

Gross Pathology of the Cerebellum in Patients Diagnosed and Treated
as Functional Psychiatric Disorders

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Nine of 33 patients diagnosed as functional psychosis, who had negative neurological examinations and laboratory studies, showed gross pathological changes of the vermis when the cerebellum was exposed for implantation of a vermal stimulator. These findings motivated us to review the CAT scans done on 264 psychiatric patients as part of their work-up to rule out organic or structural aberration. Although 132 (50 per cent) of these scans were reported as abnormal, only 17 showed pathology of the cerebellum. With careful rereading with attention to the posterior fossa, however, the incidence of cerebellar vermal abnormality proved to be much higher. Of the 96 patients in the series who were diagnosed as functional psychosis, 31 showed pathology of the cerebellar vermis (22 of 65 schizophrenics and 9 of 31 patients with other functional psychosis). Scans of seven patients who had been diagnosed and treated as functional psychosis revealed tumors of the vermis. Scans were then obtained on 20 additional patients with a diagnosis of schizophrenia. These patients were selected at random from two psychiatric services, excluding only those patients who had findings suggesting organicity or who had histories of alcoholism or electroconvulsive therapy. Twelve of the 20 patients (60 per cent) showed atrophy of the vermis of the cerebellum. Thus a total of 34 of 85 schizophrenic patients (40 per cent) had scans showing pathology of the cerebellar vermis. These data are consistent with data from animal experiments that demonstrate a role for the cerebellar vermis in behavioral pathology and epilepsy.

In reviewing the follow-up results in the 38 patients in whom we have implanted a cerebellar pacemaker for the treatment of intractable behavioral disorders, we reported, in 1978, the unexpected finding of definite gross pathological changes of the vermis of nine of the patients when the cerebellum was exposed for implantation of the electrodes (10). In every case, the diagnosis had been functional psychosis, with no evidence of structural pathology. Of the nine patients, six had a diagnosis of schizophrenia, one of psychotic depression, and two of epilepsy with episodic behavioral manifestations (psychotic depression in one and episodic, uncontrollable rage in the other). These nine patients were in addition to those few in the series of 38 who were known to have post-traumatic brain aberrations as the cause of their psychotic behavior. All nine patients had had preoperative computerized

axial tomographs (CAT scans) that were declared normal by routine reading.

Because the incidence of unsuspected structural abnormality in the pacemaker patients was high, we chose to scrutinize the CAT scans of the nine patients carefully, directing special attention to the posterior fossa. The rereading disclosed atrophic changes of the vermis in several scans that were previously read as normal. Aided by scans of higher resolution, we later set out to determine the incidence of structural abnormality of the vermis in patients diagnosed as having severe functional behavioral disorders.

Materials and Method

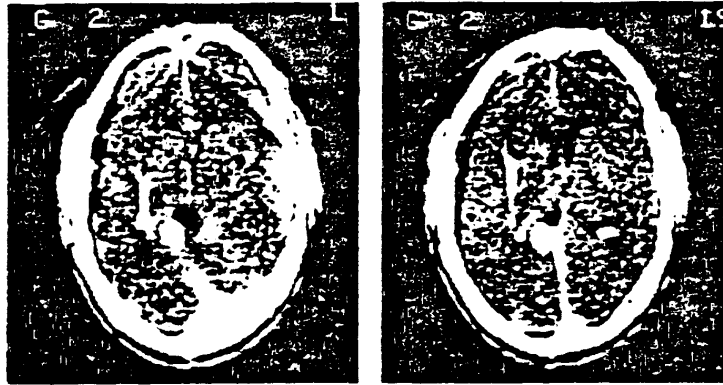
Patient Groups

Since 1975, scans have been performed by the Department of Radiology of Tulane Medical Center (TMC) on 284 patients with a psychiatric diagnosis. Scans on 264 patients (including 33 who are now pacemaker patients) were ordered as part of the evaluation of the patient and were read routinely by radiologists. Twenty of the 284 scans were done on

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TENTORIAL MENINGIOMA
 PSYCHIATRIC Dx: SCHIZOPHRENIA



(F. J.)

FIG. 2. CAT scan showing tentorial meningioma infringing on the rostral vermis of the cerebellum.

Two patients in this group of seven had cerebellar cysts. One had a history of psychiatric hospitalization, with a diagnosis of schizophrenia 16 years earlier. Six years after that, seizures developed, and a diagnosis was made of epilepsy with psychotic manifestations, as well as schizophrenia. He had had episodic catatonia, gross thought disturbance, and auditory hallucinations. Repeated neurological examinations, electroencephalograms, isotope scans, and skull roentgenograms were all negative. When ataxia, headaches, nausea, and vomiting developed in the patient, a CAT scan was performed and the cyst revealed. At operation, a large cyst of the lateral lobe and vermis was evacuated and a tentative diagnosis of hemangioblastoma was made. The other patient with a cyst was treated for a year with psychotherapy and tricyclic medications. Repeated neurological examinations, electroencephalograms, and skull roentgenograms were normal. A CAT scan (Figure 3) showing a large cyst of the lateral lobe and vermis was obtained when he developed severe headaches after a party where he sniffed amyl nitrite.

Mucormycosis was established at operation in the sixth patient in this group after a CAT scan had led to a diagnosis of cerebellar cyst. For 2 years, this patient

had had psychiatric symptoms of anxiety, mood disturbance, visual hallucinations, and, later, when a block developed in cerebral spinal fluid circulation, disorientation and impairment of memory suggestive of an organic psychosis.

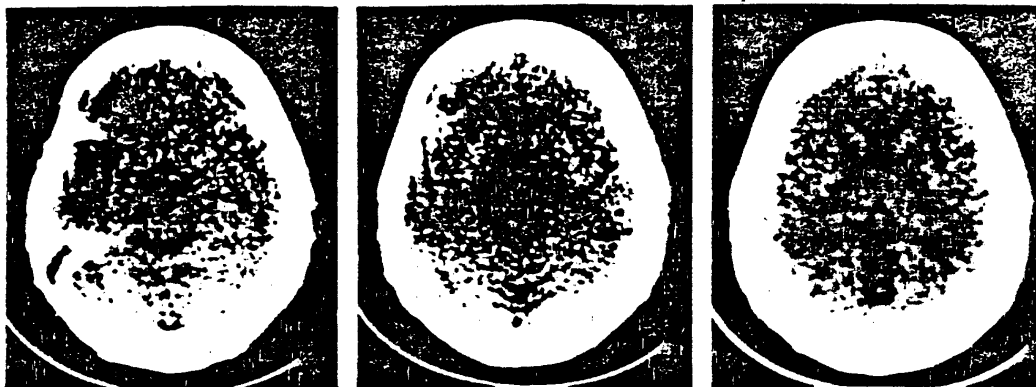
The seventh patient in this group had diffuse cerebellar calcification. Over the preceding 10 years, he had had numerous hospitalizations for psychotic depression, during which he had had repeated courses of electroshock and antidepressant medications.

Rereading of CAT Scans Originally Read as Normal

Schizophrenic patients. Among the 132 patients in whom CAT scans had originally been read as normal were 47 schizophrenics. On careful rereading, 16 of the 47 scans were abnormal, all showing atrophy of the cerebellar vermis (Table 4). Considering that 18 of the 65 scans done on patients diagnosed as schizophrenic had originally been read as pathological, the number of abnormal scans in the schizophrenic population comes to 34 (52.3 per cent). Six of the 18 scans originally read as abnormal showed cerebellar pathology (12 showed the lesion elsewhere). Thus, 22 of the 65

VERMIS ATROPHY

PSYCHIATRIC Dx: SCHIZOPHRENIA (RANDOM)



(F. V.)

FIG. 4. CAT scan showing atrophy of the cerebellar vermis in a randomly selected schizophrenic patient.

large university hospital, although the same criteria were used in both studies. Unfortunately, criteria for establishing atrophy are somewhat imprecise. It may be that we diagnosed atrophy by CAT scan more often than it occurred, despite the close clinical correlation with abnormalities seen at operation in some of our patients. At this stage, we cannot be sure. With the introduction of improved scan equipment with higher resolution, however, the incidence of abnormal findings increased. The relatively small number of CAT scans on patients with functional psychosis as a possible diagnosis (65 over a 4-year period at this large university center) is a reflection of the belief that schizophrenia is not caused by structural abnormality.

In numerous studies, we have demonstrated the midline cerebellum (vermis and fastigial nucleus) to be an integral part of the neural network for emotional expression. Anatomic connections and functional relationships have been described (7, 8). Participation of the cerebellum in emotional behavior and epilepsy has also been shown in animals (4, 5, 12, 13), as well as in a limited number of patients in whom deep and surface electrodes were used for diagnosis and treatment (3). Snider and associates (15, 16) also demonstrated anatomic connections to brain stem sites involved in emotion. In our laboratories, we have shown that the cerebellar vermis and fastigial nucleus assert a unique modulating effect on brain sites where physiological

activity correlates with pathological behavior and epilepsy. Whereas stimulation of the vermis or fastigial nucleus inhibits pyramidal cell activity of the hippocampus (previously demonstrated to be overactive in adverse emotional states and at onset of epileptic seizures), it activates cells in the septal region (where stimulation induces pleasure and where spiking abnormalities occur in association with the anhedonia of psychotic behavior; ref. 7). These findings prompted our use of cerebellar vermal stimulation to treat patients with intractable psychosis and epilepsy.

Our earlier animal studies had indicated that psychotic symptoms and epileptic seizures could be induced by certain lesions (irritative) in the midcerebellar structures when a dysrhythmia spread to involve specific supratentorial structures implicated in emotional expression (5). Gross destructive lesions of the vermis or fastigial nucleus do not consistently create the dysrhythmia. Similarly, many patients with gross cerebellar lesions do not have psychotic symptoms or epilepsy. Corresponding with animal findings, it may be that those signs and symptoms appear in patients only when a dysrhythmia evolves, as a result of a vermal lesion, to implicate rostral supratentorial structures.

Despite the evidence of cerebellar abnormality, neurological examination of these patients has been essentially negative. Minimal clumsiness has sometimes

been noted, suggesting a mild dysdiadochokinesia. Vermal lesions may be responsible for the changes in eye tracking in schizophrenic patients, suggestive of vestibular involvement, reported by Holzman and associates (11).

Atrophy of the cerebellar vermis cannot be correlated with alcoholism and electroconvulsive shock treatment, since the incidence of abnormal scans was just as high in the group of 20 schizophrenics with no history of alcoholism or electroconvulsive therapy. The possibility of neuroleptic medications as a contributory factor has not been completely eliminated.

The present findings further complicate the cloudy issue of "What is schizophrenia?" Although subtle atrophic changes in the vermis have been noted in a considerable percentage of our patients diagnosed as schizophrenic, many schizophrenic patients in this study had no evidence of abnormality of the cerebellar vermis. On the basis of animal and patient data gathered during the past 30 years, we have speculated that the clinical syndrome of psychosis derives from a specific dysrhythmia through the pathways for emotional expression. With the dysrhythmia, the same signs and symptoms emerge regardless of the initiating cause. Precise data are not yet available to determine the exact percentage of patients with "functional psychosis" who have structural disturbance of the vermis.

We have shown, in animals, that the dysrhythmia involving the cerebellar vermis and supratentorial structures associated with emotion (septal region, hippocampus, amygdala) can be induced by administration of taraxein, the fraction obtained from serum of schizophrenic patients (9).² This finding suggests that, in some patients at least, the cerebellar dysrhythmia with resultant psychotic symptoms may be due primarily to a biochemical abnormality. There may be two principal pathological categories for the clinical entity of schizophrenia: a) structural disorder of the vermis, and b) biochemical aberration; or possibly the biochemical aberration leads eventually to structural change, although this seems unlikely, since we have found no positive relationship between duration of illness and structural change in our study.

Salzman and associates (14) have discussed the complex relation between phenytoin (Dilantin) and cerebellar abnormality in patients with epilepsy. The scans of only two of our epileptic patients (of 10 reviewed), both of whom had intractable pathological behavior, showed vermal atrophy. Both are cerebellar stimulator patients who showed atrophy of the cerebellar vermis at operation. We previously reported

data from basic animal studies which suggest that the same brain sites and pathways implicated in psychotic behavior are involved in epilepsy as well (5).

At Tulane and at other centers, intractable seizures have been treated by cerebellar stimulation (2, 18). Salzman and associates (14), in a study of the lateral cerebellar lobes of epileptic patients involving biopsies of the cerebellar cortex, as well as postmortem findings, reported cerebellar pathology. Their review of evidence introduced by Spielmeier (17), as well as their own data and those of others, suggested that cerebellar abnormality might be a primary cause of epileptic seizures. Our basic and clinical findings indicate that the vermis and fastigial nucleus are more involved than the lateral cerebellar cortex.

Additional studies, including postmortem histological evaluation of the vermis, are required to clarify the relationship, if any, between an abnormal cerebellum and the two major syndromes of psychosis and epilepsy, as well as the nature of the specific underlying diseases for these syndromes.

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