Cerebellar stimulation for cerebral palsy

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Eight children with cerebral palsy, who had implanted cerebellar stimulators, were evaluated by a panel of six experienced physicians in a double-blind cross-over experiment with 3-week periods of real and sham stimulation. Neither the panel of physicians nor the patients could tell whether the stimulators were operating or not.

KEY WORDS • cerebellum • cerebral palsy • implanted stimulator

Cerebellar stimulation has held out the hope of releasing latent capacities of spastic and athetotic children.1,2,3 Because spasticity varies so much with effort, anxiety, rest, or distraction, the effect of cerebellar stimulation on cerebral palsy is difficult to measure.5,6 The method of videotaping before and after cerebellar stimulation proved inconclusive. Patients and family members sometimes reported that there was marked improvement in function when the stimulating apparatus was not even working. This double-blind study was therefore devised to control the placebo effect.

Clinical Material and Methods

Patient Population

Initially, only two criteria were required for a cerebellar stimulator implantation to be offered to a patient with cerebral palsy: the patient was required to be pathologically hyperreflexic, and the patient's family had to understand the possible advantages and disadvantages of the proposed procedure. The patient and family were told that the procedure was experimental, that there were risks which were then detailed precisely, and that the goal of the study was to determine whether cerebellar stimulation could actually affect spasticity or not. Then the procedure was discussed in detail, often at more than one meeting. Later, severe mental impairment was added as a criterion for rejection. Many patients were rejected. Some patients declined the procedure after a full explanation.

A total of 17 patients had cerebellar stimulators implanted. All patients underwent neurological examination and were found to be hyperreflexic; many had Babinski signs, and some had athetosis. All had increased muscular tone, but from the beginning it was believed that tone was an unreliable criterion of the effectiveness of the stimulator because of previous orthopedic tenotomies, muscle transplants, and arthrodeses, and some naturally occurring fibrosis of joints. Most patients were in school, but some were adults. After all 17 patients had been using their stimulators for at least 5 months, they were all invited to participate in the double-blind study to be described. For various reasons, only eight patients agreed to participate in this double-blind study. In the total group of 17 there were five males and 12 females, but in the test group there were two males and six females. Of the test group, two were ambulatory, two could walk with the aid of crutches, and four were in wheelchairs. Their ages were 3, 8, 9, 12, 15, 17, 18, and 18 years; the 3-year-old is the youngest reported child with a cerebellar stimulator. The cause of spasticity was thought to be prematurity in four, trauma in one, and unknown in three. Total time of cerebellar stimulation before this study ranged from 5 to 23 months: 5, 13, 16, 16, 16, 17, 19, and 23 months.

A brief clinical description of the eight patients included in the study follows.

Case 1. This 9-year-old only daughter was normal until she was involved in an auto accident at age 9½ months. She was unconscious, and suffered convulsions for 2 weeks. She underwent heel-cord lengthening at age 5 years, which helped only briefly. At acceptance into the study she was totally dependent; she could feed herself a little, but could not dress herself, handle her toilet, or run her own wheelchair.
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She could count to five; she underwent two recent eye operations for squint. Her head circumference was at the second percentile. She wore cockup braces on both wrists; she had severe hyperreflexia but no Babinski signs and no athetosis. Phenobarbital, 30 mg, was administered daily for seizures.

Case 2. This 17-year-old only son was delivered prematurely; his birth weight was 3 lb. He spent his first month in the hospital. At the age of 5 years, he underwent adductor tenotomy, which was repeated at age 7 years. He had alternating exotropia. His talking and intellect were normal, but he could not hold a pencil until third grade. At acceptance into the study, he used a powered wheelchair. He was an honor student in high school, with a scholarship to college. He needed help with his pants, shoes, and socks, and his toilet, but could feed himself. He could not supinate his forearm or tap his toes. There was severe hyperreflexia with bilateral Babinski reflexes. His vision was 20/20 bilaterally, and his speech was normal.

Case 3. This 17-year-old girl was a high-school senior and the eldest of three children. The mother had toxemia of pregnancy, and delivered at 7 months. The patient’s birth weight was 3 lb 6 oz. She sat at 1 year, walked alone at 2½ years, and has always talked normally. She underwent heel-cord lengthening at 2½ years of age, and a hamstring section later. Heel-cord lengthening was repeated when she was 7 years old; adductor tenotomy was performed at 10 years of age and was repeated 3 years later. At admission to the study she could drive a car with her right foot only; she had no athetosis. She was an “over-achiever,” could type, play the piano, and was teaching 13 students. She had marked hyperreflexia in her arms and legs with a right Babinski sign.

Case 4. This 8½-year-old girl was the eldest of four children, the result of a premature delivery. Her birth weight was 2 lb 13 oz, and she was sustained in an incubator for 8 weeks. She underwent obturator and iliopsoas operations at 3 years old and eye surgery at 5 years old. At entry into the study she spent most of her time in a wheelchair; she could not walk, but at home crawled with her arms. She could not dress or handle her toilet, but could feed herself. She had thick speech, and drooled. Hand patting was extremely slow and toe tapping impossible. She had hyperreflexia with bilateral Babinski signs.

Case 5. This 15-year-old boy was the third of three children, born after a normal pregnancy and delivery. His birth weight was 9 lb 4 oz. He sat alone at 1 year, and used his arms to crawl. He talked at 7 years, and was toilet trained at 3 years. He underwent a hamstring operation at 3 years old, and a foot operation and pelvic “release” at 6 years of age. At entry into the study, he used Canadian crutches, could dress and feed himself, and could handle his toilet. His speech was slow, and he did not know the alphabet. He had no athetosis or seizures. He walked with a scissors gait, with severe hyperreflexia in his legs. The somatosensory evoked responses were unchanged by 15 minutes of cerebellar stimulation.

Case 6. This 18-year-old left-handed high-school senior was the younger of two children. She was the result of a normal pregnancy and delivery, but twitching was noted in the nursery. She developed slowly. A ventriculogram at 1 year old was abnormal on the left. Hamstring and heel-cord surgery was performed when she was 9 years old. She had high average grades in a normal school. At admission to the study she used a wheelchair, but could not manage a walker or crutches because of weakness in her right hand. She dressed herself slowly, fed herself with meat cut, and handled her toilet. She had regular menses. There were involuntary movements of the right leg, hyperreflexia, especially on the right, with a right Babinski sign and ocular overshoot. She was overweight.

Case 7. This girl, aged 2 years 11 months, was adopted. Her mother was possibly malnourished in pregnancy. The patient was bright mentally; she talked early, saying full sentences at age 1½ years; she was toilet trained at 19 months. She had casts for club feet at 12 weeks. At admission to the study, she could not walk unassisted more than 10 to 15 feet and rarely tried to walk, apparently because she fell. When she did walk, it was with a stiff gait on tip-toes. She usually scooted or crawled. Her arms were normal, but she had increased tone and reflexes in her legs and normal weight.

Case 8. This 12-year-old girl was the eldest of her family. She was born in Holland with a birth weight of 4 lb. She was toilet trained at age 6 years, and started school at 9 years old. She underwent bilateral adductor tenotomies, bilateral hamstring sections, and bilateral heel-cord lengthenings at 10 years old, and a phenol block of a nerve in her left arm at age 12 years. At admission to the study she had understandable speech; she could read at the level of an 8-year-old, and write at the level of a 6-year-old. She could walk very slowly with a walker, but used a wheelchair. She could not use her left hand, and patted slowly with her right hand. She had extremely hyperactive reflexes with bilateral sustained ankle clonus and sustained patellar clonus on the right. She could not keep her eyes closed.

The Stimulator

A battery-powered radiofrequency generator supplied capacitatively-coupled pulses of 250-μsec pulse width at 100 Hz. A battery-powered radiofrequency generator supplied capacitatively-coupled pulses of 250-μsec pulse width at 100 Hz. Current was measured at the level of 8 volts.* Current was not measured. The external, un-
sterile sending antenna consisted of a simple coil of wire. The receiving antenna and electronic devices were encased in Silastic and sterilized for implantation subcutaneously. A long piece of multistrand wire connected the receiving antenna to 2-mm platinum electrodes, five-in-line, 4 mm on center. Electrodes 1, 3, and 5 were positive, and electrodes 2 and 4 were negative (Fig. 1). One patient had specially fabricated platinum strips with 20 contacts (negative) on the superior surface of the cerebellum, and 12 contacts (positive) on the posterior surface; another patient had the regular five-in-line electrodes over the superior (negative) and the posterior (positive) cerebellar surfaces. Power transmission is not affected by eccentric placement of the large sending antenna until the center of the small receiving antenna is outside the circle of the sending antenna. This allows considerable latitude for acceptance of the sending antenna on the skin.

A specially constructed testing apparatus measured power transmission in volts, pulse width, and pulse frequency at a plane parallel to and 1.0 to 1.5 cm from the plane of the patient's sending antenna. Pulse width was adjusted to 250 μsec and pulse frequency to 100 Hz. New batteries were used about every 5 days.

Surgical Procedure

For the surgical implantation, general endotracheal anesthesia with hyperventilation was always used. The patient was positioned on one side, so that a bilateral suboccipital craniectomy could be done just below the lateral sinus, allowing placement of the arrays of electrodes under the tentorium. The receiving antenna was placed over the chest on the side opposite the better hand. Electrodes were tunneled from the chest wound to the suboccipital wound by means of a specially designed instrument. Preoperative and intraoperative methicillin was given in all cases and continued postoperatively for 1 or 2 days.

There were no infections in any of the 17 patients. In one patient, subcutaneous accumulation of spinal fluid persisted long enough (2 weeks) to prevent hospital discharge at the expected time. Two patients later had broken wires; an unsuccessful attempt to splice the wires was made in one patient; these cases will not be discussed further because the patients with broken wires were not in the double-blind study. There were no other complications.

The Experimental Protocol

All eight patients included in the study and their families were thoroughly advised of the experimental nature of the double-blind procedure, and all consented to it. Most patients were enthusiastic in their participation, considering it an adventure in medical progress.

The pulse generators and sending antennas were taken away for 1 week from the eight patients. No stimulation was allowed during this week. The stimulators and antennas were checked to be sure that the pulses were being generated correctly. Numbered and color-coded sets of plastic patches† were made in such a way that one color in each set contained a hidden piece of aluminum foil, sufficient to prevent transmission of power from the sending antenna to the implanted receiving antenna. The code as to which color contained the aluminum foil was kept secret at the Clinical Technology Corporation until the completion of the full experimental protocol. The first 3-week period then proceeded with stimulation as previously.

†Plastic patches supplied by the Clinical Technology Corp., Kansas City, Missouri.
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TABLE 1
Opinions of examiners testing function in eight spastic patients*

<table>
<thead>
<tr>
<th>Examiners</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
<th>Case 7</th>
<th>Case 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. K.</td>
<td>+</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>L. M.</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>—</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>—</td>
</tr>
</tbody>
</table>

*Double-blind comparison of 3-week periods with and without cerebellar stimulation. + = power on better; — = power off better; = no difference.

The blinking light of the portable battery-powered generator indicated the stimulation was on, but, of course, the patients and families all knew the possibility that stimulation was being blocked by the patch that was now worn at all times. At the end of the 3-week period, on one day, all patients were evaluated by the panel of six experienced physicians. Objective testing was stressed, especially in activities of daily living. Records were kept, and these records were made available to the panel of physicians at the end of the second evaluation.

After completion of the first evaluation, the stimulators and sending antennas were again collected, kept for 1 week so that there was no stimulation for another 1-week period, and thoroughly checked. At the end of this week of no stimulation, the stimulators and antennas were returned to the patients with the opposite color of the numbered set of plastic patches. In all instances the opposite patch either did or did not contain the aluminum foil, exactly opposite to the first patch. (Consideration was given to double testing the placebo effect by using aluminum foil for more than one 3-week period of stimulation, but it was thought that this would unnecessarily prolong the experiment.) Stimulation again proceeded as before for a 3-week period, and then the same panel of six physicians reevaluated all eight patients on one day at the end of this second 3-week period of stimulation. The crucial question asked of the panel members was whether the patient's performance was better after the first 3-week period or after the second 3-week period.

The results were then tabulated after the code had been broken. All panel members and all the patients and their families were made aware of the results. As far as possible, nothing else but the patch was changed during the protocol. For example, if the patient was going to school or was receiving physical therapy, this was continued throughout.

The Evaluating Panel

Panel members were Charles A. Clough, M.D., David Francisco, M.D., Charles Kelly, M.D., Lana Minningerode, M.D., Edward Novak, M.D., and the author. Dr. Francisco is an orthopedist; Drs. Kelly, Minningerode, and Novak are physiatrists; and Dr. Clough and the author are neurosurgeons.

The methods of examination varied from examiner to examiner. It was hoped that the results of this double-blind study would be applicable to clinical medicine generally, and therefore no strictures were applied to the methods of evaluation, but all examiners were urged to be objective. For example, the author used only measured or timed tests of performance, such as, walking as far as possible in a specific time, clicking a hemocytometer as rapidly as possible for a measured time, and catching a falling yardstick placed next to the open hand.

Questionnaire for Patients and Families

Although the emphasis in this report is on the opinions of experienced physicians, the opinions of all eight patients and their families were also obtained by questionnaire. A questionnaire was filled out at the end of each 3-week period, before the double-blind code was broken at the end of the experiment. Thus, the opinions of the patients and their families were also blinded. The first questionnaire dealt primarily with an opinion concerning the function during the first 3-week period as compared with the prior stimulation before the protocol started; the second questionnaire asked for a comparison between each 3-week period of stimulation (the same question posed to the panel).

Results

Tables 1 and 2 summarize the results. Not a single patient was thought by more than 50% of the ex-

TABLE 2
Summary of examiners' opinions*

<table>
<thead>
<tr>
<th>Examiners</th>
<th>Power on Better</th>
<th>Power off Better</th>
<th>No Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. F.</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>E. N.</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>C. K.</td>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>L. M.</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>C. C.</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>K. W.</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

*See Table 1.
The examiner (L.M.) who seemed to sense better function when the power was on was wrong on two occasions and could not tell on one occasion, but estimated that performance was better with the power on in five out of eight patients. The next "best" examiner (C.K.), however, was wrong on four patients and could not tell on one, estimating that performance was better with power on in only three out of eight patients. All the other examiners had vastly less success in finding any real difference.

Careful inspection of the results for each individual patient (Table 3) shows that Case 1 had three positives, but also three opinions of no difference. Case 5 had an array of platinum disc electrodes (negative) over the superior surface and a separate array (positive) over the posterior surface; Case 6 had platinum strip electrodes with 20 (negative) contacts over the superior surface and 12 (positive) contacts over the posterior surface of the cerebellum; neither of these two patients with electrode arrays designed to stimulate a larger mass of cerebellar tissue seemed to perform any better than the patients with electrodes solely on the superior surface of the cerebellum (where current density and effective stimulation are very superficial). The overall results of the study showed that in 25 instances the opinion was that there was no detectable difference; in 12 instances the opinion was that the patient performed better when the power was on; and in 11 instances the opinion was that the patient performed better when the power was off. Table 4 gives the results of the questionnaire.

Discussion

The overall results seem to show that it is very difficult to detect any difference at all due to cerebellar stimulation (25 opinions of no detectable difference), and, when a difference is detected, chance alone seems to explain the difference (12 opinions "for" and 11 opinions "against").

The difficulty of the panel in telling any difference at all leads to the conclusion that there was no deleterious effect of cerebellar stimulation. Likewise, the conclusion is inescapable that no clinical efficacy was shown in this study of cerebellar stimulation. As to the patient's own opinion, chance again appears to operate. If one combines the two patients where no difference was noted with the two patients who thought they performed better when the power was off, these four patients exactly equal the four patients who thought their performance was better when the power was on (Table 4). Apparently the patients themselves and their families are no better able to detect an effect from cerebellar stimulation than the panel of experienced physicians. This study includes only eight patients, an admittedly small number.

The methods of evaluation employed in this study are used in an average office on an average patient by an experienced practicing physician. The lack of efficacy as shown by these methods does not disprove all effect of cerebellar stimulation on the spastic human; developing laboratory methods may still show some effect. However, even if some laboratory effect is eventually shown in an adequate double-blind study, clinical usefulness of cerebellar stimulation must remain unproved. Brief personal experience with the method of measuring the amplitude of the somatosensory cortical evoked potentials as affected by cerebellar stimulation has been a disappointment. The attempt by Upton and Cooper to use late waves after peripheral nerve stimulation may prove helpful, but such late waves have been notoriously capricious. Other methods (standing force-plate, resisted passive movement, torque measurements) are being developed.

This study does not confirm Cooper's claims. However, this author interprets Cooper's data to show no effect of cerebellar stimulation. The basis for dis-
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agreement, fundamentally, is whether one is allowed to discard the number of cases (always a majority in Cooper's statistics) where no change occurred with cerebellar stimulation in achieving a Z score with the Sign test. Cooper discards those with no change, and compares the number who are improved with the number who are worsened by cerebellar stimulation; he then concludes that cerebellar stimulation is effective, whereas the appropriate conclusion should be only that cerebellar stimulation does no harm. To conclude that cerebellar stimulation is effective, it is submitted, one should achieve this Z score by combining the number of cases where no detectable change was found with the number of cases thought to be worsened, and then by comparing that total number with the number thought to be improved. Such correct analysis of Cooper's data, then, does show his results to be comparable to this small study.

Cerebellar stimulation in the human remains experimental. It has not been shown to be effective treatment for spasticity when tested in a double-blind fashion.7

References
4. Larson SJ: Personal communication, 1978

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