Gilles de la Tourette's Symptoms Induced by L-Dopa

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SUMMARY

Gilles de la Tourette's and Benedek's symptoms were twice released by L-dopa in a patient suffering from the sequelae of a contusio cerebri. Attendant circumstances of the case offer a functional-neuronal explanation fitting the rules of neuronal denervation and post-denervation supersensitivity according to Cannon's law. The view of a somatogenesis of Gilles de la Tourette's syndrome is supported.

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Gilles de la Tourette's syndrome (GTS) is characterised by a peculiar pattern of motor and phonation tics.[1]

The attention paid to this rare disease has been mainly brought about by its aetiological discussion, which is still in progress since its first description by Gilles de la Tourette[2] and Brissaud.[3] Two recent articles are filled with neurological evidence of its origin on the one hand,[3] and with depth-psychologically-produced reasons on the other.[4]

The case reported here — the first one to our knowledge with Gilles de la Tourette's symptoms iatrogenically released by L-dopa — thematically supports the report of Shapiro and Shapiro[5] on GTS, 'to illustrate the erroneous reading of symptoms . . . resulting from the medical vogue of attributing psychological cause to diseases of unknown aetiology'.

CASE HISTORY

A 32-year-old White male patient suffered contusio cerebri after a car accident, and after about 24 hours regained semiconsciousness and developed extreme motor restlessness. He was treated with low-potency phenothiazines. On admission to a neurosurgical ward, he had spastic deep reflexes on the left side, a left supranuclear facialis paresis, and a positive Babinski sign intermittently on the left side, as well as marked bilateral papilloedema for the first 9 days. A right carotid angiogram was found to be entirely normal. An episode of generalised purpura occurred on the 9th day, but the clotting time, prothrombin estimations, and platelet count were normal.

When we saw the patient, on the 46th day after his accident, no papilloedema was left, but he had trigeminal hypasthenia, some slight central facialis weakness, and arm deep reflexes a trace brisker all on the left side, but no pyramidal signs and no peripheral pareses, rigor or tremor. Except for diminished synkinetic movements of his left arm, there were no deviations of co-ordination whatsoever. He was still disorientated in all three spheres, did not reveal any signs of vegetative somnolence, but a very short span of attention, and the full-blown picture of Korsakoff's syndrome, with only a few and dissociated islets of available memory left, and with a never-ending volley of colourful, rambling confabulations. Emotionally he maintained a situatively independent level of 'empty' friendliness, lacking any adequate emotional resonance to his own situation or actual themes and events in question.

During the first month he received high and various amounts of diazepam, chlordiazepoxide, and thioridazine to control an often occurring motor restlessness and a tendency to wander. Nicotinic acid, vit min B_6, and biperiden were also administered. His adaptation to his environment steadily improved, but only slight amelioration of his flat emotionality and of his amnesia were detectable.

Experience gained in Parkinsonian patients[6] and in my own previous case of Korsakoff's syndrome subsequent to carbon monoxide poisoning, led to a trial of L-dopa being administered to improve the patient's memory. An initial daily dose of 188 mg of L-dopa was slowly increased to 750 mg within 14 days and kept at this level for another 6 days. L-tryptophan 500 mg per day were added to prevent eventual side-effects of L-dopa.[7] During this whole L-dopa trial, 1 200 mg ascorbic acid, 6 mg biperiden, 60 mg diazepoxide and 25 mg amitriptyline were given daily.

After being on 750 mg L-dopa for 3 days, and 16 days after commencing the L-dopa medication, he suddenly developed a marked psychomotor restlessness, went through a few hours' episode of non-induced aggression, but became friendly and calm again as soon as he was addressed by somebody. Later that same day, for no apparent reason, he started to shout loudly, reiterating short phases or single words, mostly without any meaning. When asked about this, he would excuse himself with, 'I can't help it, I feel like shouting'. From the following day on, the shouting spells were interrupted by loudly repeating obscene words without addressing anybody, mostly while alone in his room. One could hear him producing thumping oaths and bad language in a normal low voice, suddenly switching to roaring meaningless words, interrupted by coughing and barking sounds. When someone entered the room, he immediately stopped and apologised for using these expressions and causing a disturbance. He never interrupted himself or others who spoke to him, but as soon as there was a pause in the conversation he

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would suddenly burst out shouting incoherent phrases 'My name is . . .'; 'Pretoria'; 'Kraaifontein'; '1973'; 'I'll go to bed now', etc. At times he repeated a phrase uttered or a question put to him several times and mostly in his normal voice.

From the very start of these symptoms a peri-ocular tic on the left side was observed. The shouting spells, the coprolalia, the echolalia, and the periocular tic gradually diminished 3 days after discontinuing the L-dopa.

To verify a causal connexion between these Gilles de la Tourette's and Benedek's symptoms and the administration of L-dopa, 9 days later (6 days after the last symptoms) L-dopa was readministered, 250 mg daily, and without any other additional drugs. Episodes of shouting, together with some restlessness, again occurred 6 days after recommencing the L-dopa medication, and all the symptoms returned on the next day when L-dopa was finally discontinued. During the subsequent 2 days, the whole syndrome again faded away and did not reappear during the 5 further months of his hospitalisation.

A first electro-encephalograph, 1 month after the accident, was abnormal, with bitemporal delta-activity, accentuated on the left side and enhanced during hyperventilation. A control done 3 months later was completely normal. An air encephalogram done 2 months after the second episode of Gilles de la Tourette's and Benedek's symptoms, revealed a slight dilatation of the whole of the left lateral ventricle, and a more considerably dilated, pear-shaped 3rd ventricle with a diameter of 12 mm.

DISCUSSION

Episodes of Gilles de la Tourette's symptoms and compulsory shouting resembling Benedek's klazomania[8] were twice released by L-dopa in a patient suffering from the sequelae of a contusio cerebri.

The daily doses of 750 mg and 250 mg L-dopa respectively used, were so little that any exogenous percursor excess of subsequently synthesised catecholamine transmitters can be excluded.[9] Thus a mechanism triggering off Gilles de la Tourette's symptoms, other than a substituting or over-substituting effect as in Parkinson's syndrome, is to be supposed here.

The details of the case reported fit the principle of functional neuronal denervation as a consequence of preceding brain oedema, and possible thereby reduced striatal afference, before subsequently developed postdenervation neuronal supersensitivity as a prerequisite to neuronal recovery. Minute amounts of transmitters reaching the receptor sites of supersensitive neurons, generate excessive and increased neuronal efferent activity, an effect fully in accordance with the attendant circumstances of the L-dopa-induced Gilles de la Tourette's symptoms described.

Haloperidol, a potent dopamine receptor blocker, is unequivocally the drug of choice in the treatment of GTS. Snyder *et al.*[11] deduced that hyperactivity of the dopamine system may be a factor in the pathophysiology of GTS. One of the most significant indications that the striatal apparatus and striatal afference is the neurological substrate of GTS, is given by the stereotaxic treatment of GTS by Hassler and Dieckmann.[12]

Coagulation of the medial and intralaminar thalamic nuclei resulted in recovery from both coprolalia and tics, thus demonstrating that (*i*) both motor and phonation tics are due to a hyperkinetic extrapyramidal syndrome, and (*ii*) the striatal afference and pathological pattern of striatal response is responsible for triggering off GTS.

After a hypothalamic lesion of the nigroneostriatal pathway, striatal dopamine synthesis dropped to 15% ipsilaterally,[13] with concomitant marked striatal neuronal glycogen storage,[14] providing the role of nervous afference in striatal neuronal metabolism. De-afferenting processes imply 'neuronal disuse', consequent development of functional denervation and subsequent postdenervation supersensitivity. Primary striatal processes of direct neuronal denervation and secondary de-efferenting lesions may both result in striatal neuronal supersensitivity, until a new steady state of compensatory habituation, neuronal recovery, or partial, irreversible neuronal damage is established. Taking into account the typical onset of GTS in childhood, and the frequent spontaneous remission during adult life, these items mentioned favour the view of Fisarova[15] of a causal role of perinatal lesions in their 29 patients, and accord with the childhood developmental abnormalities traced by Shapiro *et al.*[16] in 52% of their cases, 35% being left-handed. Moreover, Sweet and coworkers,[1] besides 36% left-handers, found mild motor asymmetries in 11 of their 22 patients, dismissing the allegation that neurological deviations were extremely rare in GTS.[4]

Our own observation of L-dopa-induced Gilles de la Tourette's symptoms in a brain-lesioned patient, supports the view that for heuristic gain preference should be given to objective findings instead of Freudian approaches to syndromes of yet unknown origin.

REFERENCES

1. Sweet, R. D., Solomon, G. E., Wayne, H., Shapiro, E. and Shapiro, A. K. (1973): J. Neurol. Neurosurg. Psychiat., **36**, 1.
2. Gilles de la Tourette, G. E. A. B. (1885): Arch. neurol. (Paris), **9**, pp. 19, 158.
3. Brissaud, P. E. (1896): Rev. neurol., **4**, 417.
4. Lawall, P. C. and Pietzcker, A. (1973): Fortschr. Neurol. Psychiat., **41**, 282.
5. Shapiro, A. K. and Shapiro, E. (1971): Psychiat. Quart., **45**, 159.
6. Goodwin, F. K. (1971): J. Amer. Med. Assoc., **218**, 1915.
7. Birkmayer, W. and Mentasi, M. (1972): Dtsch. Ärztebl., 686.
8. Benedek, L. (1925): Z. ges. Neurol. Psychiat., **98**, 17.
9. Romero, J. A., Lytle, L. D., Ordonez, L. A. and Wurtman, R. J. (1973): J. Pharmacol. Exp. Ther., **184**, 67.
10. Glick, S. D., Greenstein, S. and Zimmerberg, B. (1972): Science, **177**, 534.
11. Snyder, S. H., Taylor, K. M., Coyle, J. T. and Meyerhoff, J. L. (1970): Amer. J. Psychiat., **127**, 199.
12. Hassler, R. and Dieckmann, G. (1970): Rev. neurol., **123**, 89.
13. Nyback, H. and Sedvall, G. (1971): J. Pharm. Pharmacol., **23**, 322.
14. Hoffmann, P. C., Toon, R., Kleinman, J. and Heller, A. (1973): J. Neurochem., **20**, 69.
15. Fisarova, M. (1972): Cs. Neurol., **35**, 202.
16. Shapiro, A. K., Shapiro, E. and Wayne, H. (1972): J. Nerv. Ment. Dis., **155**, 335.