Stuttering: an update for physicians

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Abstract

STUTTERING IS A DISTURBANCE IN THE NORMAL FLUENCY and time patterning of speech. Developmental stuttering (DS), with or without associated psychiatric illness, is the most common form and includes all cases with gradual onset in childhood that are not the result of acquired brain damage. Persistent developmental stuttering (PDS) is DS that has not undergone spontaneous or speech-therapy–induced remission. Organic models of DS focus on incomplete lateralization or abnormal cerebral dominance. There is also evidence that DS has a significant genetic component to its cause. Neuroimaging research data and the effectiveness of dopamine receptor antagonists in DS seem to support the theory of a hyperdopaminergic origin. Speech therapy remains the main treatment for DS; however, antidepressants can be useful in selected cases. Risperidone, a serotonin-dopamine antagonist, has been shown to be more effective than placebo in decreasing the severity of stuttering. The long-term efficacy and safety of serotonin-dopamine antagonists in DS deserve further study.

The case

A 35-year-old man who stutters is very anxious when speaking outside speech therapy situations. Although he has a good relationship with his physician, he hesitates to request help from the latter. The man is worried that his family physician might conclude that he suffers from a mental illness. He is about to start a new job and is concerned that his persisting fluency problem and speech-related fears are going to interfere with his work. Eventually he contacts his family physician's office for an appointment.

Stuttering is a disturbance in the normal fluency and time patterning of speech that is inappropriate for the person's age.[1] The disturbance may interfere with academic and professional achievement or social communication. Developmental stuttering (DS), with or without associated psychiatric illness, is the most common form and includes all cases with gradual onset in childhood that are not the result of acquired brain damage (Table 1). "Developmental" indicates that this form of stuttering begins during the period of the most extensive speech and language development.[2] Normative dysfluency data for early childhood stuttering have been published recently.[3] Activities such as speaking in front of a group of people or talking on the telephone tend to worsen DS. Other activities such as singing, reading aloud or speaking alone often improve it.[1]

Studies have shown that a large number of people who stutter recover without professional treatment. It has been estimated that between 50% and 80% of children with DS will recover with or without professional treatment, generally before puberty.[2,4]

Persistent developmental stuttering (PDS) is DS that has not undergone spontaneous or speech-therapy–induced remission. Traditionally, it has been believed that about 1% of adults have PDS. A study involving 1879 university students showed a prevalence of self-reported stuttering of 2%.[5] The male:female ratio in DS is 3:1.[1]

Acquired stuttering in previously fluent individuals may be neurogenic, resulting from brain damage associated with stroke, traumatic brain injury, Alzheimer's disease, renal dialysis, Parkinson's disease and progressive supranuclear palsy.[6,7] It is much rarer than DS.

Tourette's disorder and DS have certain clinical features and symptoms in common, and both respond favourably to dopamine type 2 (D_2) receptor antagonists,[8] which may help shed some light on the nature and treatment of DS.

Review

Synthèse

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In this article we will examine the diagnostic and treatment measures that the medical profession can take when managing patients who have DS. We will also discuss pharmacological treatments that seem promising in this condition.

Diagnosis

The gradual onset of DS occurs before the age of 12 years, generally between 2 and 5 years.[2] Preschool children normally go through a transient period of dysfluency. As a result, recognition of incipient stuttering may be difficult in this age group. Knowing the characteristics of a preschooler's normal dysfluency will help the general practitioner decide whether or not referral to a speech and language pathologist is needed. Traditionally it has been considered that normal dysfluency is suggested by no more than 10 dysfluencies per 100 spoken words.[2] Parents may help in the assessment of this condition by providing a home video sample of at least 750 syllables recorded over more than 1 day but within 1 week.[3] Examples of normal preschooler dysfluency are presented in Table 2.

The most common normal dysfluencies in preschool children include word repetitions (especially words of one syllable or parts of words), interjections, and revisions or incomplete phrases. Prolongations and tense pauses (lips together, no sound produced) also occur. A limited amount of preschooler dysfluency may persist into adulthood.[2]

More recently it has been suggested that dysfluencies can be categorized as either stuttering-like dysfluencies or other dysfluencies.[3] Stuttering-like dysfluencies include repetitions of parts of words, repetitions of words of one syllable and disrhythmic phonations. The last type comprises prolongations, blocks ("…toy") and broken words ("o…pen"). Other dysfluencies incorporate interjections, revisions or abandoned utterances, and repetitions of multisyllables or phrases. The wording "normal dysfluencies" refers to dysfluencies produced by normally fluent children, and it is not equivalent to "other dysfluencies." An increase in revisions and phrase repetitions is normal. Reassurance should be provided to parents of normally dysfluent preschoolers.

Developmental stuttering should be distinguished from acquired stuttering, cluttering, Tourette's disorder and spastic dysphonia (Table 3). In contrast to neurogenic stuttering, a person with DS becomes more fluent with each successive reading of the same short text (adaptation effect).[12] Furthermore, people with DS have more difficulty with the initial syllables of words than those with acquired stuttering. The sudden onset of stuttering warrants referral to a neurologist. If a neurological evaluation is negative, a psychiatric consultation is indicated.

Developmental stuttering can coexist with cluttering, phonological disorder (failure to produce developmentally expected speech sounds), expressive and expressive or receptive language disorder, attention-deficit hyperactivity

Table I: Definitions and features of various types of stuttering

Type	Definition and features
Developmental stuttering	Stuttering with gradual onset in childhood as a disturbance in the normal fluency and time patterning of speech
Persistent developmental stuttering	Developmental stuttering that has not undergone spontaneous or speech-therapy–induced remission
Acquired stuttering	Stuttering that occurs more or less abruptly in previously fluent individuals
Neurogenic	Results from brain damage and involves • Repetitions, prolongations and blocks • No grimaces, eye-blinking or social anxiety
Psychogenic	Begins suddenly after emotional trauma and involves • Repetition of initial or stressed syllables • Indifference toward dysfluency • Dysfluency that never fluctuates • Persistence of normal eye contact

Indications for referral of children to a speech and language pathologist

- Three or more stuttering-like dysfluencies (e.g., "b-but," "thi-thi-this"; "you you you," "and and"; "mummy," "cookie"; "...toy"; "o...pen") per 100 syllables are uttered[3]
- The child exhibits reactions of avoidance or escape (e.g., pauses, interjections ["uh," "uhm"], eye blinks, head nods)
- The child appears tense and uncomfortable[2]
- The general practitioner is in doubt as to the nature of the child's speech changes

Table 2: Examples of normal dysfluency in preschoolers

Type of dysfluency	Examples
Voiced repetitions	Occasionally 2 word parts (mi ... milk) Single-syllable words (I ... I see you) Multisyllabic words (Barney... Barney is coming!) Phrases (I want … I want Elmo)
Interjections	(We went to the ... uh ... cottage)
Revisions — incomplete phrases	(I lost my....where is daddy going?)
Prolongations	(I am Toooommy Baker)
Tense pauses	(Lips together, no sound produced)

disorder and mental retardation. Signs and symptoms of chronic tetany are seen in many patients with DS.[13,14]

Pathophysiology

Although DS may be worsened by stressful situations, there is no evidence that anxiety or conflicts cause stuttering. Certain theories use organic and learning models to explain the cause of DS. Organic models focus on incomplete lateralization or abnormal cerebral dominance.[9] Such studies suggest that the right and left hemispheres play distinct opposing roles in the generation of stuttering symptoms: activation of regions in the left hemisphere appears to be related to the production of stuttered speech, while activation of regions in the right hemisphere may represent a compensatory process associated with the attenuation of stuttering symptoms.[15]

The existing data suggest that there is a genetic component to DS and that spontaneous recovery and chronicity are influenced by genetic factors.[16] Family, twin and segregation studies all have indicated that stuttering has a large genetic component to its cause. An interaction between genetic and environmental factors is probably involved. Tourette's disorder, attention-deficit hyperactivity disorder, DS, oppositional defiant and conduct disorder, and other behaviours associated with Tourette's disorder appear to be polygenic due in part to 3 dopaminergic genes (dopamine D_2 receptor, dopamine β-hydoxylase and dopamine transporter).[17] A Mendelian mode of genetic transmission has not been found in DS. As for adult male stutters 9% of their daughters and 22% of their sons will stutter; for adult female stutters the risks are 17% and 36% respectively.[18]

Developmental stuttering is increasingly considered to be a speech disorder resulting from a central neuromotor dysfunction that disorganizes the exact timing needed to generate fluent speech. This has led to increased interest in using drug therapy for PDS refractory to speech therapy. Early controlled trials of haloperidol[8] showed that the drug was effective in treating DS, particularly the secondary behaviours, but most patients discontinued treatment because of side effects. Haloperidol, which is a fairly specific D_2 receptor antagonist, is also effective in treating motor tics and Tourette's disorder. These conditions, like DS, begin in childhood, are more common in boys than in girls, have a fluctuating course and worsen under stress. In addition, some of the secondary behaviours seen in DS are reminiscent of tics. These clinical observations and single-administration experiments with haloperidol led to the hypothesis that D_2 receptor antagonists may be important in the treatment of DS.[8]

Positron emission tomography (PET) studies using 6-fluorodopa (6-FDOPA) as a marker of presynaptic dopaminergic activity showed significantly higher 6-FDOPA uptake in patients with moderate to severe DS than in nonstuttering control subjects in the medial prefrontal cortex, deep orbital cortex, insular cortex, extended amygdala, auditory cortex and caudate tail. Elevated 6-FDOPA uptake in ventral limbic cortical and subcortical regions is compatible with the hypothesis that stuttering is associated with an overactive presynaptic dopamine system in regions of the brain that modulate verbalization.[19]

The development of the new (atypical) neuroleptic medications has resurrected interest in using D_2 receptor antagonists to treat DS. The atypical neuroleptics differ from the typical ones in their profile of interaction with receptors. Human PET studies have shown that the serotonin type 2 ($5\text{-}HT_2$) receptor occupancy by atypical neuroleptics exceeds the D_2 receptor occupancy, and this correlates clinically with a low incidence of extrapyramidal side effects. Risperidone, an atypical neuroleptic with a high D_2 receptor occupancy and a high $5\text{-}HT_2$ occupancy[20] has been tried in patients with Tourette's disorder[21] and chronic tics[22] with encouraging results.

A role for serotonin systems in DS has also been proposed.[23] Serotonin-specific reuptake inhibitors (SSRIs) such as fluoxetine and clomipramine are known to be effective in the treatment of obsessive-compulsive symptoms. Patients with DS seem to display obsessive-compulsive symptoms at a rate similar to that seen in Tourette's disorder.[24] A double-blind, placebo-controlled study of fluoxetine in Tourette's disorder showed a statistically significant reduction in obsessive-compulsive symptoms but no effect on tics.[25] The fact that SSRIs occasionally cause akathisia and parkinsonism[26,27] seems to indicate a certain effect of sero-

Table 3: Differential diagnosis of developmental stuttering

Disorder	Features
Acquired stuttering	
Neurogenic	Sudden onset with neurological symptoms
Psychogenic	Sudden onset after emotional trauma; no evidence of neurological symptoms; rare occurrence
Cluttering	Unpredictable, fast and jerky outpourings of words and phrases[9] (slurred or omitted syllables, improper phrasing and pauses); no awareness of any communication problem; can coexist with developmental stuttering[10] • Cluttering: "I want to go to the st... uh... place where you get on t-t-train...subway st-st-station and I don't have muh-muh ti-ti-time money" • Developmental stuttering: "I want to go to the suuuuuubway ssssstation and I don't have muh-muh-money"
Tourette's disorder	Presence of other motor and vocal tics besides stuttering[9]
Spastic dysphonia	Patients sound as though they are speaking while being strangled. Onset in middle age; abnormal breathing pattern; no known pathological cause[11]

tonin on dopamine metabolism. Both neuroleptics and SSRIs can cause nonstuttering people with presumably normal dopaminergic function to stutter, while they can decrease dysfluency in known stutterers.[12] The effects of SSRIs on brain dopamine systems are probably more limited when compared with those of neuroleptic medications.

Thus, the hypothesis that antidopaminergic drugs may be effective in the treatment of DS seems to be supported by the similarity of tic-like symptoms seen in DS with the tics seen in Tourette's disorder, past treatment experience with haloperidol in the latter and in DS, recent studies with atypical neuroleptics in Tourette's disorder and neuroimaging studies of presynaptic dopaminergic activity in people with DS. The data supporting a role for serotonin systems in DS are more restricted.

Treatment of stuttering without associated psychiatric disorders

Speech therapy

There is no cure for DS, and speech therapy remains the main treatment option. Electronic aids can cause more harm than good and are often given up. More severe cases of DS and those treated after puberty will recover only partially or will be refractory to speech therapy.[2]

North American speech and language pathologists who provide speech therapy to adults with DS tend to hold 1 of 2 different viewpoints.[28] The first approach identifies DS as a life problem and provides various counselling techniques for building self-esteem, attitude change and avoidance reduction. The second approach relies on the direct manipulation and modification of the stuttering response to fluent-sounding speech by the systematic application of the steps and rules of speech mechanisms. Developmental stuttering is, thus, viewed as a modifiable behaviour. This behavioural speech therapy attempts to reconstruct the respiratory, phonatory and articulatory gestures used to generate speech. One clinical goal is to reshape completely the speech of the person. Another clinical goal is to teach steps allowing the termination and cancellation at will of a speech dysfluency. Behavioural programs that reshape fluency have gradually replaced the older counselling procedures.[29]

In a recent review Conture[30] concluded from the available evidence that people who stutter benefit from the services of speech and language pathologists. However, this author has also concluded that much less attention has been paid to the effects of treatment on the daily life activities of people who stutter.

A randomized controlled clinical trial of 3 types of speech therapy for stuttering in children aged 9 to 14 years indicated that the treatments were successful 1 year later for over 70% of the children.[31] A follow-up study of up to 5 years after treatment of these patients revealed that treatment gains were maintained in the long term, with rates of

Table 4: Medications for the treatment of stuttering

Drug	Indication	Side effects
Risperidone	Moderate to severe PDS	Side effects and long-term risks at low doses used for PDS remain to be clarified
	Limited high-stress periods, such as starting work or school	In psychiatric doses: insomnia, agitation, extrapyramidal symptoms, anxiety, headache, weight gain
	For the treatment of PDS, research is under way	
Paroxetine	PDS with few or no tic-like features (repetitions might be favourably influenced)	Nausea, somnolence, sweating, tremor, asthenia, dizziness, dry mouth, insomnia, constipation, diarrhea, decreased appetite and male sexual dysfunction
	Social anxiety and depressive disorders.	Discontinuation symptoms are possible
	Has not been evaluated for the treatment of PDS in controlled studies	
Sertraline	PDS with few or no tic-like symptoms (repetitions might be favourably influenced)	Nausea, diarrhea, loose stools, dyspepsia, male sexual dysfunction, insomnia/ somnolence, tremor, increased sweating, dry mouth and dizziness
	Social anxiety and depressive disorders	Discontinuation symptoms seem less significant than with paroxetine
	Sertraline has not been evaluated for the treatment of PDS in large controlled studies	

Note: PDS = persistent developmental stuttering.

dysfluency similar to those seen 1 year after the start of treatment.[32]

Adults in speech therapy behavioural programs, however, will often show regression and even total relapse if they stop practising. Equally unfortunately, there are adults who present with speech-related social anxiety so serious that it is incompatible with participation in conventional speech therapy. In other patients, speech-related social anxiety causes a return to pretreatment speech patterns whenever communication is attempted with people not included in the speech therapy process. Finally, there are patients who do well in speech therapy, but if 1 or 2 dysfluencies occur after discharge, speech-related anxiety leads to a return to pretreatment dysfluency levels.[28]

In adolescents and adults who have persistent developmental stuttering (PDS) that is refractory to speech therapy but no coexisting psychiatric symptoms, the general practitioner can do the following:

- Refer the patient to a psychiatrist or neurologist with a special interest in the pharmacological treatment of PDS
- Initiate pharmacological treatment if sufficiently conversant with the available medication

Pharmacological treatment

In a double-blind, placebo-controlled study, risperidone (up to 2 mg/d) was found to be statistically significantly superior to placebo in terms of reducing the mean percentage of syllables stuttered.[33] The study involved 16 people with DS deemed to be free of psychiatric disorders. It was also reported that the drug was well tolerated (Table 4) and that 6 of 8 subjects treated with risperidone chose to continue the drug therapy.

Ziprasidone, which is not yet available for clinical use in Canada, is unique among the new neuroleptic medications.[34] It has agonist activity at the 5-HT_{1A} receptors and inhibits the reuptake of both serotonin and noradrenaline. These characteristics suggest that ziprasidone may be effective in treating anxiety and depression, which is desirable in certain patients with DS in whom the classic neuroleptics can cause depression.[35] Moreover, there appears to be a low association between ziprasidone and movement disorders and weight gain.[34] Although there is hope that the atypical neuroleptics will be associated with a much lower risk of tardive dyskinesia,[36] only long-term studies with low-dose atypical neuroleptics will clarify their risk:benefit ratio in the treatment of PDS.

Clomipramine, an SSRI, has been shown to be superior to desipramine, an antidepressant not significantly affecting serotonin reuptake, in a double-blind crossover trial involving 17 patients with DS described as psychiatrically normal.[37] The authors speculated that stuttering symptoms may be selectively responsive to serotonergic agents and commented that stuttering is seen in 25%-35% of patients with Tourette's disorder, an indication of etiological continuity. There are also reports of effective antistuttering treatment with SSRIs (Table 4), including a double-blind, placebo-controlled N = 1 crossover study of sertraline.[23] However, double-blind, placebo-controlled studies of antidepressants in large groups of patients with DS have not yet been performed. The fact that fluoxetine decreased significantly the obsessive-compulsive symptoms seen in Tourette's disorder, but had no effect on tics seen in that disorder,[25] suggests that the tic-like secondary symptoms seen in some cases of DS will not be significantly influenced by serotonergic antidepressants and that they should continue to be studied mainly in cases of DS without substantial tic-like symptoms. In addition, the possibility that nonserotonergic antidepressants can be used in DS remains. The currently available antidepressants exhibit 7 different mechanisms of action[38] so they should not be dismissed in pharmacological research into DS.

Treatment of stuttering with associated psychiatric disorders

This presentation is most commonly seen in adults and adolescents who stutter. However, this does not mean that all adults and adolescents who stutter have psychiatric disorders. In fact, the exact prevalence of psychiatric disorders in this population is unknown.

In adults PDS can be associated with depression[9] and social phobia.[39] The diagnosis of the depressive and anxiety disorders that can be present in people with DS should be formulated on the basis of stringent DSM-IV criteria.[1] The main feature of social phobia is a marked and persistent fear of social or performance situations in which embarrassment may occur. In people with DS the social anxiety is specifically related to speaking situations.

The diagnosis of social phobia is warranted only if the avoidance, fear or anxious anticipation of encountering the social or performance situation interferes significantly with the person's functioning, or if the person is markedly distressed about having the fear. Interestingly, DSM-IV states

Indications for referral of patients with PDS to a psychiatrist

- Social anxiety, depression or other psychiatric disorder is suspected
- The patient is found not to be a candidate for behavioural speech therapy
- The patient fails to benefit from a behavioural speech therapy program
- The patient relapses soon after completing a behavioural speech therapy program

In PDS with psychiatric disorders, the general practitioner:
- Prescribes antidepressants, if indicated
- Provides cognitive behavioural psychotherapy, if able to do so
- Provides counselling aimed at education and attitude change in patients with PDS who have difficulty accepting that they have emotional problems

that if another mental disorder or general medical condition is present (e.g., stuttering, Parkinson's disease, anorexia nervosa), the fear or avoidance should not be limited to concern about its social impact. In the light of this last criterion many patients with PDS would not be given a diagnosis of social phobia, and this has been criticized[39] because it prevents people with PDS-related social anxiety from receiving a diagnosis and treatment.

Monoamine oxidase inhibitors (e.g., phenelzine), cognitive behavioural group therapy[40] and SSRIs (e.g., paroxetine[41]) have all been shown to be more effective than controlled conditions in the treatment of social phobia.

The depressive disorders seen in PDS are also treatable with antidepressants and cognitive behavioural therapy. Improvement in dysfluency paralleling improvement in social anxiety and depression after treatment with paroxetine,[28] sertraline[23] and mianserin[42] has been described in case reports and uncontrolled trials.

These anxiety and depressive disorders do not cause but can worsen DS. In addition, DS can be in certain cases a contributor to the multifactorial cause of these depressive and anxiety disorders. While tic-like symptoms and obsessive-compulsive behaviours similar to those seen in Tourette's disorder are also observed in people with DS,[24] it cannot be stated that patients with DS and tic-like symptoms suffer from Tourette's disorder or other tic disorders or that they suffer from obsessive-compulsive disorder.

In summary, the general practitioner should maintain regular follow-up of patients with stuttering after referral to a speech and language pathologist and a psychiatrist. In this way, the general practitioner will be in the best position to contribute to the identification of the psychiatric disorders that can occur in PDS and participate effectively in their multidisciplinary care.

Resolution of the case

The family physician recorded the patient's complaints of increased anxiety in social situations requiring speaking and referred him to a psychiatrist. After 10 weeks of treatment with paroxetine, 20 mg/d, this patient's stuttering decreased by 50% and his social phobia score dropped to low levels. The patient noted some temporarily increased facial sweating. After 10 weeks of treatment the paroxetine therapy was discontinued, and the patient experienced mild irritability and light-headedness for a few days. After 24 weeks of no paroxetine treatment he maintained the improvement and was enthusiastic about the increase in the frequency and quality of his social and occupational interactions that involved speaking. Over the following 6 months he gradually returned to pretreatment levels of dysfluency but never experienced again the pretreatment level of speech-related social anxiety. He began a new course of paroxetine, 20 mg/d, which lasted 15 weeks. He reported further improvement in his fluency and his residual speech-related social anxiety.

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References

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-IV)*. 4th ed. Washington: The Association; 1994. p. 65.
2. Peters TJ, Guitar B. *Stuttering: an integrated approach to its nature and treatment*. Baltimore: Williams and Wilkins; 1991. p. 71-86.
3. Ambrose NG, Yairi E. Normative disfluency data for early childhood stuttering. *J Speech Lang Hear Res* 1999;42:895-909.
4. Finn P. Establishing the validity of recovery from stuttering without formal treatment. *J Speech Hear Res* 1996;39:1171-81.
5. Ardilla A, Bateman JR, Nino CR, Pulido E, Rivera DD, Vanegas CJ. An epidemiology study of stuttering. *J Commun Disord* 1994;27:37-48.
6. Heuer RJ, Sataloff RT, Mandel S, Travers N. Neurogenic stuttering: further corroboration of site of lesion. *Ear Nose Throat J* 1996;75:161-8.
7. Brazis PW, Masdeu JC, Biller J. *Localization in clinical neurology*. 3rd ed. Boston: Little, Brown and Company; 1996. p. 515.
8. Brady JP. The pharmacology of stuttering: a critical review. *Am J Psychiatry* 1991;148:1309-16.
9. Kaplan HI, Sadock BJ. *Synopsis of psychiatry*. 8th ed. Baltimore: Williams and Wilkins; 1998. p. 1175-7.
10. Dalton P, Hardcastle WJ. *Disorders of fluency*. New York: Elsevier; 1977. p. 109.
11. Lindsay KW, Bone I, Callander R. *Neurology and neurosurgery illustrated*. 3rd ed. Edinburgh: Churchill Livingstone; 1997. p. 118.
12. Brady JP. Drug-induced stuttering: a review of the literature. *J Clin Psychopharmacol* 1998;18:50-4.
13. Costa D, Antoniac M, Berghianu S, Marinescu R, Boeru L, Bruja N, et al. Clinical and paraclinical aspects of tetany in stuttering. *Act Nerv Super (Praha)* 1986;28:156-8.
14. Steidl L, Pesak J, Chytilova H. Stuttering and tetanic syndrome. *Folia Phoniatr (Basel)* 1991;43:7-12.
15. Braun AR, Varga M, Stager S, Schulz G, Selbie S, Maisog JM, et al. Altered patterns of cerebral activity during speech and language production in developmental stuttering. An H2(15)O positron emission tomography study. *Brain* 1997;120:761-84.
16. Yairi E, Ambrose N, Cox N. Genetics of stuttering: a critical review. *J Speech Hear Res* 1996;39:771-84.
17. Comings DE, Wu S, Chiv C, Ring R, Gade R, Ahn C, et al. Polygenic inheritance of Tourette's Syndrome, stuttering, attention deficit, hyperactivity, conduct and oppositional defiant disorder: the additive and subtractive effect of the 3 dopaminergic genes - DRD2, D beta H and DAT 1. *Am J Med Genet* 1996;67:264-88.
18. Kidd K. Genetic models of stuttering. *J Fluency Dis* 1980;5:187-201.
19. Wu JC, Maguire G, Riley G, Lee A, Keator D, Tang C, et al. Increased dopamine activity associated with stuttering. *Neuroreport* 1997;10:767-70.
20. Kapur S. A new framework for investigating antipsychotic action in humans: lessons from PET imaging. *Mol Psychiatry* 1998;3:135-40.
21. Bruun RD, Budman CL. Risperidone as a treatment for Tourette's Syndrome. *J Clin Psychiatry* 1996;57:29-31.
22. Lombroso PJ, Scahill L, King RA, Lynch KA, Chappell PB, Peterson BS, et al. Risperidone treatment of children and adolescents with chronic tic disorders: a preliminary report. *J Am Acad Child Adolesc Psychiatry* 1995;34:1147-52.
23. Costa D, Kroll R. Sertraline in stuttering [letter]. *J Clin Psychopharmacol* 1995;15:443-4.
24. Abwender DA, Trinidad KS, Jones KR, Como PJ, Hymes E, Kurlan R. Features resembling Tourette's Syndrome in developmental stutterers. *Brain Lang* 1998;62:455-64.
25. Scahill L, Riddle MA, King RA, Hardin MT, Rasmusson A, Makuch RW, et al. Fluoxetine has no marked effect on tic symptons in patients with Tourette's Syndrome: a double-blind placebo-controlled study. *J Child Adolesc Psychopharmacol* 1997;7:75-85.
26. Bauer M, Hellweg R, Baumgartner A. Fluoxetine-induced akathisia does not

reappear after switch to paroxetine [letter]. *J Clin Psychiatry* 1996;57:593-4.
27. Di Rocco A, Brannan T, Prikhojan A, Yahr MD. Sertraline-induced parkinsonism. A case report and an in vivo study of the effect of sertraline on dopamine metabolism. *J Neural Transm* 1998;105:247-51.
28. Costa D, Kroll R. Treatment of stuttering with paroxetine: a case study. *Proceedings of the First World Congress on Fluency Disorders*. vol 2; 1994 Aug 8-12; Munich (Germany). Nijmegen, the Netherlands: University Press; 1995. p. 511-3.
29. Kroll R, Beitchman JH. Stuttering. In: Sadock BJ, Sadock VA. *Kaplan & Sadock's comprehensive textbook of psychiatry*. 7th ed. Philadelphia : Lippincott Williams and Wilkins; 2000.
30. Conture EG. Treatment efficacy: stuttering. *J Speech Hear Res* 1996;39:S18-26.
31. Craig A, Hancock K, Chang E, McCready C, Shepley A, McCaul A, et al. A controlled clinical trial for stuttering in persons aged 9-14 years. *J Speech Hear Res* 1996;39:808-26.
32. Hancock K, Craig A, McCready C, McCaul A, Costello D, Campbell K, et al. Two- to six-year controlled-trial stuttering outcomes for children and adolescents. *J Speech Hear Res* 1998;41:1242-52.
33. Maguire GA, Gottschalk LA, Riley GD, Franklin DL, Potkin SG. Risperidone in the treatment of stuttering: a double-blind placebo-controlled study. *New Research Program and Abstracts of the American Psychiatric Association Annual Meeting*; 1998 May 30-Jun 4; Toronto. Washington: The Association; 1998. p. 207.
34. Kaplan HI, Sadock BJ. *Synopsis of psychiatry*. 8th ed. Baltimore: Williams and Wilkins; 1998. p. 1080.
35. Bloch M, Stager S, Braun A, Calis KA, Turcasso NM, Grothe DR, et al. Pimozide-induced depression in men who stutter. *J Clin Psychiatry* 1997;58:433-6.
36. Casey DE. Will the new antipsychotics bring hope of reducing the risk of developing estrapyramidal syndromes and tardive dyskinesia? *Int Clin Psychopharmacol* 1997;12(Suppl 1):S19-27.
37. Gordon CT, Cotelingham GM, Stager S, Ludlow CL, Hamburger SD, Rapoport JL. A double-blind comparison of clomipramine and desipramine in the treatment of developmental stuttering. *J Clin Psychiatry* 1995;56:238-42.
38. Stahl SM. Basic psychopharmacology of antidepressants, part 1: antidepressants have seven distinct mechanisms of action. *J Clin Psychiatry* 1998;59(Suppl 4):5-14.
39. Stein MB, Baird A, Walker JR. Social phobia in adults with stuttering. *Am J Psychiatry* 1996;153:278-80.
40. Heimberg RJ, Liebowitz MR, Hope DA, Schneier FR, Holt CS, Welkowits LA, et al. Cognitive behavioural group therapy vs. phenelzine therapy for social phobia: 12th-week outcome. *Arch Gen Psychiatry* 1998;55:1133-41.
41. Lydiard RB. The role of drug therapy in social phobia. *J Affect Disord* 1998; 50(Suppl 1):S35-39.
42. Costa D. Antidepressants in the treatment of stuttering [letter]. *Am J Psychiatry* 1992;149:1281.

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