearance of swollen cholinergic neurons in the locus ceruleus indicate the possible accumulation of noradrenaline in the neurons of the locus ceruleus in hydrocephalic animals. Our results, which showed an increased density and thickness of DBH-IR axonal fibers around the locus ceruleus with a loss of these fibers in the terminal areas, also indicate dense accumulation of noradrenaline in the locus ceruleus with impairment of axoplasmic flow of the chemical. More detailed investigation with specific anterograde tracers will be necessary to clarify the changes in this pathway.

Reversibility With Shunt Placement

There have been several reports of animal models in which hydrocephalus was treated using VP shunts. The body weight and growth rate data recorded after shunt placement are very similar to those presented in this report. The response in activity levels to shunt insertion

![Graphs illustrating the change in the numbers of TH-IR neurons in the unilateral ventral segmental area (VTA) and medial part of the substantia nigra compacta (med. SNC). Values reflect the average number of TH-IR neurons at 0, 2, 4, and 8 weeks and their standard deviations (vertical bars) in Group 3 (nonshunted) and Group 2 (shunted) animals. Asterisks denote values that are statistically different from the control value (p < 0.05).]

![Photomicrographs showing changes in Nissl staining in the medial septal nucleus. A: Tissue section from a control animal revealing many round and strongly stained neurons projecting their axons to the fornix–fimbria. B: Tissue from a rat with a severe case of hydrocephalus demonstrating extremely compressed neurons (arrowheads) with remarkable loss in number as well as in staining density. C: Tissue section displaying a few vacuolated neurons surrounded by morphologically normal neurons in a rat in the subgroup that underwent shunt placement at 4 weeks and was killed at 8 weeks. Bar = 100 μm.](B)
was also as rapid as in the animals in our study that underwent shunt placement. However, in our series there was one exception, in an animal that underwent shunt insertion at 4 weeks and whose hindlimb weakness and spasticity worsened after shunt placement. This animal had been proven to have some degenerative neurons on Nissl staining. This is probably one model example of irreversible neuronal damage in hydrocephalus treated with delayed shunt placement.

Our data demonstrate that early shunt placement (at 2 weeks) is better than late shunt placement (at 4 weeks) in reversing functional and behavioral deficits. Other investigators have shown that delayed shunt installation results in increased injury to the periventricular white matter and in reduced noradrenaline levels in the cerebral cortex.12,14,30,38,45 In patients treated with shunt placement for posthemorrhagic hydrocephalus, it has been reported in several studies that poor neurological development is correlated with an increased interval between the diagnosis of hydrocephalus and shunt installation.6,11 These results indicate that the timing of CSF shunt placement could determine the prognosis of patients with hydrocephalus. However, some patients with normal-pressure hydrocephalus demonstrate rapid improvement from longstanding dementia after shunt installation. This impressive recovery can only be explained by reversal of functional cessation and/or injury of some neuronal systems related to intellectual ability. Although the recovery could not be fully elucidated in our experimental model, this fact suggests that functional impairment may be longstanding and at least partially reversible in some cases of chronic hydrocephalus. Further study of neonatal and infant models of hydrocephalus would illustrate to what extent similar mechanisms are operative in younger age groups.

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References

Functional reversibility in shunt-treated hydrocephalus


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