

*1. Behavior, Mental Health and Medications***Medication, Behavior, and Fragile X Syndrome**

By Andrew Levitas, MD

The use of medication in the treatment of the behavioral problems associated with fragile X syndrome (FXS) begins with an understanding of the behavioral characteristics of the condition.

CHARACTERISTIC PATTERN OF BEHAVIORS IN FRAGILE X SYNDROME

Full Mutation	Premutation
Attention deficit/hyperactivity disorder	Attention deficit/hyperactivity disorder
Autism spectrum disorders, with following conditions:	Avoidant disorder
Panic disorder, other anxiety disorders	Major depressive disorder
Mood disorders	Increased risk of social deficits, shyness, anxiety, mood disorders
Aggression (primarily in adolescent and adult males)	

Of these disorders, attention deficit/hyperactivity disorder, anxiety disorders, and mood disorders can potentially be treated through the use of medication.

In attention deficit/hyperactivity disorder (ADHD), motor overactivity (sometimes seen as aimless activity or exploration), inability to concentrate or focus, distractibility, and inability to inhibit impulses (alone or as part of FXS), may continue into adolescence or adulthood.

Medication for these behaviors, often begun in childhood, can sometimes be successfully tapered or discontinued in mid- to late adolescence when hyperactivity/distractibility/impulsivity declines. Where this is not the case, persons with FXS can continue to benefit from these medications into adulthood.

To some extent, the behaviors typical of ADHD overlap with those seen in adolescents and adults with anxiety disorders, making it difficult to distinguish between them. The person with an anxiety disorder may have any or all of these symptoms, plus difficulty sleeping, obvious fright in some situations, or signs of emotional arousal not seen in ADHD. (For example: flushing, pallor, rapid breathing, rapid pulse, sweating, or panic episodes characterized by sudden panicky running, aggression or self-injury, accompanied by signs of emotional arousal.) It is possible for a person to have both ADHD and an anxiety disorder, evolving separately or together, making complete treatment a matter of a combined approach.

Panic disorder, with increasingly frequent panic responses to novelty, change, sudden sounds, social situations, or for no obvious reason at all, can either begin—or because of the person's adult size—become more severe in adolescence and adulthood. It is important when considering treatment to recognize the anxiety response underlying any aggression or self-injury that may be part of the panic response, and treat this by minimizing known causes of anxiety in the environment and by using anti-anxiety medications (typically the SSRIs) when necessary. Where aggression is a prominent part of the episodes, mood-stabilizing medication may also be of benefit, and can help some persons tolerate otherwise problematic side effects of SSRIs (irritability and “behavioral activation”—similar to what one feels if one has too much coffee).

Anxiety can exacerbate the effects of ADHD, and vice versa. Treatment must begin with consideration of which set of symptoms appears most in need of remediation, and which medication type is most likely to be tolerated by the patient. Stimulants and adrenergics used for ADHD, and SSRIs used to treat anxiety disorders (see below), are both usually well tolerated by adolescents and adults with FXS, and can be used together.

Obsessions and compulsions can continue from childhood and increase or decrease in intensity. When they become a problem for a person or his or her family, both behavioral and medication approaches can be of benefit. Medications are the same as for panic disorder and generalized anxiety (the SSRIs).

When mood disorders occur, they typically have their onset in adolescence or adulthood. They can take the form of depression, mania, or mixed mood states. Major depressive disorder can be recognized by sleep disturbance, appetite disturbance, loss of energy or enthusiasm for usual sources of pleasure, and either sadness or irritability. The person may take to bed, or refuse to leave home. Anxiety and obsessions/compulsions may intensify. Antidepressants (SSRIs) will also treat this disorder.

Mania, the manic component of bipolar disorder, also causes sleep disorders, usually major decrease in sleep, along with elated or irritable mood, easily changeable mood (“mood lability”), and an increase in energy and personal intrusiveness. Treatment is built around mood-stabilizing medications. Depending upon the severity of mania when it is encountered, various adjunctive medications may be necessary to treat the initial episode until the regime can be tapered to a maintenance program of mood stabilizers.

Mixed mood episodes, with features of both mania and depression, may require careful use of both antidepressant and mood-stabilizing medications. Where hallucinations or delusions occur, antipsychotic medication may be necessary. In the case of both bipolar disorder and major depressive disorder, the person may need to be maintained on mood-stabilizing or antidepressant medication to prevent recurrence.

The National Fragile X Foundation provides detailed information on different medications used in the treatment of FXS at www.FragileX.org.

Additional Medication Information

By Elizabeth M. Berry-Kravis, MD, PhD

It is important to recognize that although psychiatric diagnoses are applied to individuals with fragile X syndrome (FXS) to help describe, categorize, and guide treatment for behavioral symptoms, the symptoms are actually driven by the underlying biological disorder of FXS. Thus, individuals with FXS have overlapping symptoms in many psychiatric diagnostic categories and may not present “typically” for any one diagnosis. Further, because the underlying problem is FXS and not the psychiatric diagnosis, medications are not always effective, and when they are effective, they tend to make symptoms milder but do not fully treat the problem behavior. For instance, a person with FXS may respond to stimulants for the distractibility portion of their symptoms, but with a much less complete response than a person who has ADHD only. Thus, it is important for caregivers not to expect a complete response to medications, or to rely on medication treatment alone for management of symptoms. Rather, they should consider medication treatment as an adjunct, which can take the edge off behavior sufficiently to allow other behavioral and environmental strategies to be more effective.

Because medications do not always work as predicted in individuals with FXS, it is important to apply a systematic strategy for medication management. If a medication is not helping at all for a targeted behavior, it is not likely to work with other medications added. In order to prevent “polypharmacy” with the use of four or five medications (some of which may be of no benefit), medications that are not helpful should be weaned before replacing them with an alternative. Medication changes should be done systematically, with one change occurring at a time if possible, in order to best determine what is helping and what is not.

Many individuals with FXS have episodic symptoms. They may be adequately managed most of the time, but occasionally, when really stressed or bothered, will have dramatic outbursts. Medication increases are not necessarily needed simply because an outburst has occurred—often the outburst was situational and will not respond to medication changes until the individual is so sedated from medication as to be under-reactive to everything, including normal life events. These kinds of episodic behaviors are best managed with a combination of medication and proactive strategies designed to 1) identify when the individual with FXS is becoming overwhelmed, and to diffuse the situation before the outburst occurs, and 2) modify the environment to reduce the stimuli that are keeping the person with FXS constantly “on edge.”

It is further important to recognize that individuals with FXS tend to have many odd behaviors that are just part of the syndrome, do not represent any disorder other than FXS, and do not need to be treated with a medication if they are not getting in the way of function. Examples of this would be the tendency of individuals with FXS to talk to themselves, exhibit eye aversion, and have non-obtrusive routines. These are not psychotic behaviors, and most of the time they do not impair function and do not need or respond to medication treatment. Treatment should be focused on anxiety and OCD behaviors, distractibility, and aggressive behaviors that limit daily life.

Behavior Issues: Mood Disorders

Developed by the Project Work Group

(Note: There is a vignette on the DVD based on this material.●)

BIPOLAR DISORDER

People with fragile X syndrome can have moods that are disruptive to their daily lives. These are not just transient fluctuations in mood, or angry outbursts, but sustained changes in mood over days to weeks, with disturbances of sleep, appetite, and activity level.

Characteristics:

- Unable to sit for long
- Remains off task
- Paces aimlessly, sometimes tries to leave the building/house
- Aggressiveness
- Sleeplessness
- Irritability

Bipolar disorder can be treated, and future episodes minimized or eliminated, with mood-stabilizing medication. Blood tests are needed to check the medication blood levels, and parents and staff need to watch out for side effects. The parents should inform the work/house staff that their child is on a medication. They should have ongoing communication as mood, activity levels and sleep quality return to normal.

DEPRESSION

Depression can cause huge disruptions to the daily lives of people, but it can be diagnosed, and it can be treated.

Characteristics:

- Loss of interest in favorite activities and people
- Irritability
- Lack of appetite
- Moodiness
- Lack of motivation
- Sleeplessness
- Increased rigidity in routines
- Nervousness

Modern antidepressants can be extremely effective, but they can take weeks to work completely. Some require EKG monitoring. They also help with anxiety and compulsions, which are also common in persons with FXS.

PANIC EPISODE

People with fragile X syndrome can sometimes have a panic response to harmless but startling stimuli, or to no obvious event at all.

Characteristics

The person may:

- Become flushed
- Look frightened
- Try to flee
- Fight with anyone trying to restrain him
- React with self-injury, commonly hand-biting
- Sweat heavily
- Breathe rapidly
- Have a racing pulse

If such incidents are frequent, disruptive, or frightening, consult a psychiatrist about anxiety-reducing medication.
