Current PSYCHIATRY

New therapies can help patients who stŭt'tər

Stuttering, which impairs social and occupational functioning, has been receiving more attention as a clinical psychiatric disorder. Treatment based on neurophysiology and advancements in psychopharmacology can offer these patients hope.

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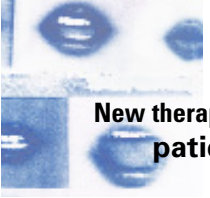
Despite its prevalence, stuttering has not received as much attention as other psychiatric disorders from patients or psychiatrists—with good reason. Until recently, little was known about the neurophysiology of stuttering, and treatment was generally ineffective especially in adults (*Box 1*). Despite their own personal struggles with the disorder, patients have questioned the need for psychiatric treatment.

That has now changed. We know now that stuttering is likely a disorder of brain chemistry. Studies suggests that olanzapine, a novel dopamine antagonist, is a useful, well-tolerated medication for the treatment of stuttering. As a result, psychiatrists are now equipped to play an important role in its management.

Furthermore, we can give patients the therapeutic opportunity to discuss what often has been a lifetime of frustration with stuttering. We can enable them to understand the course and treatment of this disorder and encourage them to take advantage of the opportunities to lessen the symptoms of stuttering and, ultimately, improve their quality of life.

How stuttering develops

Stuttering is a speech disorder characterized by frequent prolongations, repetitions, or blocks of spoken sounds and/or



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Box 1

Neither tongue cutting nor psychoanalysis has worked

Stuttering has occurred throughout history, with descriptions from the ancient Egyptians and Greeks. For centuries, theories on its etiology involved abnormalities in the tongue or larynx, and the treatments addressed such ideology. Even today, some stuttering treatments involve such archaic methods as cauterizing or cutting the tongue. Treatments focused on the tongue or larynx have not demonstrated consistent efficacy.

The pioneering work of Orton[21] and Travis[22] signaled a significant change in the understanding of stuttering. They postulated that stuttering may arise from abnormal cerebral activity, signaling a significant change in the theories of the etiology of stuttering. Unfortunately, stuttering treatments did not reflect this new understanding until fairly recently.

Psychoanalytic theorists believed that stuttering arose from the individual's attempt to fulfill some type of unconscious neurotic need, usually resulting from disturbed early parent-child interaction.[23] Psychoanalytic therapy was largely ineffective, however.

Most stuttering treatment practiced today involves speech therapy utilizing cognitive and behavioral methods. Such methods are often limited in their efficacy, especially in adults.[24] Some forms of therapy involving speech motor training have been shown effective in young children while the brain is still in development.[25] The pharmacologic treatment of stuttering is not widespread today, but new and recent research identifying certain cerebral abnormalities is providing clues for pharmacologic interventions.

syllables. A common disorder affecting 1% of adults and 4% of children, stuttering is classified in DSM-IV as an Axis I disorder (*Box 2*).[1]

By definition, stuttering can interfere with social, academic, or occupational functioning. Persons who stutter often develop secondary behaviors such as avoidances of words, phrases, or even social situations, which in turn leads to a high level of social anxiety.[2]

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Stuttering usually begins in childhood and is likely a developmental disorder. Rare cases of acquired stuttering begin in adulthood but are related to secondary causes such as medications, brain trauma, or stroke.[3] Some 80% to 90% of developmental stuttering begins by age 6; onset after age 9 is likely to have some psychogenic or neurogenic basis.[4] In approximately 60% of the children who stutter, the symptoms will remit by age 16. Children who stutter require early intervention, given the importance of communication in a child's development.[5]

Stuttering shares many similarities with Tourette syndrome. Both begin in childhood, follow a waxing or waning course, have a 4:1 male-to-female ratio, are made worse by anxiety, involve abnormalities in the basal ganglia, and respond to dopamine antagonist therapy.[6] Persons who stutter often exhibit tic motions, similar to those seen in Tourette syndrome, which are associated with the struggles to produce speech. Genetic studies have shown possible high additive genetic effects; pair-wise concordance for stuttering was significantly higher in identical twins (63%) than it was in fraternal same-sex twins (19%).[7,8] Researchers are investigating potential molecular genetic markers for stuttering.

Functional brain imaging studies suggest that stuttering is associated with abnormal cerebral activation primarily involving abnormally low metabolism of the cortical speech areas and the striatum. The defects in stuttering occur primarily in the timing and initiation of spontaneous speech, with such tasks as singing and reading in chorus being spared. A clue to understanding stuttering lies with these "induced fluency" tasks.

Functional positron emission tomography studies utilizing ^{18}F-deoxyglucose showed that stuttering is associated with abnormally low metabolism of speech cortical areas (Wernicke's and Broca's) and low metabolism of the basal ganglia, notably the striatum. During the induced fluency, Wernicke's and Broca's areas normalize but the striatum remains abnormally low.

Riley postulates two "loops" of speech, an inner or medial system and an outer or lateral system.[9] The lateral system is preserved in stuttering and can be activated through singing, rhythmic speech, etc., but the inner loop, as mediated by the

Box 2

DSM-IV diagnostic criteria for stuttering

A. Disturbance in normal fluency and time patterning of speech (inappropriate for the individual's age), characterized by frequent occurrences of one or more of the following:
   1. Sound and syllable repetitions
   2. Sound prolongations
   3. Interjections
   4. Broken words (e.g., pauses within a word)
   5. Audible or silent blocking (filled or unfilled pauses in speech)
   6. Circumlocutions (word substitutions to avoid problematic words)
   7. Words produced with an excess of physical tension
   8. Monosyllabic whole-word repetitions (e.g., "I-I-I-I see him")

B. The disturbance in fluency interferes with academic or occupational achievement or with social communications

C. If a speech-motor or sensory deficit is present, the speech difficulties are in excess of those usually associated with these problems.

Coding note: If a speech-motor or sensory deficit or a neurological condition is present, code the condition on Axis III.

striatum and influenced by dopamine, remains impaired. Once a person who stutters initiates speech, he or she often avoids taking a breath as the whole system must again be jump-started. The low striatal metabolism may be the common-state phenomenon underlying this timing.

The dopamine hypothesis of stuttering

Stuttering is likely related to abnormal elevations of cerebral dopamine activity. Stimulant medications, which increase dopamine activity, have been shown to increase stuttering symptoms.[10] As will be reviewed later, dopamine antagonist medications have been shown to improve the symptoms of stuttering. Also, the striatal hypometabolism in stuttering seen in PET imaging may be a result of a hyperdopaminergic state.

To investigate this dopamine hypothesis of stuttering, Wu et al measured presynaptic dopamine levels in individuals who stutter.[11] These were found to have 50% to 200% higher levels of dopamine activity than did the controls. Dopamine is inhibitory to striatal metabolism, providing an

explanation for the striatal hypometabolism seen in stuttering. Also, risperidone was found to increase striatal metabolism in those whose stuttering improved on this medication.[12]

Evaluating the patient

One should begin with a comprehensive psychiatric history. Because many patients began stuttering in childhood and have had difficulty dealing with their disorder, other psychiatric disorders such as social phobia may be present. Moreover, other medical etiologies (e.g., stroke) may cause a speech disorder that resembles stuttering.

Stuttering involves abnormalities in fluency as well as tic motions and cognitive avoidances. Inquiries should be made as to the patient's fluency of speech during work, during introductions, speaking in front of an audience, with family, etc.; the level of stuttering can vary depending on the particular environment.

Stuttering fluency can be rated through an objective scale known as the Riley SSI-3.[13] This scale measures the duration of each stuttering event, the percentage of syllables stuttered versus syllables spoken, the severity of associated tic motions, and a global score of the aforementioned components. Because most psychiatrists cannot routinely perform this scale to assess the patient's progress, it is best to partner with a speech-language pathologist who can also assist the patient through speech therapy.

Nonetheless, you may assess the progress of treatment by relying on your own "ear," the patient's own assessment, and the input of a significant other or family member.

In addition to considering DSM-IV criteria, comprehensive treatment should address all aspects of this disorder, including not only the fluency enhancement but improvement in social avoidances and cognitive restructuring. Be aware that stuttering waxes and wanes over time. You should expect to see some "dips" in efficacy during the course of therapy. A longitudinal assessment over several months is needed to determine if the stuttering treatment is efficacious.

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What we've learned about drug therapy

Many medications have been tried to treat stuttering but few have shown efficacy in well-controlled trials. Most pharmacologic studies did not include a placebo control or employ objective measures of stuttering severity, nor did they provide multiple baseline and treatment measures.

The critical new knowledge is this: Medications that lower dopamine activity have shown replicated efficacy in improving stuttering. The benzodiazepines have been shown to reduce anxiety short-term but have not been shown to improve fluency in stuttering. Limited studies of serotonergic antidepressants suggest a possible role in reducing the social anxiety of stuttering but have not been shown in well-controlled trials to improve stuttering fluency directly.

Multiple studies of haloperidol in the 1970s showed that this medication improved fluency in individuals who stutter. Long-term compliance with this medication, however, was poor given its dysphoric side effects, sexual dysfunction, extrapyramidal concerns, and risks of tardive dyskinesia. Limited research with calcium-channel-blocking medications (e.g., verapamil, nimodipine) showed limited efficacy in stuttering.[14,15] Calcium-channel blockers, however, may exert a mild antidopamine effect.

Further supporting dopamine hyperactivity in the pathology of stuttering, Stager et al compared pimozide (n = 6), a selective dopamine (D_2) antagonist, paroxetine (n = 5), a highly selective serotonin reuptake inhibitor, and placebo (n = 6). The researchers found a positive clinical response in those on pimozide compared with those taking placebo, whereas the paroxetine group exhibited no clinical response.[16] Although small, such a study supports the hypothesis that dopamine may be a principal transmitter involved in stuttering pathology, and serotonin may play a minor role, if any.

> Medications that lower dopamine activity have shown replicated efficacy in improving stuttering

Risperidone, a newer-generation dopamine antagonist with a side-effect profile more favorable than haloperidol, has been shown in a well-controlled, double-blind, placebo-controlled study to improve stuttering symptoms (0.5 mg to 2

mg/d). Although generally well tolerated, long-term compliance was hindered by prolactin-related side effects such as sexual dysfunction, galactorrhea, amenorrhea, and dysphoria.[17] Dysphoria with risperidone has also recently been reported to occur with its use in Tourette disorder.[18]

Olanzapine is a novel psychotropic medication that possesses dopamine-blocking qualities but is not associated as much with prolactin-related side effects or dysphoria. A preliminary open-label study suggests that it too improves the symptoms of stuttering.[19]

A multicenter study of olanzapine in the treatment of adult developmental stuttering involved 23 adults in a 3-month, double-blind, placebo-controlled trial preceded by a 1-month baseline rating period. At the end of the double-blind phase, subjects were followed for 1 year. Olanzapine (2.5 mg titrated to 5 mg/d) was shown to exert a statistically significant improvement over placebo in multiple objective measures of stuttering severity. The medication was well tolerated without prolactin-associated side effects. Concerns of appetite increase and weight gain with olanzapine were minimized through simple education. The average weight gain was 4 lb in the treatment group, compared with 1 lb in the placebo group. Compliance was also high. All subjects elected to enter the open-label phase of the protocol.

In many patients in the study, stuttering symptoms have continued to improve over 6 months to 1 year or even longer, suggesting that an adequate treatment trial should be measured not in days or even weeks, but possibly months. Also, some individuals in the open-label phase have shown even further efficacy with dose escalation to 7.5 mg to 10 mg/d or higher of olanzapine.[20]

It is likely, however, that pharmacologic treatment will not be the total answer. In the studies cited earlier, the novel dopamine antagonists led to significant—yet only partial—reductions in stuttering symptoms. The future of optimal stuttering treatment will likely involve the active collaboration between a speech language pathologist and a psychiatrist, using speech therapy to enhance the positive benefits of the medication.

References

1. American Psychiatric Association. *DSM-IV-R*. Washington, DC: American Psychiatric Association, 2000.
2. Maguire GA, Riley GD, Franklin DL, Wu JC, et al. The dopamine hypothesis of stuttering and its treatment implications. *Intern J Neuropsychopharmacology* 2000;3(1).
3. Ludlow CL, Dooman AG. Genetic aspects of idiopathic speech and language disorders. *Otolaryngol Clin N Am* 1992;25(5):979-94.
4. Manning WH. *Clinical decision making in fluency disorders*. 2nd ed. San Diego, Calif: Singular, 2001;107-8.
5. Riley G, Ingham J. Acoustic duration changes associated with two types of treatment for children who stutter. *J Speech Language Hearing* 2000;43:965-78.
6. Wu JC, Maguire GA, et al. A positron emission tomography [18F] deoxyglucose study of developmental stuttering. *Neuroreport* 1995;6:501-5.
7. Felsenfeld S, Kirk KM, Zhu G, et al. A study of the genetic and environmental etiology of stuttering in a selected twin sample. *Behav Gen* 2000;30(5):359-66.
8. Howie PM. Concordance for stuttering in monozygotic and dizygotic twin pairs. *J Speech Hearing Research* 1981;24(3):317-21.

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Related resources

- National Stuttering Association http://www.nsastutter.org
- University of California-Irvine Medical Center: Facts About Stuttering. http://www.ucihealth.com/News/ UCI%20Health/stutter2.htm
- Hulstijn W, Peters HFM, Van Lieshout PHHM, eds. *Speech Production: Motor Control, Brain Research and Fluency Disorders*. International Congress Series 1146. Amsterdam, Netherlands: Excerpta Medica, 1997.

DRUG BRAND NAMES

Haloperidol • Haldol
Nimodipine • Nimotop
Olanzapine • Zyprexa
Paroxetine • Paxil
Pimozide • Orap
Risperidone • Risperdal

DISCLOSURE

Drs. Maguire and Franklin report that they receive grant/research support from, serve as consultants to, and are on the speaker's bureau of Eli Lilly & Co.

Dr. Maguire also reports that he receives grant/research support from Johnson & Johnson, and serves on the speaker's bureau of Pfizer Inc. and GlaxoSmithKline.

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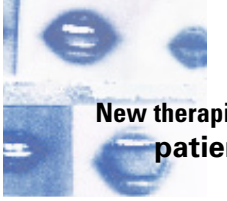
Bottom Line

Stuttering is a speech disorder characterized by frequent prolongations, repetitions, or blocks of spoken sounds and/or syllables. With what has been learned recently of the dopamine hypothesis, novel pharmacologic treatments, particularly with olanzapine, appear to be effective.



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9. Riley GD, Wu JC, Maguire GA. Pet scan evidence of parallel cerebral systems related to treatment effects. In Hulstijn W, Peters HFM, Van Lieshout PHHM (eds.), *Speech Production: Motor Control, Brain Research and Fluency Disorders.* Amsterdam: Excerpta Medica, 1997.
10. Burd, L; Kerbeshian, J. Stuttering and stimulants [letter]. *J Clin Psychopharmacology* 1991;11(1):72-3.
11. Wu JC, Maguire G, Riley G, et al. Increased dopamine activity associated with stuttering. *Neuroreport* 1997;8(3):767-70.
12. Maguire GA. The Dopamine Hypothesis of Stuttering and its Treatment Implications. Presented at Collegium Internationale Neuro-Psychopharmacologicum. Brussels, Belgium, July 2000.
13. Riley G. *Stuttering Severity Instrument.* 3rd ed. Austin, Tex: ProEd, 1994.
14. Brady JP, McAllister TW, Price TR. Verapamil in stuttering [letter]. *Biol Psychiatry* 1990;27(6):680-1.
15. Maguire G, Riley G, Hahn R, Plon L. Nimodipine in the treatment of stuttering. *ASHA Journal* 1994;36:51.
16. Stager S, Calis K, Grothe D, et al. A double-blind trial of pimozide and paroxetine for stuttering. In: Hulstijn W, Peters HRM, van Lieshout PHHM, eds. *Speech Production: Motor Control, Brain Research and Fluency Disorders.* International Congress Series 1146. Amsterdam: Excerpta Medica, 1997:379-82.
17. Maguire GA, Riley GD, Franklin DL, Gottshalk LA. Risperidone for the Treatment of Stuttering. *J Clin Psychopharmacology* 2000;20:479-82.
18. Margolese HC, Annabel L, Dion Y. Depression and dysphoria in adult and adolescent patients with Tourette syndrome treated with risperidone. Presented at the American College of Neuropsychopharmacology, Waikoloa, Hawaii Dec. 10, 2001.
19. Lavid N, Franklin DL, Maguire GA. Management of Child and Adolescent Stuttering with Olanzapine: Three Case Reports. *Ann Clin Psychiatry* 1999;11(4):233-36.
20. Maguire GA, et al. Olanzapine in the Treatment of Adult Developmental Stuttering. Presented at the American College of Neuropsychopharmacology, Waikoloa, Hawaii Dec. 10, 2001.
21. Orton ST. Studies in stuttering. *Arch Neurology Psychiatry* 1927;18:671-2.
22. Travis LE. *Speech Pathology.* New York: Appleton-Century-Crofts, 1931.
23. Sadock BJ, Sadock VA. *Kaplan and Sadock's Comprehensive Textbook of Psychiatry.* 7th ed. Baltimore, Md: Lippincott Williams & Wilkins, 2000.
24. Manning WH. *Clinical Decision Making in Fluency Disorders.* 2nd ed. San Diego, Calif: Singular Publishing, 2001;311-14.
25. Riley G, Ingham J. Acoustic duration changes associated with two types of treatment for children who stutter. *J Speech Language Hearing* 2000;43:965-78.