Stereotactic Thalamotomy and L-dopa Induced Involuntary Movement in Parkinsonism

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Involuntary movement is one of the most disturbing and problematic side effects of L-dopa in the treatment of Parkinsonism. Several attempts have been made to reduce this complication, such as an addition of adjuvant, (4) and use of slow release L-dopa. However, the problem remains unsolved probably because hyperkinesis occurs when the akinesis of Parkinsonism is overcorrected by L-dopa and produces hyperkinesis (15).

For more than 15 years we have been treating Parkinsonian patients with stereotactic thalamotomy or pallidotomy or both and began to use L-dopa since 1968. We found that the previous operation reduces the incidence and severity of L-dopa induced involuntary movements in the treated limbs suggested by several authors (1) (15) (17) (20).

This paper is an analysis of L-dopa induced involuntary movements seen in 29 cases in 121 Parkinsonian patients treated with L-dopa, 94 cases with the previous stereotactic procedures and 27 non-surgical cases.

Methods

121 Parkinsonian patients have been treated with L-dopa since 1968 usually as in-patients. Among these, 94 cases had undergone stereotactic operation, unilaterally or bilaterally with 126 lesions before the trial of L-dopa. 13 of these cases (10.7%) had some history suggesting encephalitis. After the initial admission for the drug therapy, patients have been followed up in the out-patient clinic in one to six month intervals or by proforma completed by the patient or his relatives.

The dosage of L-dopa ranged from 0.5 Gm. to 8.0 Gm. daily with the average of 4.2 Gm. for 60 males and 3.2 Gm. for 59 females. The average interval between the onset of Parkinsonism and the L-dopa therapy was 9.9 years for males and 10.0 years for female group, with the average onset of the disease of 49.0 years old and 51.1 years old respectively. The average dose was 3.9 Gm. daily in the involuntary movement group and 3.6 Gm. in the non-involuntary movement group.

Results

1) General comments:

Among 121 patients with L-dopa, 29 cases (24.0%) developed involuntary movements. 2 patients developed dyskinesia with relatively small doses of 1.5 Gm. daily.

Key words: Parkinsonism, L-DOPA, Thalamotomy, Involuntary movement.

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Post-encephalitic patients were more inclined to have involuntary movements (5 in 13 cases—38.5%) than other patients (24 in 108 cases—22.2%). Patients who developed involuntary movements had developed Parkinsonism at an earlier age (43.8 years) than the whole group (50.0). This is evidently due to the preponderance of involuntary movements in post-encephalitic Parkinsonism with an earlier onset of Parkinsonism than other idiopathic or arteriosclerotic groups. The average age at the onset of the disease was 38.9 years old in the post-encephalitic type and 50.0 years old in whole group.

Mones et al (15) remarked that patients with a longer history of Parkinsonism had a greater incidence of L-dopa induced dyskinesia. In our series there was no such tendency. The average history of 9.6 years in dyskinesia group and 9.9 years in the whole group, did not differ significantly.

The interval between the start of L-dopa and the appearance of the involuntary movement varied greatly from person to person; one developed movement only 3 days after the administration of the drug and one after 8 months of usage. The average interval was 2.7 months. There was a tendency for the post-encephalitic patients to have a shorter interval (x=0.7 months) than other patients (x=3.1 months).

As reported by the several authors (2) (5) (14) (16) (22) (23), face, jaw and tongue are most frequently affected by involuntary movement (23 in 29 cases), limbs 16 cases, neck or trunk 10 cases, chest 2 cases and one of the swallowing muscles.

2) Effects of the previous operation.

94 cases among these 121 cases treated with L-dopa had undergone stereotactic operations, 58 cases unilaterally, 34 cases bilaterally and 2 cases uncertain (Table 1).

Table 1. Stereotactic lesions in 94 cases with L-Dopa. (1968-1971)

<table>
<thead>
<tr>
<th>Sites of Lesion</th>
<th>Unilateral operation</th>
<th>Bilateral operation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right Hemisphere</td>
<td>Left Hemisphere</td>
<td>Right Hemisphere</td>
</tr>
<tr>
<td>VL.</td>
<td>10</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>VL + P</td>
<td>10</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>VL + P + IC.</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>P</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>P + IC.</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>VL + IC.</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>SUB.</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>IC.</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>34</td>
<td>34</td>
</tr>
</tbody>
</table>

Table 2. Sites of L-Dopa induced involuntary movements

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>Number of cases</th>
<th>Number with IM.</th>
<th>Limb Right</th>
<th>Limb Left</th>
<th>Face Right</th>
<th>Face Left</th>
<th>Tongue</th>
<th>Trunk</th>
<th>Neck</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-surgical cases</td>
<td>27</td>
<td>8 (29.6%)</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Right hemisphere</td>
<td>24</td>
<td>5 (20.8%)</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Left hemisphere</td>
<td>34</td>
<td>9 (257.7%)</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bilateral hemispheres</td>
<td>34</td>
<td>7 (20.5%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>121**</td>
<td>29 (24.0%)</td>
<td>6</td>
<td>11</td>
<td>5</td>
<td>7</td>
<td>10</td>
<td>10</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

** Including 2 other cases of which operative record is missing.
* Chest, deglutition muscle etc.
IM; involuntary movement

Number, frequency and sites of the L-DOPA induced involuntary movement according to the previous stereotactic procedure.

Table 3. Stereotactic lesions and L-Dopa induced involuntary movement

<table>
<thead>
<tr>
<th>Sites of IM.</th>
<th>Operated cases</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contralateral to lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VL</td>
<td>P.</td>
<td>VL* P.</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ipsilateral to lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VL</td>
<td>P.</td>
<td>VL* P.</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Other parts</td>
<td>VL</td>
<td>P.</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Number of lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM.; involuntary movement, VL.; ventrolateral thalamotomy, P.; pallidotomy, IC.; internal capsulotomy.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note the rare occurrence of the L-DOPA induced involuntary movement of contralateral body to the previous stereotactic lesion.

The sites of lesions are shown in Table 1, usually the ventrolateral thalamotomy or the thalamo-pallidotomy. The stereotactic procedure has been described in detail somewhere (8) (9). Briefly, using the Guiot-Gillingham's Frame, a high frequency electrocoagulation is made in the ventrolateral nucleus (v.o.a., v.o.p., v.i.m.), via a postero-anterior parasagittal track with a laterality of 15 mm. Deep electrode monitoring is usually used to confirm the position of the electrode. If the rigidity remained
after the thalamic lesion an additional additional pallidal lesion would be made by the same track. The size of the lesion is usually 6 mm. in length and 5 mm. in diameter.

The incidence of L-dopa induced involuntary movement differs considerably according to the previous operation (Table 2). 8 cases among 27 non-surgical cases (29.6%) developed dyskinesia, 14 cases among 58 cases (23.7%) with the unilateral and 7 among 34 cases (20.6%) with the bilateral operation.

It is noteworthy that in the operated groups dyskinesia of limbs or face contralateral to the brain lesion is rare compared to that of the ipsilateral limbs or face and that of non-surgical group. This agrees with the observations of other authors (1) (11) (15) (20) (22). We noticed involuntary movement of the contralateral side of the body only in 4 cases among the 126 lesions but 10 cases in the ipsilateral side, and in 27 non-surgical group 5 cases developed movement of the limbs or face.

Table 3 shows the frequency and the sites of the involuntary movement according to the location of the lesions made. It appears that double lesions (thalamopallidotomy or thalamo-capsulopallidotomy) are more effective to prevent the involuntary movement than single lesion. But Stellar, 1971 (20) reported the prevention of contralateral dyskinesia by a single lesion in the thalamus.

We paid attention to the “unsuccessful” 4 cases who developed the L-dopa induced involuntary movement of contralateral side of the body. Fig. 1 is the map of the lesions which we made in the previous operation on the frontal section of Schalten-and-Bailey’s atlas (19). The black circles are lesions of “unsuccessful” cases and open ones are those of “successful” cases, “successful” means they developed no L-dopa induced involuntary movement of contralateral limbs to the brain lesion though they developed dyskinesia of other parts of the body. All lesions in “successful” cases were located in the pathway, the interruption of which relieves Parkinsonian tremor and rigidity (8). It is obvious that in “unsuccessful” cases lesions were made too laterally or too high or low.

We are convinced that stereotactic thalamotomy or thalamopallidotomy for Parkinsonian tremor or rigidity prevents L-dopa induced involuntary movements of the contralateral limbs, if the lesion is made in the correct place. However, it is difficult to prevent movement of the ipsilateral limbs or of tongue, jaw or neck.

Discussion

Though it is generally accepted that thalamotomy and L-dopa are the two major methods for relieving Parkinsonism, the mechanisms are still obscure. It is said that the stereotactic procedures interrupt the pathway of dopamine transmitter neurons (8) or the striatopallidodugal system (6) and that L-dopa replaces the deficiency of dopamine in the substantia nigra or striatum (10). Yuill (24) concluded “Parkinsonism and Huntington’s Chorea, which is similar to L-dopa induced involuntary movement, might be regarded as being at opposite ends of the biochemical spectrum with normality at its centre.”

According to our results, stereotactic thalamotomy or pallidotomy for Parkinsonian tremor or rigidity prevents L-dopa induced involuntary movement of the
Fig. 1. Locations of the previous thalamic lesions of cases with L-DOPA induced involuntary movement. On the frontal section of Schalten & Baily’ Atlas. (4.0 mm posterior to mid. AC-PC line.)

Empty circles are the lesions which stopped the involuntary movement of “operated” limbs though the patient developed those of other part of the body. Black circles are lesions of cases who developed involuntary movement of “operated” limb. Note the empty circles are almost totally located in the pathway (the dotted zone), the interruption of which relieves the tremor and rigidity of Parkinsonism (Gillingham, 1966).
"operated side" of the body as well, as has been reported by several authors (1) (11) (15) (20) (22). Why interruption of the striopallidothalamocortical circuit stops the Parkinsonian features as well as L-dopa induced involuntary movement which is pathogenetically at the opposite end of the former, according to Yuill (24), is difficult to explain.

Manfred (13) explained L-dopa induced involuntary movement as a releasing phenomenon of the motor cortex from inhibitory impulses via the striatopallidothalamocortical circuit, which also receives an inhibitory input from dopaminergic neurons of the substantia nigra. He stated "by the administration of L-dopa, the striatopallidothalamocortical circuit receives more inhibitory powers from dopaminergic neurons, this in turn would lead to the release of cortico-motor function and results in the involuntary movements.” He explained the relation to the previous thalamotomy in “on the side of the thalamotomy the striatopallidothalamocortical pathway is permanently interrupted thus the cortical release can not be expected in the operated side.”

This hypothesis explains our results that stereotactic lesions in the circuit for Parkinsonian tremor and rigidity is effective for L-dopa induced movements, and the fact that the post-encephalitic Parkinsonian patient who is known to have marked dopamine deficiency (10), is likely to develop L-dopa induced involuntary movements.

The transitory ballistic movement of “operated” limbs, which is sometimes experienced post-operatively, is also explained by Manfred’s theory, as the interruption of striatopallidothalamocortical circuit implies the "transitory” release of the motor cortex.

It is noteworthy that L-dopa induced involuntary movement of neck muscles is difficult to prevent by the previous operation, and that spasmodic torticollis is also difficult to cure by ventro-lateral thalamotomy (18).

No matter what the explanation stereotactic thalamotomy prevents this side effect of L-dopa, this phenomenon is of considerable importance clinically (17).

We applied this theory to three bradykinetic Parkinsonian patients who had been unable to tolerate L-dopa because of vigorous involuntary movement of limbs. All of them became able to endure this drug after stereotactic thalamotomy (or thalamopallidotomy), although they still had some involuntary movements of the jaw or neck.

Summary

(1) We investigated 121 Parkinsonian patients on L-dopa, from the standpoint of L-dopa induced involuntary movements. 94 cases had undergone stereotactic operation previously, unilaterally or bilaterally.

(2) 29 cases among these 121 patients developed L-dopa induced involuntary movement.

(3) Post-encephalitic Parkinsonian patients are more likely to be subject to this side effect.

(4) Stereotactic thalamotomy (or Thalamopallidotomy) is helpful not only in
diminishing Parkinsonian tremor or rigidity but also to prevent L-dopa induced involuntary movement, as this procedure definitely stops drug induced dyskinesia of the “operated” limbs.

References


20) Timberlake, W. H.: Double blind comparison of Laevodopa and Procyclidine in Parkinsonism, with illustrations of L-dopa induced movement disorders. Neurology (Min-
