LONG-RANGE RESULTS IN THE TREATMENT OF INTRACTABLE PAIN BY STEREOTAXIC MIDBRAIN SURGERY*

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Stereotaxic lesions in the midbrain (mesencephalotomy) were first carried out by us in 1947, and the lesions were planned in such a manner that not only the spinothalamic and quintothalamic tracts but also adjoining areas of the tegmentum dorsal to the red nucleus were included.11,15 In those patients in whom pain was associated with pronounced emotional reactions mesencephalotomy was combined with dorsomedial thalamotomy (mesencephalothalamotomy) since the effect on anxiety and emotional responses obtained by lesions of the dorsomedial nuclei was similar to that following prefrontal lobotomy but without most of the undesirable side effects of the latter. This report deals with the long-range results in 54 patients treated by this method.

The operation seems to be indicated only after all conservative methods such as drug therapy, physical therapy, including electroshock therapy and psychotherapy, have failed. Of our 54 patients, 31 not only had been treated by conservative methods but in addition had various surgical procedures performed such as nerve blocks, sympathectomy, rhizotomy, chordotomy and lobotomy or combinations of such procedures.

METHOD

The initial method was modified in varying directions so that eventually the following method seemed to be the most suitable. The puncture is made parallel to the median plane; it is inclined backward 34° to the interaural plane and passes through the posterior commissure which serves as a reference point. Such an oblique direction intersects with the spinothalamic tract at a larger angle than the interthalamic plane and thus the chance of injuring this system is enhanced. While at the level of the pineal center the spinothalamic tract lies close to the arm of the inferior colliculus, at the level of the posterior commissure the relatively much larger internal geniculate body lies lateral to the spinothalamic tract. There is less danger of extensive injury to the auditory system at the latter level than more posteriorly because at the more anterior level the auditory system occupies a larger area than in the arm of the inferior colliculus, where a small lesion may easily interrupt all cochlear impulses.

In a dorsoventral direction the lesion has to extend from the level of 1 mm. below the posterior commissure to 5 mm. ventral to this structure. One should bear in mind that secondary pain-conducting pathways probably exist in the reticular formation so that an attempt should be made to interrupt these systems as extensively as possible without injury to other functionally important structures. The stylet electrode is inserted 7.5 mm. lateral from the midline, and lesions are made with the stylet protruded in a medial and lateral direction.

In order to avoid undesirable side effects as much as possible, stimulation of the area should precede production of lesions. Subjective pain and paraesthesia or their absence may indicate the proper or improper position of the electrode. Ocular movements on the homolateral side would indicate that the electrode lies too close to the oculomotor fibers, whereas tinnitus or other auditory sensations would point to a too far lateral position. If the electrode is too deep, then movements of the contralateral extremities

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may occur. In some cases recording evoked potentials from this area on stimulation of a contralateral peripheral nerve may be of additional help in correct orientation of the electrode. Subsequently, stereotaxic mesencephalotomy with slight modifications has been used successfully by Leksell (reported by Torvik\(^1\)), Roeder and Orthner,\(^2\) and Mazars \textit{et al.}\(^3\)\(^4\)

**CLINICAL OBSERVATIONS**

1. *Atypical Facial Pain*. Seven patients had undergone section of the 5th nerve root in other hospitals without relief or were even worse following operation. In 1 of these cases a tumor of the cerebellopontine angle had been suspected. Initially definite relief was obtained in 6 cases. In 4 cases the pain recurred 5 months to 4 years after operation, in 2 of them in a milder form, in 2 as severe as before operation. One patient died at home several months following surgery, the cause of death not being ascertained. In this case the period of observation was too short to warrant a definite conclusion. The longest period of observation was in the following case:

A 47-year-old white female was admitted to the hospital Sept. 16, 1947 because of severe pain in the right temple. Her disorder had been diagnosed as tic douloureux in 1941 and nerve blocks had been attempted without relief. Subsequently a Spiller-Prazier retrogassarian rhizotomy was performed by another neurosurgeon but the pain became more severe. Her pain persisted for 7 years despite analgesic drugs. There was complete loss of all forms of sensation involving the right trigeminal field including the cornea. The temporal and masseter muscles were atrophied on the right.

On Oct. 30, 1947 a left mesencephalothalamotomy was performed. Postoperatively there was impairment of sensation to pin prick, heat, cold and light touch on the entire right side of the body; this disturbance regressed within 1 year. The face was anesthetic from the previous rhizotomy. Immediately after operation she stated that her former pain was gone. There were no complications except for an occasional slight paresthetic sensation ("zig-zag flash") in the right upper lip and transitorily impaired sensation of position of the right large toe. There was also transient slight bilateral tremor more pronounced on the right.

On repeated examinations during a 13-year period she is still free from pain and reports only occasional slight paresthesia on the right side of the face and head.

2. *Postherpetic Pain*. All 5 patients with postherpetic facial pain experienced initial relief after mesencephalotomy or mesencephalothalamotomy. The beneficial effect was maintained 8 years after contralateral mesencephalothalamotomy in the first patient. This was a 70-year-old woman who had a left-sided severe herpes zoster opthalmicus in July 1945. A retrogassarian rhizotomy in November 1945 had offered no relief and a plastic repair of the lids had been performed in December 1945. The pain was so great that on admission in March 1952 she threatened suicide. On March 20, 1952, a right mesencephalothalamotomy was performed with almost total relief which lasted until her death (December 1960) from a cerebrovascular accident. The hypalgesia induced by the mesencephalotomy involved the upper trunk and entire arm on the left side. The left side of the face was anesthetic from the previous retrogassarian rhizotomy. The second patient estimated after 3 years that she had obtained 50 per cent relief. The third patient experienced a gradual return of pain 1½ years postoperatively but not of sufficient intensity to interfere with work or sleep. The fourth patient had a recurrence 9 months postoperatively, although the hemianalgesia produced by the mesencephalotomy was still present 6 years after surgery. The fifth patient, with "severe burning and aching" of the left forehead, scalp and eye, had been relieved for 5 years when the pain gradually returned.

In summary there was permanent, nearly complete relief in 1 case, and partial relief in a second case. Partial relapse was experienced in 1 patient and complete relapse in 2 others. It seems of interest that in 1 of these 2 cases the pain reappeared in full intensity more than 3 years postoperatively.

Of 2 patients with postherpetic pain of the lower segments, partial relief of dyesthesias was obtained on the right side of the neck in 1 case. The other patient, a morphine addict, was unrelieved despite correct inter-
rupture of the spinothalamic system as evidenced by the appearance of hemi-analgesia.

3. Tabes Dorsalis. One patient with gastric crises received no benefit from bilateral prefrontal lobotomy but was relieved by bilateral mesencephalotomy for 9 weeks. When the right side of the body again became sensitive, the gastric crises returned. The second patient with lancinating pain in both thighs was relieved for 2 months after which time the hypalgesia regressed.

4. Trauma of Cord and Spinal Roots. Of the 6 patients in this group, 1 was completely relieved by mesencephalotomy for the duration of observation (1 year), 1 was relieved temporarily and 1 obtained no relief. Mesencephalotomy combined with thalamotomy was performed in 3 cases; it resulted in complete relief in 1 case (duration of observation 10 years), partial relief in 1, and in 1 there was a transient effect of not caring about the pain, as after prefrontal lobotomy.

5. Tumors. There was 1 patient with Dercum’s disease (adiposis dolorosa) who had relief for 11 months following mesencephalotomy.

Of 11 patients with metastatic malignancies 2 died a few days after operation, cachexia being a contributory factor. One patient with a tumor of the pulmonary sulcus had complete relief after contralateral mesencephalotomy until his demise 6 weeks later. Two patients with uterine carcinoma were relieved by bilateral mesencephalotomy and required only mild sedation (survival 3 months and 3 years respectively; in the latter patient the pain partially recurred). In 1 patient with carcinoma of the tongue the pain was reduced for the survival period of 5 months. A patient with metastatic carcinoma causing facial pain was relieved after a second mesencephalotomy; he succumbed 3 months postoperatively. Four patients were not relieved (1 with bronchogenic carcinoma, 1 with carcinoma of the epiglottis and metastases in the neck, and 2 with pelvic carcinomas).

6. Central Pain. There were 16 patients with “thalamic” pain; in 14 there probably was a thalamic lesion of vascular origin; 1 had a parietal-lobe cyst extirpated and 1 had had a hemorrhagic cystic lesion of the left parietal region; whether there also was involvement of the thalamus in the latter 2 cases is uncertain. Two patients died, apparently from hemorrhage, subsequent to mesencephalotomy; probably their vascular hypertension was, at least partly, responsible. Initial relief or at least reduction of pain could be obtained in 11, an experience that demonstrated the importance of afferent impulses entering the diencephalon in the genesis of this type of so-called spontaneous pain. However, there was a complete recurrence of pain in 4 patients within 1–5 months, probably because of compensatory collateral systems. In 2 patients the pain reappeared with slighter intensity within 1–5 months. There was no relief in 3 cases.

In 1 patient with a pontine hemorrhage there was a relief for 6 weeks and in another with an aneurysm of the anterior communicating artery there was no relief.

7. Amputation Neurona and Phantom-Limb Pain. Two such patients not only had been unrelieved by prefrontal lobotomy but also had development of mental changes following this procedure. The first patient likewise was unrelieved by nerve blocks, sympathectomy and neurolysis of the stump neuroma. He was completely free of pain following contralateral mesencephalotomy (duration of observation 10 years). The second patient had a slight injury to a finger caused by a cactus thorn. Gradually increasing pain was refractory to roentgen-ray therapy, removal of cervical disc, scaleneectomy, resection of the carpal ligament and finally amputation of the arm. Pain subsided after contralateral mesencephalotomy; however, preceding her discharge from the hospital there was a slight injury to the ankle on the side of her original pain. Her pain is now transferred to this member while she no longer complains of her former pain (duration of observation 6 years).

COMPLICATIONS

Mortality. This was restricted to two
groups: patients suffering from thalamic pain following cerebrovascular accidents caused by vascular hypertension (2 cases) and patients with malignancies (2 cases). The mortality of 4 in 54 cases (7.4 per cent) is in contrast with that of 24 per cent reported by White and Sweet\textsuperscript{14} in their survey of 29 cases of mesencephalitic tractotomy.

*DYSESTHESIA.* There were 8 patients (14.8 per cent) with dyesthesia. In 1 of them the phenomenon was only transient; it attained a severe degree in but 2 cases (3.7 per cent).

In the earlier group of cases in which the puncture was performed several mm. behind the center of the pineal gland and the lesion was produced near the arm of the posterior colliculus, disturbances of hearing were noted in audiometric studies in about 50 per cent, the usual finding being a bilateral low-tone defect, while high-tone loss prevailed in the opposite ear. Occasionally a gradual sloping at both ends occurred with better acuity for middle tones, so that a contraction of the auditory field resulted. In 25 per cent of the initial cases the threshold of discomfort was lowered, and tinnitus lasting 2–3 weeks was reported in 3 instances. Of practical importance is the fact that recovery in auditory functions developed to a variable degree in all cases, also in patients in whom the initial auditory disturbance was pronounced.\textsuperscript{8}

In our later group of patients, the lesions were placed at more anterior levels in the region of transition from the superior colliculus to the thalamus where there is less chance of damaging the acoustic pathways. Since this change in technique, disturbances of hearing were slight and their frequency was reduced to 16.6 per cent. Disturbances of taste were noted in 2 patients.

*MOTOR DISTURBANCES.* There was a facial weakness of 2 months' duration in 1 patient, a monoparesis of 1 week's duration in a second patient and a hemiparesis of 2 weeks' duration in another. A permanent hemiparesis occurred in 1 case, and transient hemiparesis with slight residual weakness of the right hand in another case.

*OCULAR DISTURBANCES.* Difficulty in convergence of the eyeballs for 1 week occurred in 1 case, and partial oculomotor paresis affecting particularly the superior rectus was observed in 3 instances. Parinaud's syndrome in 1 case lasted 5 months, while it seems permanent in 2 other patients. A unilateral Horner's syndrome in 1 patient lasted for 3 weeks and loss of the light reflex occurred in a patient with carcinoma.

*OTHER DISTURBANCES.* Two patients had ataxia and 1 had intention tremor, and 1 had a combination of these two symptoms lasting up to 3 weeks. In 1 case the ataxia was still present 1 year postoperatively. A transient dysphasia for 3 weeks occurred in 1 patient.

One patient was irrational and had visual hallucinations for 5 days after bilateral mesencephalothalamotomy. He also had increased sexual desires following operation that lasted several months. One patient was disoriented for 1 month after unilateral mesencephalotomy.

A summary of the results in these 54 cases is given in Table 1.

**DISCUSSION**

Mesencephalotomy has the decided advantage over mesencephalitic tractotomy in that the operation is less formidable, has fewer complications, avoids particularly the extensive lesions of the occipital lobe reported by various authors, and has a much lower mortality rate. In our material of 54 cases of mesencephalotomy, there were 4 deaths (mortality rate 7.4 per cent). According to White and Sweet\textsuperscript{14} the operative mortality for mesencephalitic tractotomy in 29 cases (their 5 cases plus 24 from the literature) was 24 per cent which they considered too high to warrant use of this procedure. One of the most distressing complications following mesencephalitic tractotomy is the appearance of annoying dyesthesias. It was for this reason that Drake and McKenzie\textsuperscript{2} abandoned the procedure. White and Sweet likewise concluded that the disagreeable dyesthesia was too much of a risk to warrant Walker's\textsuperscript{13} mesencephalitic tractotomy. Schwartz\textsuperscript{9} observed this phenomenon in both of his cases. In our material post-
operative dysesthesia occurred in 8 patients (14.8 per cent); however, the phenomenon was transient in 1 case and was disturbing in but 2 others (3.7 per cent). In this connection it may be mentioned that dysesthesia may appear also after chordotomy (e.g. in 15 per cent of Sjöqvist's series10).

In comparing our operation with other neurosurgical approaches it is important to stress the long-range effects. Particularly the Boston group (Mark et al.3) described good results with lesions of the nucleus ventralis posterior. However, these were short-term observations, and those authors who observed a long-range effect of thalamic lesions (Riechert,6 Bettag and Yoshida1) found recurrence of pain in about the same high percentage as we did with mesencephalotomy. In evaluating the small number of patients in whom permanent relief of pain was obtained, one has to consider that in these patients all other conservative and in one-half of them also surgical procedures had failed and that many of them were close to suicide.

We do not claim that mesencephalotomy is the final answer to the problem of pain but only a refinement of producing a lesion in the spinothalamic and quintothalamic tracts and adjacent pain-conducting systems. Whether the final solution of the problem of intractable pain will be found in surgical or conservative methods will depend on further studies.

REFERENCES

8. SALEMAN, M. Audiometric studies following mes-


DISCUSSION

Dr. J. LAWRENCE POOL: The authors of this presentation deserve our praise and admiration for their long years of truly arduous and most meticulous pioneering work in tackling one of the most difficult problems of neurological surgery—the treatment of intractable pain. As we have heard, many of their patients suffered from the most difficult types of painful syndromes to treat.

Their particular technique is one fraught with risks of complications such as hemorrhage in a very critical area and the hazards of oculomotor and auditory disturbances and dysesthasias, as described by Dr. Wycis. Mesencephalotomy is therefore not to be undertaken lightly, as they have been careful to state at the outset of their paper.

In going over their paper prior to this meeting, which was very kindly submitted to me, several points occurred to me. First of all, it was of interest that most of their patients with atypical facial pain had already had, elsewhere, section of the trigeminal root with no relief. In other words, the wrong operation had been done for the wrong syndrome. This, I think, is worthy of note in this Society. I think we should all beware of this trap, not only for the sake of the patient, but also because of “neurosurgery and the law.”

Secondly, it was stated that lobotomy had been done in some of these patients without benefit. However, I found allusions in these authors’ text to only three lobotomies. This is mentioned because I feel lobotomy still has a place for the emotionally distraught patients with cancer who were too often not helped by stereotactic procedures. Similarly, cordotomy properly done can certainly be effective for pain caused by pelvic malignancy, for example.

With respect to emotional factors, as in some of the reported cases, one might think that a good psychiatric evaluation would be advisable prior to a decision as to what type of surgical procedure should be done. Dr. Wycis has told us that the psychiatrists, in most cases I understand, have thrown up their hands prior to this clinical procedure. I would like to ask Dr. Wycis whether he would recommend psychiatric evaluation and consulation as to what procedure should be done for a given patient.

The whole problem of relief of pain, of course, brings up the matter not merely of severeing sensory pathways, but also involves our concept of the individual psychology of a given patient. Melzack, R. (The perception of pain. Sci. Amer., Feb. 1961, 204: 41-49) stresses this very well with respect to the sensory and affective components of pain. The latter factor, the affective, may well account for some of the failures of surgery. We should all be on our guard for this affective or emotional factor.

I would like to ask Dr. Wycis why he thinks his procedure has failed to relieve a number of the patients suffering from the so-called thalamic syndrome.

In this connection, in the text one case was mentioned that touched my interest, the matter of central pain caused by aneurysm of the anterior communicating artery. I would be interested to know the mechanism of pain in this patient.

The reported work also brings up consideration of the possible role of collateral sensory channels that may develop, because pain returned in some patients some months later. Does Dr. Wycis think collateral sensory channels are a factor in such cases?

Finally, one would like to know more about the location of the lesions that were made; that is, has he more autopsied cases than the one he showed us?

Dr. GEORGE M. AUSTR: I would like to add my congratulations to those of Dr. Pool for Dr. Wycis and Dr. Spiegel’s many years of endeavor and, of course, their pioneering work in the use of the stereotactic instrument in the human.

One is impressed not only by the quality of their work but their honesty in evaluating their results. The over-all figure of 31 per cent cure I think we as neurosurgeons can well appreciate and understand. I am not so sure if we were to present this figure to other groups of our colleagues that they would be deeply appreciative or even sympathetic, since people who refer patients to us for relief of pain feel that a 31 per cent guarantee is not quite enough.

I am impressed that in a number of their patients they felt that it was necessary not only to make a mesencephalic lesion but also a lesion in the medialis dorsalis nucleus. I would like to ask Dr. Wycis if he believes that perhaps in some of these patients it might be worth while evaluating them after the medialis dorsalis lesion before going ahead with mesencephalotomy.

We have had 2 patients in whom we did coagulation of the medialis dorsalis nucleus with complete relief.

Now a word about the very important point that they brought out, namely, the fact that a number of patients were relieved transiently only to have return or variation in return of their original syndrome of pain. Dr. Pool has touched on this, I believe, when he questioned the possibility of collateral pathways of pain. We all know, of course, that even though one completely sections the afferent pathways of pain in the mesencephalon there are lower portions in the medulla and pons where collaterals are given off. It is, therefore, entirely possible that sprouting of new synaptic ter-
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minals could occur over a period of time and that subsequent conditioning of these terminals by the original lesion causing the pain could make them effective in synaptic transmission.

DR. ELDON L. FOLTZ: I would like to compliment Dr. Wycis because of his long efforts toward achieving relief of pain. The 81 per cent good results which Dr. Wycis reports in these patients treated for pain by subcortical stereotactic lesions might be related to the basic "personality" substrate of the individuals. His deeper lesions are in some instances affecting the same system that our cingulotomy procedure does, and consequently his results also may be related to emotional and personality factors.

In a broad study of human reaction to sensation in general, Petrie has used the Köhler kinesthetic after-image technique to demonstrate how differently people may reproduce a quantified sensory stimulus. One-third were found to be "augmenters," who significantly enlarged the sensory image. One-third likewise were classed as "reducers" who consistently reduced or diminished the sensory image. And the last one-third were "moderates" who reproduced the image relatively accurately. This classification has nothing to do with sensory thresholds, but is related to personality and emotional make-up. These groups might be likened to patients with marked emotional reactivity to pain (augmenters), marked emotional tolerance to pain (reducers), and the normal or mid-group (moderates). Psychological testing can divide patients on this basis and may institute new methods of preparative selection of operations designed to relieve the suffering of painful states. It would seem we might do a great deal for the "augmenter," less for the "moderate," and possibly help the "reducer" little at all. It is possible that Dr. Wycis' group of 31 per cent good results was made up mainly of "augmenters" who are generally 33 per cent of our populace.

DR. HENRY T. WYCIS: Those patients who originally were operated on by the Spiller-Frazier method, the previous diagnosis having been tic douloureux, and who had subsequent anesthesia of the face, were referred to us because they had either a recurrence of their pain or a burning type of dysesthesia of the face. This group did quite well; 1 of the patients in this group who was operated upon in 1947 has remained free from pain up to the present time.

Chordotomy still has a very definite role, particularly when pain is in the lower one-half of the body. We have found more difficulty relieving the pain in the lower-body segments by mesencephalotomy than in the upper extremities, head, face and neck.

Regarding psychotherapy, I didn't have time to go into this. Some of these patients already had had psychotherapy. A number of them also had had electroshock therapy. These were desperate cases. Many of them had rhizotomies, chordotomies, sympathectomies, lobotomies and other surgical procedures. This may account for the relatively low incidence of permanent relief.

I would say that the patients with the thalamic syndrome were the most difficult to relieve, partly because, as Dr. Foltz said, of the spreading of these pain pathways as one gets to higher levels. One also has to consider that afferent pathways carrying pain impulses end in various subcortical areas. Walker has called attention to the possible importance of the colliculi; however, there are also other areas that may serve perception of pain, such as the reticular formation, the diffuse thalamic projection system and the hypothalamus. Experimentally, Spiegel, Kletzkin, Szekely, and Wycis have shown that after destruction of the area of the ventral posterior nuclei of the thalamus, stimulation of afferent nerves evokes potentials in the hypothalamus that have a higher amplitude than preceding the ablation of these thalamic nuclei.

The patient who had the aneurysm of the anterior communicating artery had a central type of pain. That patient was not relieved by mesencephalotomy.

Lesions of the dorsomedial nuclei were added to those of the mid-brain in patients who had cancer or emotional disturbances associated with their pain. Most of the patients with carcinoma died before the long-range results could be evaluated. For a similar reason, the dyesthesias that Walker observed following his mesencephalic tractotomies were not pronounced; in practically all of his cases the patients had carcinoma, and most of them died before dysesthesia had a chance to develop.

Going back to tic douloureux, if you operate upon enough patients with this condition, a burning type of pain in the face will develop in a few of them.

I agree with Dr. Foltz that one has to do more than simply interrupt pathways of pain. The individual has to be studied as a whole and one must know his response to pain before one considers any operative procedure. This applies particularly to the question of addiction, since patients addicted to narcotics give a very poor prognosis regarding relief of pain by any operative procedure.