Response of Tardive and L-Dopa-Induced Dyskinesias to Antidepressants

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ABSTRACT: We report two patients with dyskinesia responding to antidepressants. The first is a 70-year-old man with depression, Parkinsonism and neuroleptic-induced tardive dyskinesia who presented with hysterical mutism. After recovery from the mutism, he was started on desipramine for depression. One week later the dyskinesia improved markedly. The second patient is a 61-year-old man with Parkinson's disease, dementia, depression and L-dopa-induced oro-lingual-facial dyskinesias. He was taking levodopa, trihexyphenidyl and bromocriptine. The depression was treated first with desipramine and later with trazodone. The dyskinesia improved significantly on both drugs. The response of the dyskinesias to antidepressant medication may be due to the fact that antidepressants decrease beta-adrenergic receptor sensitivity and density which in turn may result in a diminished release of dopamine since beta-adrenergic receptors mediate the noradrenaline-stimulated release of dopamine.

RÉSUMÉ: Réponse au traitement par les antidépresseurs des dyskinésies tardives et de celles qui sont induites par la L-dopa. Nous rapportons les cas de deux patients dont les dyskinésies ont répondu au traitement par les antidépresseurs. Le premier est un homme âgé de 70 ans souffrant de dépression, de la maladie de Parkinson et de dyskinésies tardives induites par les neuroleptiques et qui a présenté un mutisme hystérique. Après avoir recouvré l'usage de la parole, il a reçu de la désipramine pour traiter sa dépression. En une semaine, les dyskinésies se sont améliorées de façon appreciable. Le second patient est un homme âgé de 61 ans souffrant de la maladie de Parkinson, de démence, de dépression et de dyskinésies oro-lungo-faciales induites par la L-dopa. Il prenait de la lévodopa, du trihexyphénidyle et de la bromocriptine. La dépression a été traitée d'abord avec de la désipramine et ensuite du trazodone. Les dyskinésies se sont améliorées de façon significative avec ces deux médications. La réponse des dyskinésies à la médication antidépressive est peut-être due au fait que les antidépresseurs diminuent la sensibilité et la densité des récepteurs bêta-adrénergiques ce qui peut occasionner une diminution de la libération de la dopamine, les récepteurs bêta-adrénergiques servant de médiateurs pour la libération de la dopamine sous stimulation noradrénénigique.

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Case reports

Patient 1 A 70-year-old, right-handed man was admitted to the Baycrest Hospital Behavioural Neurology Unit with a one-year history of mutism. The mutism began one month following insertion of a cardiac pace maker for complete heart block complicating a myocardial infarction. He also became completely withdrawn, sitting in a chair all day, rising only to eat. He was able to dress and feed himself but extremely slowly. Eleven years earlier he was admitted to hospital following a right
On admission he was mute and had a stooped posture, shuffling gait, and at times seemed stuck to the floor. He had a positive glabellar tap. He was able to match letters but did not read aloud. Reading comprehension to questions with words and short phrases. This occurred during a 1/2-hour period. Later that day he began to speak in complete sentences spontaneously and the patients were medication free. DePorter et al 12 reported a patient with rapid cycling between mania and the euthymic state. The patient had neuroleptic-induced oro-buccolingual dyskinesias and signs of parkinsonism. The dyskinesia was drug resistant, but remitted during the manic phase and relapsed during the euthymic phase. The parkinsonism did not change.

Unlike the above cases, our first patient did not have a bipolar affective disorder and the tardive dyskinesia improved in response to medication. The response occurred by about one week after the introduction of desipramine. It is of note that the depressive symptoms had not improved by that time.

Rosenbaum et al 13 report improvement in depressed patients who have tardive dyskinesia. In their patients both the depression and the tardive dyskinesia improved in response to a combination of tricyclic antidepressants and lithium carbonate. The improvement occurred one to two months after the beginning of treatment.

The alleviation of tardive dyskinesia by antidepressants may be explained by the fact that antidepressants decrease beta-adrenoceptor sensitivity14 and density. 15 Since beta-adrenoceptors mediate the noradrenaline-stimulated release of dopamine, a decrease in beta-adrenoceptor density would result in a diminished spontaneous release of dopamine with diminished dopaminergic dyskinesia. Slightly offsetting this mechanism is the fact that long-term antidepressants appear to sensitize animals to the post-synaptic locomotor effects of dopamine-mimetics.19-20 This post-synaptic sensitizing action may result from an antidepressant-induced subsensitivity of pre-synaptic dopamine receptors.21,22 This sensitizing factor, however, is small compared to the decrease in beta-adrenoceptors. The alleviation of tardive dyskinesia by beta-adrenoceptor sensitivity cannot here be accounted for by a spontaneous reduction in the dyskinesia, since such spontaneous reductions occur gradually over a matter of months.

In the second patient both desipramine and trazodone improved the dyskinesias. Trazodone shares with the tricyclic antidepressants the property of decreasing adrenoceptor sensitivity and density.

Although the dyskinesias in our two patients each had a different etiology, the implication of the above effect and mechanism of action of desipramine and trazodone, if further validated, is that antidepressants could be a useful treatment for tardive dyskinesia and levodopa-induced dyskinesias, even in the absence of depression.

DISCUSSION

In manic-depression, tardive dyskinesia may improve during mania and may be exacerbated during the depressed or euthymic phases.11,12 Cutler et al 11 described two patients with state-dependent dyskinesia. Rapid switches between the two states were accompanied by recurrence of the dyskinesia during depression and disappearance during mania. The switches were spontaneous and the patients were medication free. DePotter et al 12 reported a patient with rapid cycling between mania and the euthymic state. The patient had neuroleptic-induced oro-buccolingual dyskinesia and signs of parkinsonism. The dyskinesia was drug resistant, but remitted during the manic phase and relapsed during the euthymic phase. The parkinsonism did not change.

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ACKNOWLEDGEMENTS

We are indebted to the late Dr. Norman Geschwind, whose creative insights into the relationship between depression and tardive dyskinesia stimulated us to observe the findings reported in this paper.

This study was supported by grants from the Medical Research Council of Canada (#MA-8908), the Ontario Mental Health Foundation (#948-86-88), and a scholarship from the Gerontology Research Council of Ontario to Dr. Freedman.

We thank Vicki Gilchrist for secretarial assistance.

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