Unified Theory of Behavior Change (UTBC), which illustrates a full range of social, cognitive, and environmental influences on adherence. This model identifies five core variables associated with the intention to engage in a certain health behavior: expectancies, affect, self-efficacy, self-image, and social norms.

## Results

Twenty-seven parents in all participated in the focus groups. Their mean age was 45.27 years, and 78% were women. Their children's mean age at the time of study participation was 9.35 years; 20 of the 27 children were boys.

The themes that were elicited from group transcripts and that researchers believe can inform physician interventions with families were: defining adherence; attitudes that promote or impede adherence; and parent perceptions about their child's medical providers. On the definition of adherence, while parents initially indicated in the sessions that medication was administered consistently for their child, further discussion found that in many cases exceptions were made based on daily activities and other factors.

On the factors promoting or interfering with adherence, the researchers found that the most prominent facilitator of adherence was a perception that medication for ADHD is effective, and that symptom stabilization will lead to numerous improvements in functioning at home and in school.

In regard to parent perceptions about providers, parents conveyed positive attitudes about physicians who involved them in a collaborative care process for their child, taking a careful history and listening intently to parent accounts. The parents added that physicians should convey an openness to non-medication treatment options, and should strike a balance between being too technical in the information they share and talking down to the parent.

The deductive analysis using the variables in the UTBC also revealed several informative patterns. For example, parents believed that their positive expectations about medication treatment efficacy needed to be balanced by the understanding that treatment can be a trial-and-error process. Also, the researchers found that the self-image of parents with an ADHD child was heavily influenced by social groups, as in some cases they encounter significant peer disapproval of the decision to put a child on medication.

Parents in the study described deeply ambivalent feelings about medication, influenced by numerous factors. Many worried about the effects of stigma from an ADHD diagnosis, but they also pointed out that a physician's explanation of ADHD as a medical illness helped them better understand the role of medication.

## Implications

The findings suggest several possible strategies for physicians to employ to encourage medication treatment initiation and adherence. These include assessing parental attitudes about medication before a medication recommendation is even made; helping parents to understand the relative efficacy of non-medication treatments in which they might be interested; and taking the time to understand the child and family and to show empathy.

"These qualitative data suggest that clear information and an unequivocal recommendation to try medication, balanced with patience and acceptance of a parent's decision as a process, are likely to facilitate successful initiation," the researchers wrote. ■

*Study co-author Elizabeth Pappadopulos, Ph.D., is employed by Pfizer, Inc.; two other co-authors report research support or consulting arrangements with pharmaceutical companies. None of the cited companies were involved in the data analysis for this study.

Coletti DJ, Pappadopulos E, Katsiotas NJ, et al. Parent perspectives on the decision to initiate medication treatment of attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol* 2012; 22(3):226–237. E-mail: dcoletti@nshs.edu.

# Study proposes new criteria for intermittent explosive disorder in DSM-5

précis

- Authors review all current data on intermittent explosive disorder and propose research criteria for diagnosis.
- Authors recommend new criteria for inclusion in DSM-5.

The authors of a new study suggest that a broader and more comprehensive definition and diagnostic criteria are needed for intermittent explosive disorder and recommend that this be used in the upcoming DSM-5.

A disorder of impulsive aggression has been included in DSM since the first edition, note the authors. In DSM-III, this disorder was included as intermittent explosive disorder, though it was thought to be rare. However, the authors of the current study suggest that the diagnostic criteria for the disorder were poor and research was limited until more recent research criteria were developed. They outline this criteria and outline current evidence and data.

## Study details

The research criteria adopted by the authors state that intermittent explosive disorder can be diagnosed when high-frequency/low-intensity or low-frequency/high-intensity aggressive outbursts are present. The first threshold was set at an average of two outbursts a week for at least 1 month, because this level responds to pharmacological and cognitive-behavioral interventions. The second threshold was set at three severe outbursts a year because this level distinguishes more aggressive individuals.

The research criteria also state that the aggressive behavior must be impulsive and that some kind of distress or dysfunction must be linked to the aggressive behavior. Individuals with antisocial or borderline personality disorder or with disruptive behavior disorders were allowed to be diagnosed with intermittent explosive disorder and included in the study. Exclusion criteria included a current history of major depression, mania, or psychosis.

The authors describe aggressive outbursts in intermittent explosive disorder as: having a rapid onset and often little or no prodromal period; lasting less than 30 minutes; involving verbal assault, destructive and nondestructive property assault, or injurious or noninjurious physical assault; and occurring in response to a minor provocation by someone close to them.

## Findings

A more recent series of community-based studies has documented intermittent explosive disorder to be as common as many other psychiatric disorders. The prevalence of DSM-IV intermittent explosive disorder in the United States is about 6.9% (~21 million people) for all intermittent explosive

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disorder and 5.4% for the narrow definition (~16 million people), according to more recent data. It appears to be more frequent in males than in females, by a 2:1 ratio, and disorder is nearly twice as prevalent among individuals in the "other" race category (those who are not white, black, or Hispanic).

It is more prevalent among younger (< 35–40 years) compared with older (>50 years) individuals (6, 25, 34). Onset of the disorder precedes onset of other comorbid disorders (6, 7), and intermittent explosive disorder is persistent and follows a chronic course of at least 12 years. Existing family history data suggest that intermittent explosive disorder is familial.

Compared with healthy and psychiatric comparison subjects, individuals with intermittent explosive disorder demonstrate: 1) greater hostile attribution bias and greater negative emotional responding to socially ambiguous stimuli, suggesting a psychological trigger for impulsive aggressive outbursts; 2) greater affective lability intensity; and 3) a greater degree of immature defense mechanisms, including acting out, dissociation, projection, and rationalization.

Findings also suggest the presence of serotonergic abnormalities globally and in the limbic system (the anterior cingulate) and in the orbitofrontal cortex. The research also shows important differences between subjects with intermittent explosive disorder and healthy comparison subjects in differential activation of corticolimbic structures.

Data suggest that effective treatments for intermittent explosive disorder include fluoxetine, divalproex, oxcarbazepine, and cognitive-behavioral therapy.

## Conclusions

The research indicates that compared with DSM-IV criteria for intermittent explosive disorder, the research criteria used in this study for the disorder better identify individuals with elevated levels of aggression, impulsivity, familial risk of aggression, and abnormalities in neurobiological markers of aggression.

"In addition, other data strongly suggest important delimitation from other disorders previously thought to obscure the diagnostic uniqueness of intermittent explosive disorder," they write. "Overall, these data suggest that the diagnostic validity for the integrated research criteria is substantial and is now sufficient for recognition and inclusion in DSM-5." ■

Coccaro EM: Intermittent explosive disorder as a disorder of impulsive aggression for DSM-5. *Am J Psychiatry* 2012; 169(6):577–588. E-mail: ecoccaro@yoda.bsd.uchicago.edu.

# Donepezil not effective for fragile X syndrome

## précis

- 12-week, randomized, double-blind, placebo-controlled study of donepezil for boys with fragile X syndrome.
- Results showed no significant difference on intelligence quotient and behavioral scales.
- Authors recommend further large-scale studies.

In a 12-week, randomized, double-blind, placebo-controlled pilot study evaluating the effectiveness and safety of donepezil in boys with fragile X syndrome, results were inconclusive, with no significant improvements in intelligence or behavior.

According to the authors, fragile X syndrome is one of the most common causes of inherited intellectual disability in males. Therapeutic measures to improve cognition are important since most children with this condition have intellectual disability and behavioral problems. The authors note that at present there are no proven palliative or curative treatments for fragile X.

## Study details

Current research suggests that remodeling acetylcholinergic abnormalities in boys with fragile X syndrome may improve intellectual and behavioral function. Donepezil inhibits the enzyme acetylcholinesterase and enhances cholinergic function in the brain, and though its effectiveness has been studied in patients with mild to moderate Alzheimer's disease, research in a population without dementia has been limited. Recent evidence suggests that donepezil may be effective for the cognitive and behavioral function in patients with Down syndrome, Tourette's syndrome, attention-deficit hyperactivity disorder, and autism.

Hence, the authors examined whether children with fragile X treated with donepezil would show greater improvement in intellectual and behavioral function than those treated with placebo and whether the treatment would be tolerable and safe.

Researchers randomized 20 boys (ages 6 to 15) with fragile X syndrome to receive 12 weeks of treatment with either placebo or donepezil (2.5 mg daily for initial 4 weeks and 5 mg daily for following 8 weeks). The outcome measures included change in intelligence quotient scores on Stanford-Binet Intelligence Scale (Hindi adaptation by Kulshrestha), change in behavioral scores by the Conners 3 Parent Rating Scale (Short) and Childhood Autism Rating Scale, safety, and tolerability of donepezil.

## Results

The study failed to show a significant difference in intelligence quotient and behavioral scales with donepezil therapy over 12 weeks. However, donepezil appeared to be safe and well tolerated. There were no significant differences between groups in posttreatment scores of mean intelligence quotient, mean t-scores of various behavioral domains of the Conners 3 Parent Rating Scale, or scores on the Childhood Autism Rating Scale.

The authors noted several important study limitations that may have impacted the findings: 1) the small number of patients meant that the study was not adequately powered to detect small effects; 2) treatment duration was only 12 weeks due to limited funding for the study; 3) children with fragile X syndrome may have a spectrum of behavioral problems, including externalizing (e.g., aggression, self-injurious) and internalizing (e.g., anxiety) behavior, and this study only looked at some aspects of the behavioral phenotype; and 4) the sample was predominantly nonautistic phenotype boys, so the effect of donepezil on autistic behavior was not studied.

## Conclusions

The study did not show a significant difference in intelligence quotient and behavioral scales with donepezil therapy over 12 weeks. "Further large, adequately powered, long-follow-up, multicenter, randomized, placebo-controlled, blinded trials are needed to test the efficacy and safety of donepezil in children with fragile X syndrome," conclude the authors. ■

Sahu JK, Gulati S, Sapra S, et al.: Effectiveness and safety of donepezil in boys with fragile X syndrome: A double-blind, randomized, controlled pilot study. *J Child Neurol* 2012 Jun 29. Epub ahead of print. E-mail: sheffaligulati@gmail.com.