Brit. J. Psychiat. (1971), **119**, 277–8

ABSTRACT

L-DOPA in the Treatment of Depressive Symptoms

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The reports on the good effect of L-DOPA on Parkinson's syndrome and on some forms of depression have prompted us to investigate if it might alleviate mental disorders not responding to conventional methods. Pare *et al.* (1962) suggested distinguishing between types of depression according to how they respond to antidepressant drugs. If L-DOPA were shown to be effective, it would provide another means of differentiating between obscurely defined mental states. We present five cases of psychic disorders in which depression was a prominent symptom. All were treated with L-DOPA after a wide range of conventional treatments over many years had proved of little use.

Case 1. Woman, now aged 50. When aged 20 she began vomiting after meals. At 40 her vomiting increased so much that she became severely undernourished; she was hospitalized several times and underwent thorough hormonal and X-ray examinations, but no explanation was found. At 44 she began getting attacks of severe despondency, psychomotor retardation, anxiety and diurnality. She made several attempts to commit suicide. Thymoleptics, ECT, oral doses of tryptophan, lithium and anxiety-relieving agents were all tried, none with any lasting relief. At 47, X-ray examination finally revealed diaphragmatic hernia, not observed in earlier examinations. After surgery she vomited far less often, yet her depression continued.

At 49 she was put on L-DOPA in increasing doses. When given 1 g. a day, her despondency, anxiety and retardation began to lessen. By the time she reached 3 g. daily she was lively, alert and active. She was discharged on this dose, but five weeks later she again became depressed. When the L-DOPA was raised to 3·75 g. daily, she again recovered; after two weeks on this dose, the depression returned. The L-DOPA was now reduced to 2·25 g., and imipramine was added in doses up to 75 mg.; however, she grew still more depressed. L-DOPA was stopped and ECT started. She recovered partially and was again put on a combination of L-DOPA and imipramine but without effect.

Case 2. A man of 40 was hospitalized for depression at 30, 36 and 38 years of age. During the next two years, he was readmitted six times for attacks of psychomotor retardation, discontent, loss of vitality, muscular hypotension and great fatigue, together with attacks of anxiety combined with pain sensations in different sites. He responded only slightly and briefly to tricyclic antidepressants, anxiety-relieving agents, lithium (he had had one period of apparent hypomania), carbamazepin (because of an abnormal EEG), phenothiazines, butyrophenones and ECT. Finally he was put on L-DOPA. When he reached about 4 g. a day he became more active and more contented and calm: however, he began to vomit and have tremor. The dose was reduced, but the side effects persisted and after about a month the drug had to be stopped. After another four weeks of well-being his depression recurred, but he quickly improved after four ECTs.

Case 3. Man aged 48. At 42 he had a traffic accident and was knocked unconscious for 20 minutes, probably sustaining a fracture at the base of his skull. He had always had a tendency to fits of despondency. After the accident these grew worse, and he was admitted ten times to a mental hospital, suffering from apathy, lack of enterprise, a feeling of intense fatigue, anxiety, irritability, hypersensitivity to light and noise, and a feeling of muscular hypotension. Physical examination showed only an abnormal EEG. The depression resisted tricyclic antidepressants, phenothiazines, anxiety-relieving agents, butyrophenones and anticonvulsants.

At 48 he was started on L-DOPA. When he reached 2 g. daily, he began to improve, and he was discharged free of symptoms on a dose of 3·5 g. A month after the L-DOPA was started, he grew apathetic, despondent and irritable. He was readmitted to hospital, but the drug continually lost its effect. Five months after it was started he was back to his old state and L-DOPA was stopped.

Case 4. A man of 33 with attacks of fatigue and despondency beginning in adolescence, growing gradually worse, and from the age of 29 on making it impossible for him to work. His complaints were: a constant feeling of tiredness and weakness (he got so tired after sexual intercourse with an orgasm that he had to stay in bed for several days afterwards); insomnia, constipation; diffuse stomach and urination complaints; extreme irritability at times. He had taken phenothiazines, tricyclic antidepressants, carbamazepin and sedatives of conventional types, even in overdoses, without any lasting effect. He had been in a mental hospital ten times. Comprehensive neurological, endocrinological and medical examinations showed nothing definitely abnormal. Examination of the lumbar CSF for 5-HIAA and HVA before and after administration of probenicid gave normal values (Roos and Sjöström, 1969).

He was started on L-DOPA, and at 3 g. a day his

condition changed dramatically; he began to sleep well and became normally alert; his subjective complaints disappeared; he could exercise vigorously; psychometric testing showed that he performed at twice the rate he had done two years before and that he functioned well intellectually; he regained his sexual power. To maintain this state, however, larger and larger doses were needed. At 8 g. a day he got a tremor and a feeling of akathisia. Three months after the drug was started its effect began to wane, and five months after it had so little effect that it was stopped.

Case 5. Woman aged 61 with hypertension and splenomegaly of unknown origin. During the last two years she had a few episodes with unconsciousness, probably caused by cerebral ischaemia. After such an episode she showed increasing depressive symptoms with psychomotor retardation, depressed mood and depressive delusions. Air encephalography showed cortical atrophy, and the EEG showed a focus in the left hemisphere. ECT brought about rapid normalization of her depressive state, but some kind of bradyphrenia persisted. She relapsed, however, after a month, and in the course of the last six months she was admitted four times to mental hospital. ECT and various antidepressant drugs were tried with only temporary effects. She received L-DOPA in doses up to 2 g. daily. She has now been on L-DOPA for 22 weeks, is discharged from hospital and is free from depressive symptoms.

Discussion

All five patients, treated over several years with the conventional psychiatric methods with brief or negligible results, recovered or improved markedly on treatment with L-DOPA. However, the drug began to lose effect after a month in the first three cases and after three months in the fourth. In the fifth case, however, the remission hitherto has lasted for about 22 weeks. The vanishing effect could not be influenced by increasing the dose of L-DOPA. In these five cases, no euphoria was observed in spite of the obvious activation. The short-lived effect we observed in at least four cases bears out the experience of other authors that L-DOPA is usually of no definite use in depression, at least in the treatment of chronic depressive states (Goodwin *et al.*, 1970). However, our observations will form the basis for further investigations as to the effect of L-DOPA on psychic disorders.

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(*Received 2 November 1970*)