Aripiprazol and Tourette syndrome

Dear Editor,

Tourette syndrome (TS) is characterized by chronic motor and vocal tics. In the 60s, neuroleptics started to be used on TS and became the most efficient medications. Most used neuroleptics which have been reported in controlled studies or case reports are haloperidol, pimozide, sulphiride, risperidone, olanzapine and ziprazidone.1 Since then, typical neuroleptics have been increasingly prescribed due to their side-effects. We will present a resistant TS case that responded with aripiprazol, whose mechanism of action differs from both typical and atypical antipsychotics.2

Up to now, there is no publications about aripiprazol on TS. P., 20 years old, male, single, student, born at the countryside of the state of São Paulo and living at the state’s capital, has had his first multiple motor and vocal tics since the age of five. These tics have increasingly worsened causing much suffering for the patient and his family. Additionally, the patient showed obsessive-compulsive symptoms, besides major depressive episode, separation anxiety and panic with agoraphobia. He has unsuccessfully undergone all conventional (haloperidol, pimozide, trifluoperazine, sulphiride, olanzapine, ziprazidone, clonidine, butulonixin) and alternative (pergolide, nicotine, clonazepan, reserpine) tic treatments without success. It was added aripiprazol (15 mg/day) to the previous scheme a (sertraline + olanzapine, the latter gradually withdrawn) with tic improvement. Improvement was observed since the second week onwards using the medication and has persisted after three months of continuous treatment with 15 mg/day.

The floating nature of tics hampers to assess if the improvement occurred due to the medication or to a remission phase of the disease proper. However, vocal tics, always extremely resistant to pharmacological treatment, decreased significantly, along with the motor tics, when aripiprazol was introduced.

In the current model about the pathogenesis of TS which involve cortical-subcortical circuits, it is believed that the increase in the dopaminergic stimulation in the striatal region implies higher release of glutamate in the thalamic-cortical projections, leading to release of involuntary movements.3-4 Aripiprazol has been described as a stabilizer of the dopaminergic system. Its suggested mechanism of action is the partial agonism on D2 receptors, as it binds more to D2 G-protein bound receptors than to those which are not.2 The affinity of the drug for D2 is 4- to 20 times lower than that of haloperidol, chlorpromazine or other typical antipsychotics.5 Besides, it shows a partial agonist activity on 5HT1A receptors and antagonism on 5HT2A receptors. Most neocortex 5HT1A receptors are situated in glutamatergic pyramidal neurons. These receptors have a inhibitory action, which would reduce the excitatory glutamatergic output. It is believed that part of the control of tics would stem from this control in the glutamatergic projection pathways.

Aripiprazol, therefore, with a profile of side-effects characterized by lower weight gain, lower sedation, absence of prolactine levels elevation and of widening of QT space of electrocardiogram compared to other antipsychotics, becomes an interesting option for TS cases which do not respond to conventional therapies. It has, however, a high cost and needs official support to allow the poorest layers of the population to benefit from its effects. Controlled studies comparing aripiprazol to the conventional treatments for TS are needed.
Dear Editor,

Problems of auditory sensation have been associated with autism: auditory hyposensitivity (i.e., ‘tuning out behavior’), hyper-sensitivity (e.g., covering ears), and over selectivity to sound have been observed. Autism is associated with an abnormal pattern of activation of the temporal cortex (auditory associative cortex and the superior temporal sulcus).1

Auditory integration training (AIT) is an audiological approach for the treatment of ‘auditory distortions’ and hyperacusis, which its proponents believe are central to the dysfunction experienced by persons with autism.2

The goal of AIT is to reduce the symptoms that are interfering with auditory functioning.

The treatment requires that an accurate audiogram be obtained, which has to be evaluated to determine if the subject shows ‘hyper-sensitive hearing’ or has ‘uneven hearing’. The client is then considered as a candidate for treatment. Treatment consists on listening to music for half an hour twice a day for 10 days. The music is filtered to eliminate the frequencies to which the person is ‘hypersensitive’, or where the audiogram demonstrates peaks and is also modulated so that different parts of the frequency band are randomly modified in intensity. Audiograms are repeated midway and at the end of the training sessions, to document ‘progress’ and to determine whether additional sessions are needed.

AIT is based on the theory that listening to altered music can improve the listener’s ability to process auditory stimuli. The effectiveness of the treatment is determined by changes in both hearing and behavior.2

Several research studies have been published on the efficacy of AIT in autism.3,4 The most frequently reported improvements include improved attention, improved auditory processing, decreased irritability, reduced lethargy, improved expressive language and auditory comprehension and reduction in sound sensitivity. Unfortunately, little scientific documentation exists to support these assertions.

Although two investigations indicate that AIT may help some children with autism, there are no controlled studies to support its use yet.4,5

It is the position of the American Academy of Pediatrics that AIT has not been scientifically proven and currently should be considered as an experimental approach.4

Several problems contribute to the lack of consensus: the available literature provides little information on outcome variables and their means on experimental and control groups; The statistically significant changes in the subjects’ thresholds were less than 1-5 dB (normal clinical variation test-retest); AIT use behavioral audiometric data to support their claims of benefit, although many children are difficult to test. Long-term follow-up study of this method is necessary for fair and empirical evaluation.

It is recommended that consumers be informed that AIT is experimental in nature and a controversial treatment option for autism before they participate in the treatment. There is still much to learn about AIT. It may be useful to ask under what conditions AIT does demonstrate effectiveness. Its effectiveness should be further investigated, as for instance in a randomized controlled trial with evaluators blind to treatment type.

References