Neurogenic stuttering and lateralized motor deficits induced by tranylcypromine

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A case of neurogenic stuttering induced by the monoamine oxidase inhibitor tranylcypromine is described. The association of neurogenic stuttering with acquired lateralized motor deficits in the patient described is discussed with reference to current theories regarding the pathogenesis of neurogenic stuttering.

Keywords: Dominance – Stuttering – Tranylcypromine

INTRODUCTION

Although there is currently no universally accepted definition of primary developmental stuttering, Wingate's description appears to be the most accurate and succinct definition of the disorder, i.e. "Stuttering is a disruption in the fluency of verbal expression characterized by involuntary audible or silent repetitions or prolongations in the utterance of short speech elements, e.g. sounds, syllables, and words of one syllable" (Wingate, 1964). Neurogenic stuttering (also referred to as "acquired stuttering") has also not been clearly defined but it may probably be most accurately, and simply, described as a "stutter-like" speech disruption secondary to nervous system damage (Canter, 1971). Neurogenic stuttering has been associated with a number of neurological conditions including cerebrovascular accidents, head trauma, Parkinson's disease and haemodialysis dementia (Rosenbek *et al.*, 1975, 1978; Soroker *et al.*, 1990). In addition, neurogenic stuttering has been reported to have been induced by psychotropic agents including phenothiazines (Nurnberg and Greenwald, 1981), alprazolam (Elliott and Thomas, 1985), tricyclic antidepressants (Quaker, 1977) and theophylline (McCarthy, 1981). Most of the case reports of verbal dysfluency occurring in association with antidepressant medications describe speech blockage and word finding difficulties, rather than phonation difficulty (i.e. stuttering), as the predominant characteristic of the patient's verbal dysfluency (Brady, 1991). Helm *et al.* (1978) identified five characteristics that apparently differentiate acquired stuttering from primary developmental stuttering. These are: (1) no

adaption effect (i.e. the subject does not exhibit increasing fluency with practice); (2) repetitions, prolongations, and blocks not restricted to initial syllables; (3) stuttering on small grammatical words as well as substantive words; (4) possible annoyance but not anxiety; (5) rare secondary symptomatology such as facial grimacing and fist clenching.

This report describes a case of neurogenic stuttering induced by the monoamine oxidase inhibitor tranylcypromine. It is interesting to note that although a review of the literature reveals one previous report of neurogenic stuttering by phenelzine (another monoamine oxidase inhibitor), another recent case report describes a patient whose verbal dysfluency actually improved on tranylcypromine (Goldstein and Goldberg, 1986; Oberlander, 1993).

The occurrence of neurogenic stuttering with concurrent lateralized motor deficits in this case report is a provocative clinical finding that is discussed in the light of current theories regarding the pathogenesis of stuttering. This clinical association is particularly interesting in the context of current theories of stuttering that propose a dysregulation of the left hemisphere's usual dominance for fluent speech production.

CASE REPORT

The patient, a 14 year old left-handed female, was admitted to the adolescent psychiatric unit following repeated runaways, suicidal ideation and conflict with her parents. Upon admission, she met DSM-III-R

TABLE I. Patient's speech productivity and lateralizing hand motor function on and off tranylcypromine

Measure	On tranylcypromine	Two days post- tranylcypromine	Eleven days post- tranylcypromine	Comments
Grooved pegboard test	L, 75 s R, 71 s	L, 61 s R, 60 s	L, 65 s R, 68 s	Measures the time required to complete pegboard (normal range: dominant hand 62.6-77.6 s, non-dominant 53.2-79.8 s)
Finger oscillation test	L, 31.4 R, 33.8	L, 40.6 R, 31.4	L, 41.0 R, 37.2	Measures average number of taps in 10 s (normal range: dominant hand 40.8-49, non-dominant 35.5-44.5)
Verbal fluency	14	29	32	F-A-S words (normal 37.3-5.3 words in 2 min).
Non-verbal agility	12	26.5	29	From the Boston Diagnostic Aphasia Examination (16).
Verbal agility	8	25	43	Qualitative From the Boston Diagnostic Aphasia Examination. Qualitative (16)

criteria for a severe major depressive disorder with suicidal ideation and melancholia. As the patient was adopted, no formal biological family history was available. The patient and her family were unaware of any traumatic birth injury or delayed developmental milestones. There was no significant previous medical history. She had no identified allergies.

Upon admission, physical examination revealed a left-handed female with normal physical and sexual development. Neurological examination was normal with no focal neurological deficits identified. Prior to receiving tranylcypromine she exhibited no unusual facial movements and made good eye contact.

Psychological evaluation demonstrated a severe level of depression, an external locus of control and features consistent with a borderline personality disorder. The patient produced a verbal IQ of 113, performance IQ of 106 and full score IQ of 111 on the WAIS-R.

The patient was started on desipramine and maintained on a dose of 200 mg orally for approximately 2 months. Despite this, her affective disorder failed to improve and following an appropriate "washout" interval of 2 weeks and tyramine-free diet she was placed on tranylcypromine starting at 10 mg p.o. twice daily. Three days following the introduction of the monoamine oxidase inhibitor the patient was noted to have developed mild stuttering. Following

an increase of the tranylcypromine to 30 mg daily, there was a further increase in the patient's verbal dysfluency.

Assessment of the patient's speech pattern demonstrated a severe dysfluency characterized by audible repetitions, prolongations, hesitations and blocks of initial phonemes. Dysfluent behaviors were noted on 304 of a 900 word, 10 minute speech sample. Secondary speech characteristics included poor eye contact, circumlocutions and laryngeal and labial tensions. The verbal dysfluencies persisted with singing and miming. These speech characteristics were therefore characteristic for stuttering rather than word finding difficulties.

Neuropsychological testing at this time revealed reduced verbal and non-verbal agility as measured by components of the Boston Diagnostic Aphasia examination (Goodglass and Kaplan, 1983). The patient exhibited decreased performance in her left dominant hand on the grooved pegboard and finger oscillation tests (Table I). Auditory verbal learning and written fluency were measured to be within normal limits. In view of the patient's increasing dysfluency, tranylcypromine was discontinued 11 days after starting it. The neuropsychological battery described above was repeated on Days 2 and 11 after discontinuing the drug. This serial testing demonstrated that the patient's improving verbal fluency directly correlated with an improvement in her left-sided motor skills.

Electroencephalography performed several weeks after discontinuation of tranlylcypromine demonstrated a minor background dysrhythmia bilaterally which consisted of scattered sharp forms, no paroxysmal abnormalities and an alpha background frequency of 12 Hz.

In the 6 month period following the discontinuation of tranlylcypromine the patient has exhibited no further stuttering.

DISCUSSION

A number of theories have been proposed to describe the pathogenesis of neurogenic and developmental stuttering. The production of normal fluent speech is a complex function involving both cerebral hemispheres. In the left hemisphere-dominant individual, the left hemisphere with its greater neural mass in the left planum temporale area and its specific left thalamic functions appears to be specialized for time-dependent, non-segmental (i.e. semantic) speech functions (Moore, 1984).

Early speech theorists postulated that primary developmental stuttering occurs as a consequence of inadequate dominance by the "appropriate" dominant (usually left) hemisphere with a resultant desynchronization of speech production (Orton, 1927). More recent research utilizing regional cerebral blood flow studies (Stump and Williams, 1980; Denays *et al.*, 1989; Pool *et al.*, 1991), electroencephalographic mapping (Boberg *et al.*, 1983) and tachistoscopic visual procedures (Moore, 1976) have suggested left frontal and peri-sylvian dysfunction in patients who stutter. Poole *et al.* (1991), utilizing ^{133}Xe single photon emission computed tomography, demonstrated significant relative flow asymmetries (left < right) in the anterior cingulate superior and middle temporal gyri. This lateralized dysfunction is postulated to produce a reversed cerebral dominance with right hemispheric semantic functioning assuming a dominance for speech among stutterers. In the light of these findings, neurogenic stuttering may be postulated to occur as a result of an acquired dysregulation of the left hemisphere's usual dominant role in the production of fluent speech. This hypothesis is not supported however by a review of 10 patients who developed chronic acquired stuttering after sustaining penetrating brain lesions. This study reported that the penetrating lesions associated with acquired stuttering most frequently involved the internal and external capsules, frontal white matter and striatum with a uniform bilateral distribution (Ludlow *et al.*, 1987). In the light of current conflicting clinical evidence the pathophysiology of stuttering therefore remains unclear.

The fact that the patient described in this paper normally exhibited left hand motor dominance raises doubts about her hemispheric specialization for "phonologic" and "semantic" speech production. In view of the theories described above it is possible that she possessed reversed dominance for speech production. The mechanism by which tranlylcypromine produced apparent right hemisphere motor dysfunction and verbal dysfluency in the patient described is uncertain. It is interesting to note that the patient had previously received desipramine at therapeutic oral dosages without any adverse effect upon her speech production. This would suggest that, as has been postulated previously (Schatzberg *et al.*, 1978), the anticholinergic activity of tranlylcypromine is probably not implicated in the pathogenesis of this patient's stuttering.

Haloperidol has demonstrated efficacy in improving the verbal fluency of "developmental" stutterers. Wood *et al.* (1980) have demonstrated shifts in regional cerebral blood flow from the non-dominant (i.e. right) to the dominant (i.e. left) hemisphere in patients whose dysfluency improved on haldol. It is possible therefore that the dopaminergic activity of tranlylcypromine may be implicated in this described patient's shift in motor dominance and concomitant dysfluency. The apparent laterality of tranlylcypromine's action upon this patient's right hemisphere is intriguing. Whether this represents an idiosyncratic neurodevelopmental vulnerability in this patient or relative specificity of tranlylcypromine's activity to the right hemisphere is open to speculation. It is interesting to note a single case study which demonstrated a differential effect of lithium upon the right hemisphere as measured by dichotic listening indices (Haran *et al.*, 1987). Although there is literature to support the concept of a differential involvement of right and left hemisphere structures in primary and secondary mood disorders (Flor-Henry, 1983; Robinson and Starkstein, 1990), and the biogenic amines serotonin and dopamine have been shown to exhibit modest lateralization to the right and left hemisphere, respectively (Glick, 1983; Arato *et al.*, 1991), there has been very little work attempting to identify any lateralizing specificity in the effect of psychotropics. Further research in this area offers the opportunity for a better understanding of psychotropic drug action and the genesis of behavioral disorders.

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