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The Cerebellar Pacemaker for Intractable Behavioral Disorders and Epilepsy: Follow-Up Report[1]

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Thirty-eight patients who were intractably ill with a variety of behavioral disorders have been treated at Tulane with a chronically implanted cerebellar pacemaker. Included in the series are schizophrenics, depressives, epileptics with behavioral pathology, and patients with severe organic brain pathology. The patients who have responded best to the treatment are those with depression, those with behavioral pathology consequent to epilepsy, and those with psychotic behavior consequent to structural brain damage. Results obtained in the chronic schizophrenic patients have been less favorable. The follow-up period ranges from a few months to 27 months. Overall, the results continue to be encouraging. Twenty-one percent of the patient group displayed structural evidence of cerebellar pathology that was not detected before operation, a finding which suggests that cerebellar damage may induce psychotic behavior.

At the Society meeting a year ago, we gave a preliminary report on the first 11 patients in whom we had implanted a cerebellar pacemaker (Clinical Technology Corporation, Kansas City, Missouri) as treatment for intractable behavioral pathology (Heath, 1977). This series has now increased to 38 patients. Three of the 38 patients had second operations, making a total

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of 41 operations. The present report reviews the types of patients and the results obtained to date, describes modifications made in the procedure, and describes the principal problems we have encountered. We have elected to use anecdotal accounts, rather than tabulated data, because of the nature of the observations. Because the patients in this series were intractably ill, many being violent or potentially violent, and because we were bound by ethical considerations, it was not possible to plan controls for this therapeutic procedure. Some inadvertent controls which developed, due to mechanical problems with the apparatus, are considered in the Discussion.

On the basis of initial gratifying results, we applied the procedure to patients representing a wider variety of behavioral disorders. The requirements we initially established were maintained: (i) The patient had to have had a thorough trial with all other forms of treatment without beneficial results. (ii) Our staff had to agree with the patient's referring physician that all possible therapeutic approaches had been used and the patient's illness was indeed intractable.

METHODS

As a result of findings that evolved in laboratory work in our animal models (Heath *et al.*, 1978), we have introduced some modifications in techniques during the past year. These have included changes in electrode configuration, sites of electrode implantation, and parameters of stimulation. These modifications introduce variables in evaluating the results.

In 29 of our patients, cerebellar electrodes were placed only over the superior surface (Fig. 1). Current probes indicated that spread of effective stimulation with those electrodes was limited to 4 mm beyond the electrode sites (Sances *et al.*, 1977). Superior surface placements only were also used by Cooper *et al.* (1976) in the treatment of epilepsy and by Larson *et al.* (1977/78) and Davis *et al.* (1976) in the treatment of spasticity. Studies with our animal model (cat and rat) have demonstrated that stimulation of deeper underlying folia of the vermis, down to and including the fastigial nuclei, as well as over the vermis, activated cells of the septal region and focal sites of the amygdala (sites in the brain's pleasure system) while inhibiting unit activity in the hippocampus and focal sites in the amygdala (sites in the brain's adversive system) (Heath and Gallant, 1964; Heath, 1966, 1972, 1975; Heath *et al.*, 1974; Heath and Harper, 1976). In an attempt to stimulate as many as possible of the cerebellar cells capable of producing these effects on supratentorial structures, we modifed techniques to allow stimulation from the superior surface to the inferior surface of the vermis. On the superior surface, there were three chains of platinum

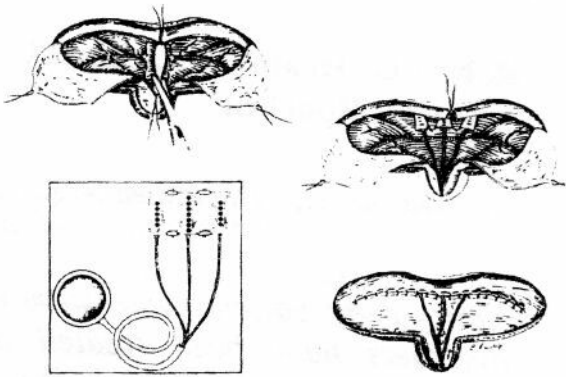

Fig. 1. Drawing illustrating placement of the superior surface electrodes. Upper left: Exposure of the cerebellum. Lower left: The electrodes: the middle chain consists of seven platinum contacts, each 2-mm diam; the lateral chains each consist of five platinum contacts, each 2-mm diam. Upper right: Electrodes in place. Lower right: Dural closure showing exiting electrode wires.

contact points, each contact point 2 mm in diameter: one chain of six contact points embedded in silicone was placed on the midline vermis and two chains, each made up of five contact points in silicone, were placed on either side of the midline about 5-mm lateral to the middle chain. On the inferior surface, the electrode was made up of two chains, each consisting of five platinum points, each 2-mm diam, embedded in silicone. One such electrode was placed on the inferior surface of each cerebellar hemisphere. The superior surface electrodes were made cathodal and those on the inferior surface anodal so that the stimulus would be more intense at the superior surface. This configuration has been used in nine patients (Fig. 2).

Evaluating the results is difficult because of the multiplicity of variables, but some of the nine patients in whom the configuration was used appear to have responded better than others. In reviewing the placements, we conclude that those responding the poorest to stimulation had electrodes on the more lateral aspect of the inferior surface. Our findings in our animal model (cat and rat), as well as in an early pacemaker patient with lateral placements, are consistent with this observation, since stimulation to the lateral cortex and dentate nucleus failed to produce the desirable effects. Our most recent innovation has been to reduce the length of the two inferior chains on each side from five to four platinum points, and to suture them

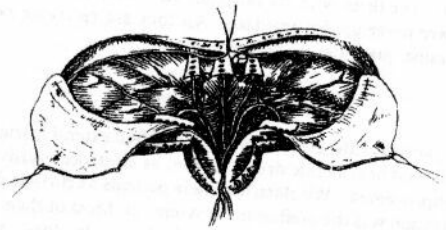

Fig. 2. Drawing of the superior-inferior electrode configuration with the inferior electrodes placed under the lateral hemisphere. On the superior surface, there are six contacts in the midline chain and five in each of the lateral chains. Inferior electrodes consist of two chains on each side, each made up of five contacts.

together for fitting against the vermis on the inferior surface. This technically involves the insertion of a piece of gel foam under the electrodes at the midline to hold them tightly against the underside of the vermis while the dura is being closed (Fig. 3). The stimulation can thus be confined largely to the vermis. Although the number of patients is small and the follow-up period short, initial results indicate these placements may be more effective than the more lateral inferior placements.

Many parameters of stimulation have been tried. The most effective is at 100 Hz with a pulse width of 150 to 250 μsec at a voltage setting determined by sensory evoked potentials recorded from the scalp and the patient's clinical response. The stimulator is set to apply the stimuli sequentially 5 min on and 5 min off. Patients initially wear the stimulator during waking hours and some, depending on clinical disorder, wear it through the

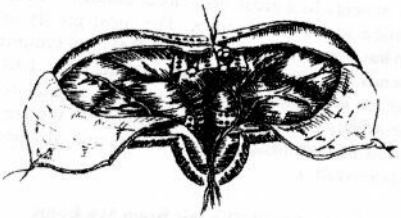

Fig. 3. Drawing of the superior-inferior electrode configuration with the inferior placements at the midline.

night as well. In our experience, epileptic patients with nocturnal seizures and profoundly disturbed psychotic patients require stimulation around the clock. Some of the less deteriorated patients, on the other hand, particularly the depressives, can determine with experience how much or how little they need it to maintain the beneficial effects.

Use of evoked potentials to determine current strength is based on earlier anatomic and physiologic studies that showed the higher subcortical sensory relay nuclei to be integral units in the network for emotional expression (Heath, 1975; 1976a). Cerebellar stimulation, by influencing the network, also affects response to sensory stimuli. With cerebellar vermal stimulation, evoked responses are usually reduced in amplitude. Measurement of averaged evoked responses has therefore been helpful in establishing the effective stimulus level to apply to the cerebellum. Obtaining evoked sensory potentials permits a rough quantitation of the effectiveness of the stimulation. And, finally, the evoked responses, somatosensory and auditory being of equal value, give some indication of the functioning of the implanted equipment (Figs. 4 and 5).

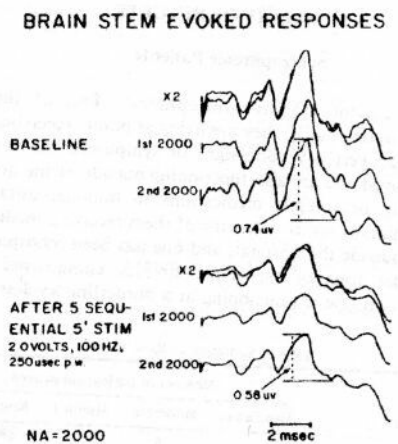

Fig. 4. Recordings of averaged brain stem responses to auditory stimuli before and after sequential cerebellar stimulation. Note reduction in amplitude without change in delay time.

Fig. 5. Scalp recordings of averaged somatosensory evoked responses to median nerve stimulation before and after sequential cerebellar stimulation. Note reduction in amplitude of responses.

SUMMARY OF RESULTS

Schizophrenic Patients

Of the 38 patients 15 are schizophrenic. Two of the 15 have significantly improved, that is, they are living at home, receiving no drugs, and displaying no overt psychotic signs or symptoms. Six patients have moderately improved and are also functioning outside of the hospital, five of them receiving neuroleptic medications in minimal dosages. Three patients have minimally improved, none of them receiving medication; two are functioning outside the hospital, and one has been rehospitalized.

We consider four of the schizophrenics unimproved: three are institutionalized and one is functioning at a borderline level at home with

Table I. Summary of Results

Classification	Number of patients improved				
	Significant	Moderate	Minimal	None	Total
Schizophrenia	2	6	3	4[a]	15
Depression	5	0	0	1[b]	6
Epilepsy	5	2	1	0	8
Organic brain syndrome	1	4	0	0	5
Miscellaneous	2	0	2	0	4
Total	15	12	6	5	38

[a] Three of the four patients are not wearing the stimulator.
[b] Patient not wearing the stimulator.

family support. The three who are hospitalized are not now using the pacemaker and have never used it regularly. All four are receiving neuroleptic drugs in the same quantities as before operation.

Patients with Depression

All six patients with severe depression had had extensive trials on both antidepressant and neuroleptic drugs, as well as electroconvulsive therapy, all without improvement. We classified these patients as chronic depressives because depression was the predominant symptom. Most of them, however, reported almost lifelong histories of anhedonia. In four of the six, obsessive-compulsive symptoms were predominant. One was notably paranoid and had profound hyperchondriacal symptoms with his depression.

Five of the six patients in this group are largely free of depressive symptoms and require no medication. With stimulation, the sixth patient, the paranoid-hyperchondriacal man, experienced prompt relief of symptoms. He soon began to complain, however, that the stimulus was uncomfortable and that the wires in his neck were painful. He subsequently stopped wearing the pacemaker and insisted that it be removed and replaced with another. Because we had some evidence he felt the stimulus turning on, and because it was possible that a current spread to the tentorium was causing his discomfort, we replaced the electrodes and receiver. After prompt relief of depressive symptoms for a few days, he once again began to complain of pain from the "cord" (electrodes) in his neck, he ceased to stimulate himself, and he insisted that the wires be cut but not removed. Eventually the entire implanted device was removed.

Epileptic Patients

All eight patients had gross behavioral abnormalities, both interictal and in association with their seizures. The most gratifying result in the epileptic group has been the elimination of behavioral symptoms, with associated improvement in personality. The treatment has had only nominal effect, however, on grand mal or absence seizures. Fortunately, those kinds of seizures are usually controlled with medications. We are treating grand mal seizures with phenytoin sodium (Dilantin) and absence seizures with valproic acid (Depakene).

Patients with Organic Brain Syndrome

Two of the five patients in this group had severe head trauma from automobile accidents and consequent psychotic behavior, which became

uncontrollable with neuroleptic drugs. Both patients had extensive brain atrophy, as demonstrated by computer axial tomography (CAT head scan), and severe spasticity. In both patients, psychotic behavior was alleviated, and neuroleptic medication is no longer required. Spasticity was not significantly reduced.

One of the five patients, spastic at birth, began having seizures shortly thereafter. The apparent cause was *in utero* infection, the mother having had German measles during the pregnancy. Neuroleptic and anticonvulsant medications failed to control behavioral manifestations, which consisted largely of paranoid psychosis with episodic violence. The patient has now significantly improved and requires no medication.

Another patient in the original series, who had extensive brain damage from gunshot injury and consequent uncontrollable homicidal rage, remains well controlled 18 months after activation of her pacemaker.

The fifth patient in this group showed some mental retardation and poor coordination from birth, suggestive of mild organic brain syndrome. Decompensating obsessive-compulsive symptoms and antisocial behavior were unrelieved by medications, and psychosurgical intervention was ultimately tried (and subsequently repeated in 6 months) with no beneficial result. Since implantation of the pacemaker 6 months ago, the patient's antisocial behavior has disappeared, but his obsessive-compulsive symptoms have been only minimally reduced.

Miscellaneous Group

Four patients are included in this miscellaneous group. One, a patient with hystero-epilepsy in the original series of 11, continues to be essentially symptom-free. Similarly, the first patient in whom we implanted a pacemaker and who was mildly mentally retarded and displayed extreme, uncontrollable violent-aggressive behavior, remains free of violent-aggressive symptoms. He has now finished rehabilitation school and has part-time employment.

Two patients in this group have shown only minimal improvement. One, with severe anorexia nervosa for 12 years and amenorrhea during most of the 12 years, has been continuously tube-fed and completely amenorrheic during the past 5 years. She displayed intense, bizarre compulsive-ritualistic behavior and at times was catatonic. Opposed to the operation, she was interdicted and the pacemaker was implanted as a life-saving measure. Her improvement since implantation of the pacemaker has been gradual. Initially, she refused to wear the pacemaker, and restraints were required to keep it operating. During the past year, however, she has shown gradual change. Compulsive rituals have been significantly reduced, and she states

she wants to wear the pacemaker because it makes her feel pleasant and relaxed. She is, indeed, more outgoing and displays more pleasant affect. Her menstrual cycle returned to normal about 4 months after stimulation began. She steadfastly refuses, however, to eat, and tube-feeding therefore continues. Before operation, she had taken large doses of antidepressant and neuroleptic medications, as well as having electroconvulsive therapy without benefit. During the past few months she has been receiving 3 mg Navane daily.

DISCUSSION

Cerebellar stimulation has consistently produced its best therapeutic results in patients whose principal symptoms are related to profound adversive emotion, that is, in those with intractable depression and those with violent-aggressive behavior consequent to epilepsy or an organic brain syndrome. Results in schizophrenic patients have been less gratifying. An obvious cause of failure in three of the severely deteriorated, long-term chronically ill schizophrenics was their refusal to wear the stimulator. On the other hand, some patients who have conscientiously used the pacemaker have had only limited beneficial effects. In these patients, the effects of stimulation on the evoked responses to sensory stimuli have differed from those in patients with good therapeutic results. In the group in whom results have been less favorable, evoked responses are characteristically inconsistent. A drop in amplitude will occur after one or two stimulations, only to be followed by an increase. This phenomenon suggests some kind of intermittent interference in the complex subcortical neural network for emotion—as if the effects being asserted by the cerebellar stimulator somehow cannot prevail.

We have considered two possible explanations for the poorer results obtained in schizophrenics. It may be that the complex, underlying disease, that is, the biochemical lesion of schizophrenia, impairs response to the stimulation. Or, it may be that neuronal function has been damaged by prolonged and heavy use of neuroleptic drugs. Every patient in the schizophrenic group had had long-term, maximal drug therapy and most had displayed side effects of varying degrees, up to and including profound tardive dyskinesia. Cell membranes have possibly become so hypersensitized that stimulation can assert little effect. This possibility can be evaluated only when it can be considered ethical to perform the operation on patients who have not had an exhaustive trial on neuroleptic drugs.

In some schizophrenic patients, effects of cerebellar stimulation have been strikingly enhanced by administration of very small doses of neuroleptic drugs. Whereas half of the schizophrenics are receiving no medication,

the other half are taking 100 mg Thorazine per day or 10 to 15 mg Navane or Moban per day with good results. Before operation, these patients had shown no response to 20 times (or more) that amount of medication.

Technical problems with the equipment still occur frequently, the most common being antenna breakage. The breakage, coupled with nonusage of the stimulator in the three very disturbed patients, points up the need for a programmable, totally implantable power source, and efforts are under way to develop such equipment.

The surgical procedure is not extensive. The only complication encountered thus far has been bothersome rather than serious: About a third of the patients have had an accumulation of spinal fluid in the electrode track between the receiver in the chest and the electrodes in the posterior fossa. Only one patient, who had extensive brain atrophy, required closure of the fistula. In a few patients, the fluid was withdrawn by a syringe after the needle was introduced under the receiver. The problem was resolved by having the other patients wear a pressure bandage over the electrode track.

A provocative and unexpected finding in this series of patients has been the presence of gross cerebellar abnormalities. In 8 of the 38 patients (21%), we have found gross scarring of the vermis with adhesions to the overlying tentorium. Even retrospectively, the cause has been hard to establish. In animals, cobalt implanted into the midline cerebellum induced dysrhythmia at supratentorial sites of the type associated with psychosis (Heath, 1976a; 1976b). These findings suggest that structural anomaly of the cerebellar vermis is a cause of psychotic behavior.

Although the deliberate establishment of controls for this type of study is difficult, a number of satisfactory controls have inadvertently developed. With each patient, there is, for comparison, a long preoperative course involving many treatments. Serving as control for suggestion consequent to this new treatment have been numerous and varied technologic failures. In two patients, in whom electrodes were not implanted over the correct site, a second operation was necessary. In the early patient with hystero-epilepsy, electrodes were placed too far laterally and only partial symptomatic control resulted (Fig. 6). With replacement of the electrodes over the vermis, the patient is almost completely free of symptoms (Fig. 7). Because of extreme asymmetry of the cerebellum in another patient, not suspected before operation, the electrodes were placed too far posteriorly (Fig. 8). After several weeks of stimulation, the patient failed to show improvement and another operation was performed to place the superior electrodes correctly over the rostral vermis (Fig. 9). Stimulation then caused prompt improvement, and she has continued to improve over the past 6 months.

About one-third of the patients in the series have had antenna breakdown of which they were unaware because of the thick insulation embed-

Fig. 6. Anterior-posterior and lateral skull X-rays of Patient BP-3. Lateral placement of electrodes after the first operation.

Fig. 7. Anterior-posterior X-ray of Patient BP-3 after second operation. Note more medial placement of electrodes.

Fig. 8. Anterior-posterior and lateral skull X-rays of Patient BP-31 after first electrode placement. Note that the superior electrodes are posterior.

ding the wires. Following such breakdowns, symptoms began to recur. When a patient's condition begins to deteriorate, the family knows that the first step is to check the equipment. This technologic problem was most readily apparent in patients with violent behavior as a result of epilepsy or organic brain disease and in schizophrenics, none of whom has been able to function very long without the stimulation. Only the depressive patients seem able to abstain from stimulation for prolonged periods.

Fig. 9. Anterior-posterior and lateral X-rays of Patient BP-31 after second operation. The superior electrodes are now over the midline rostral vermis.

In summary, results obtained with the cerebellar pacemaker continue to be encouraging. Most of the patients, all of whom were previously intractably ill, have benefited. We have gained more information about the types of patients who are most apt to respond. Those who are ill because of a preponderance of profound adversive emotion (depression, rage, violent behavior) benefit significantly. The stimulation also works well with the clinical diagnostic entity of depression, including anhedonia. Psychotic manifestations of epilepsy have also been largely eliminated, and the therapeutic procedure has removed many symptoms in patients with organic brain syndrome. Whereas some schizophrenics have been notably helped when stimulation has been possible, they have been less responsive as a group for reasons that are still obscure. Changes in techniques have been made, and more modifications are likely to be introduced as a result of further data from the animal studies and technologic advances.

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