Neuropsychiatric and Behavioral Profiles of 2 Adults With Williams Syndrome: Response to Antidepressant Intake

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ABSTRACT

Background: Individuals with Williams syndrome, a rare genetic disorder, are characterized by specific medical, cognitive, and behavioral phenotypes and often have high anxiety levels as well as phobia. Studies of the psychiatric phenotype in adults affected by Williams syndrome or literature on the management of their mental pathologies are lacking.

Method: In this article, we report the neuropsychiatric profile of 2 adult patients with Williams syndrome who also have generalized anxiety disorder and depressive symptoms (*DSM-IV-TR* criteria), along with their anxiety profiles and the strategies that were adopted for pharmacologic intervention.

Results: Neuropsychiatric profiles revealed a prefrontal cortex affliction that includes an alteration in executive functions. The patients had high scores for trait-anxiety and responded to treatment with a low-potency antipsychotic. A selective serotonin reuptake inhibitor (SSRI) was coadministered with the antipsychotic to alleviate the depressive symptoms. The treatment led to an improvement in self-control, mental concentration, and social skills, as well as decreased irritability and aggressiveness and stabilization of mood.

Conclusions: The combination of SSRIs and low doses of low-potency antipsychotics seems to be the most suitable medication to treat generalized anxiety disorder and related disorders in individuals with Williams syndrome. Manic reactions and increase in anxiety must be closely monitored during treatment. Control of anxiety and sleep should be a priority in these patients, even as a preventative measure.

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Williams syndrome is a rare genetic disorder affecting 1 in 25,000 to 50,000 births, although new prevalence estimates are as high as 1 in 7,500.[1] Williams syndrome is caused by a hemizygous deletion of ~1.6 megabases, containing ~28 genes, on chromosome 7q11.23.[2,3] The classical presentation of Williams syndrome has referred to the well-known clinical features (growth retardation, cardiovascular abnormalities, and infantile hypercalcemia),[4–6] and neurologic problems have recently been added to the clinical features (coordination difficulties, hyperreflexia, hyperacusis).[7–9]

This syndrome is characterized by a mild-to-moderate mental retardation and a relative preservation of linguistic and social-affective skills alongside relative strengths in auditory rote memory and facial recognition. These features contrast with the profound impairment of visual-spatial abilities and numeric processing.[7–12] Since this syndrome is characterized by striking verbal and musical features and by impairment of visual-spatial abilities, which have been subject to many studies,[11–13] the psychiatric symptoms[7,14–19] have been largely ignored by researchers and medical doctors. Individuals with Williams syndrome have also been strongly associated with high anxiety levels, as well as phobia development,[17,18] hyperacusis,[12] attention-deficit/hyperactivity disorder (ADHD; 70% of individuals with Williams syndrome have been diagnosed with ADHD),[7,14,15] and related psychological symptoms such as poor concentration.[16]

Recently, more information about psychiatric medication intake by patients affected by Williams syndrome has been demanded,[20] and new evidence suggests that an alteration in executive functions such as working memory and attention shifting exists in these individuals.[21–23] In this article, we report the neuropsychiatric profiles of 2 adult patients with Williams syndrome who also have generalized anxiety disorder, and we characterize their anxiety profiles and the strategies that were adopted for pharmacologic intervention. We found that the patients were responsive to selective serotonin reuptake inhibitors (SSRIs), suggesting that the combination of SSRIs and low doses of antipsychotics is the most suitable medication to be given in these cases. The patients presented to Clinica San Juan de Dios, Madrid, Spain. Patients and caregivers provided consent, first, to allow treatment and, second, to publish the findings.

CASE REPORTS

Mr A

Mr A, a 26-year-old man, was diagnosed with Williams syndrome at the age of 11 years, with confirmed positive fluorescence in situ hybridization to an elastin gene deletion in chromosome 7. Mr A lives with his mother, is dependent for activities of daily living, and attends an occupational center on weekday mornings. Mr A is unlikely to integrate in the workforce, except in jobs specially designed for him. He needs supervision to take care of household chores, although he can perform most of them. Mr A also has difficulties in making and maintaining friendships and needs to be supervised by his family when trying to be autonomous in social relationships. The quality of his leisure time is low and unsatisfactory, with no hobbies apart from going to shopping malls to try to have social contact. In this regard, he has

Clinical Points

- In patients with Williams syndrome, control of anxiety and sleep problems should be a priority and included as a preventative measure.
- Low doses of low-potency antipsychotics are recommended to treat anxiety and insomnia, but mild depressive states might appear.
- Treatment with a selective serotonin reuptake inhibitor is recommended to treat depressive states, but an increase in anxiety and a manic reaction might appear; low doses of antipsychotics are recommended to counteract these side effects.

difficulties in respecting social norms, exhibiting behaviors such as intensive eye contact that becomes obsessive and problematic and especially with regard to excessive proximity to strangers. He also is quite irritable in the family environment and presents a mild decline in sexual conduct, with an intense dissatisfaction. In addition, Mr A suffers from various disorders and diseases that can be framed within the Williams syndrome diagnosis, such as chronic pain conditions and gastrointestinal complaints, including chronic gastritis and gastroesophageal reflux (Table 1).

Mr A fulfills *DSM-IV-TR* criteria for generalized anxiety disorder. The onset of this disorder can be dated from the age of 13 years until present. Although Mr A has a slight worsening of anxiety symptoms during spring and autumn, he fails to meet the criteria for seasonal affective disorder. Mr A also fulfilled *DSM-IV-TR* criteria for a mild depressive state when he first came to the clinic. This state was characterized by a decrease in his ability to concentrate, increased self-absorption, apathy and lack of motivation, stereotyped movements, and intensified obsessive symptoms, such as repetitive speech and a marked intensity in his compulsive behavior.

Independently from Williams syndrome, Mr A has also been diagnosed with Behcet's syndrome, an autoimmune disease characterized by recurrent mucocutaneous lesions and sight threatening uveitis that may involve the central nervous system.[24] His family estimates the first appearance of symptoms at the age of 13 years. Interestingly, they also report that he may have experienced a mild depressive state when he was 12 to 13 years old.

Ms B

Ms B, a 35-year-old woman, was diagnosed with Williams syndrome at the age of 20 years, with confirmed positive fluorescence in situ hybridization to an elastin gene deletion in chromosome 7. She lives with her mother and is dependent for activities of daily living; she is unable to work outside the home or do household chores unsupervised, although she can perform most of them. Ms B is unable to maintain friendships outside the family even though she unwinds well in a known social environment, with apparently no major difficulties in respecting social norms apart from effusively approaching strangers and excessive visual contact, which becomes problematic. Ms B has hobbies, including playing the piano and attending piano classes. She also shows a mild decline in sexual conduct.

Ms B's medical disorders framed within the Williams syndrome organic symptoms include dyspepsia and postprandial acute pain associated with gastroesophageal reflux. Ms B has developed a phobia to certain types of foods, as she suffered from celiac disease and was not diagnosed for years. The phobia to foods has resolved. The celiac disease is currently being treated, and, thus, Ms B eats gluten-free foods.

With regard to psychiatric disorders, Ms B has a specific phobia to swallow, fulfilling *DSM-IV-TR* criteria for phobias, leading to weight loss. Moreover, she presented with increased anxiety episodes that fulfill *DSM-IV-TR* criteria for generalized anxiety disorder and irritability that fulfills *DSM-IV-TR* criteria for a mixed state with mild depressive symptoms and dysphoria, characterized by anhedonia, reduced motivation and initiative, neglect of normal activities (piano lessons, outings with family and friends), and insomnia with increased sleep-onset latency and early wake-up. In addition, Ms B currently fulfills *DSM-IV-TR* criteria for a mild obsessive-compulsive disorder (OCD) (Table 1).

NEUROPSYCHIATRIC PROFILES AND ANXIETY

Both patients were given the following tests: the Weschler Adult Intelligence Scale, Third Edition (WAIS-III)[25]; Test of Memory and Learning[26]; Benton Facial Recognition Test[27]; Trail Making Test parts A and B[28]; verbal fluency test[29]; Purdue Pegboard Test[30]; Rey-Osterrieth Complex Figure Test[31]; Woodcock-Muñoz Battery[32]; and the Stroop task.[33] All scores were transformed to *z* scores for comparison. The total intellectual quotient (IQ) score was calculated as a mean, so if the score for a given test was 1 or more deviations above the total IQ score, the feature was considered as a strong ability and vice versa. Mr A's total IQ score per the WAIS-III was 56. Ms B's total IQ score per the WAIS-III was 66.

Auditory verbal processing, abstract verbal reasoning, phonetic verbal fluency, and memory for stories scored as peaks for both patients and fit within the strong abilities described for individuals with Williams syndrome.[14,34] Gestaltic closing, visual-constructional praxis, and executive functions were the valleys of their abilities, as have been previously suggested.[22,23,35] All other processes were adjusted to the level expected given the patients' overall intellectual level (Figure 1).

In addition to their neuropsychiatric profile, we also assessed the patients' emotional state with the State-Trait Anxiety Inventory (STAI)[36] and Beck Depression Inventory (BDI).[37] Both patients were in a depressive state when they first started treatment. Mr A's BDI results indicate that he was not currently in a depressive episode, although his score could be interpreted as at risk for depression. Ms B's BDI results are suggestive of depressive state I. The STAI profile reveals that both patients have a high score for anxiety as a

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Table 1. Summary of the Medical and Psychiatric Conditions and Effects of the Psychiatric Medication in 2 Patients With Williams Syndrome

Variable	Mr A	Ms B
Medical condition		
Gastrointestinal (stomachache)	Yes	Yes
Acid reflux	Yes	Yes
Dental problems	Yes	Yes
Constipation	Yes	No
Hernia	Yes	No
Autoimmunity problems	Yes	No
Celiac disease	No	Yes
Diabetes mellitus	No	No
Metabolic/physiologic (fast heart rate, high blood pressure, weight gain, weight loss)	No	No
Problems with growth	Yes	No
Joint problems	Yes	No
Scoliosis	No	Yes
Sensitive to sound	Yes	Yes
Frequent ear infections	No	Yes
Eye/vision problems	Yes	No
Neurologic (anxiety, headache, muscle tics, sleep problems, tremors)	Yes	Yes
Psychological (hallucinations)	No	No
Psychiatric condition		
Anxiety disorder	Yes	Yes
Depression	Yes	Yes
Attention-deficit/hyperactivity disorder	Some characteristics	Some characteristics
Bipolar disorder	Some characteristics	Some characteristics
Sleep disturbance	Yes	Yes
Behavior problems (fighting/aggression, irritable)	Yes	Yes
Obsessive-compulsive disorder	No	Yes
Medication effect		
Use of combined antidepressive and antipsychotic medications		
Any side effect	No	No
Useful for:		
Behavior problems	Yes	Yes
Anxiety disorder	Yes	Yes
Depression	Yes	Yes
Sleep disturbance	Yes	Yes
Obsessive-compulsive disorder	Yes	Yes
Autism spectrum disorder	Yes	Yes

feature. This finding was expected on the basis of previous literature.[17] Mr A improved his anxiety state to reach normal values, probably due to his medical treatment. Ms B's anxiety symptoms slowly decreased to baseline values (Figure 2).

PSYCHOTROPIC RESPONSE

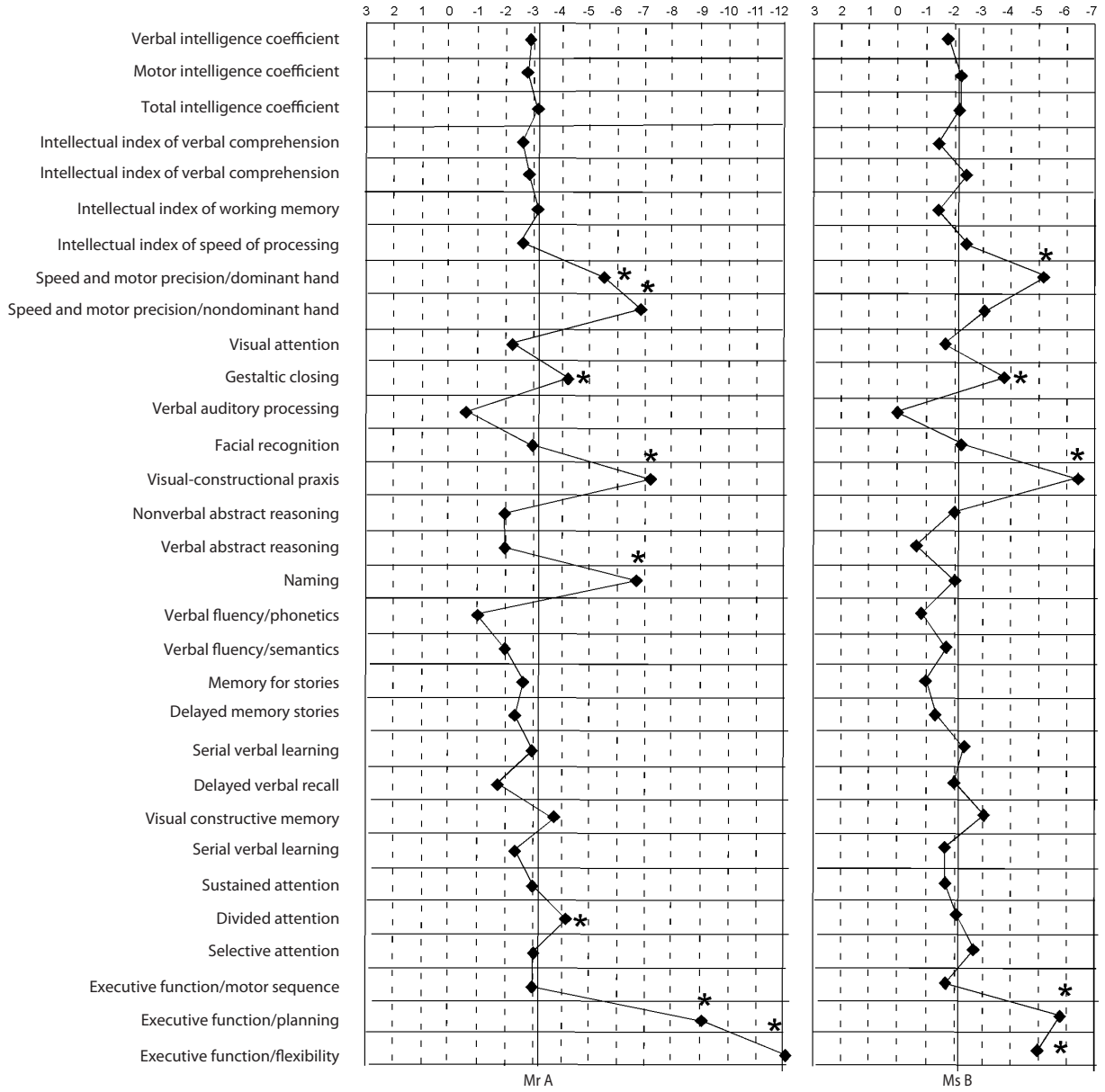
Mr A

For the last 3 years, Mr A has been maintained with a combination of low-potency sedative antipsychotics (levomepromazine oral drops 21 mg/d) and very low doses of an SSRI (citalopram 10 mg/d), well below the effective doses used for adults, which tend to be in the range of 20–60 mg/d. The variations of his treatment are summarized in Table 2.

Treatment with levomepromazine was initiated, aiming for an improvement in Mr A's anxiety and hypomanic state (irritability, aggressiveness). Once these symptoms were under control, a mild depressive state arose and was treated with the use of citalopram, as trials with the benzodiazepine lorazepam and sulpiride did not yield any improvements in the depressive state. The mild depressive state disappeared within 2 weeks following the SSRI intake (citalopram 20 mg/d). After this treatment, Mr A experienced a short hypermanic state, encompassing an increase of uninhibited sexual behavior and irritability that lasted less than 1 week. The citalopram was reduced to the current maintenance dose of 10 mg/d along with levomepromazine 21 mg/d. Low doses of levomepromazine are maintained to counterbalance the side effects (hypomania) of SSRI intake and to help his anxiety and sleeping problems. It is noteworthy to say that Mr A has remarkably improved in autonomy and social skills since the beginning of treatment.

Mr A did not experience adverse effects in response to the SSRI treatment, apart from 1 occasion when he suffered a psychotic episode, most likely in response to an intramuscular bolus dose of corticosteroids (methylprednisolone 40 mg) administered to control a mild anaphylactic shock of unknown etiology. This episode was regulated by suppressing the SSRI for 1 month and increasing the dose of levomepromazine to 25 mg. We did not aim at that time to improve the psychotic symptoms (paranoid and megalomaniac poorly structured delusions, increased disorganization of speech), as these symptoms were assumed to be an acute response to the corticosteroids.

Figure 1. Neuropsychiatric Profiles of 2 Adults With Williams Syndrome[a]



[a]All scores was transformed to *z* scores for comparison. Intellectual quotient scores were taken as mean, so all scores that were 1 deviation above or below the mean were considered as strong or weak abilities. The left panel corresponds to Mr A, and the right panel corresponds to Ms B.
*Asterisks point out the weak abilities of both individuals.

In addition, since Mr A has the autoimmune disease Behcet's syndrome, unknown to the psychiatrist, he was treated with corticosteroids for months, which resulted in mood variations (such as irritability, depressed mood, anxiety) as expected from a hypercortisolemic state.[38,39] Interestingly, corticosteroids have been suggested to act directly on the serotoninergic system.[40] In order to control these mood variations, the dose range of levomepromazine varied between 10 and 25 mg/d (maximum). Although the antipsychotic doses of levomepromazine given to normal adults are usually higher (over 100 mg/d), we adjusted our dose range based on the observation of clinical outcomes both to regulate the sleep and to alleviate the irritability and dysphoria. Mr A currently reports that his mood has been stabilized. Depression, irritability, and aggressiveness are under control. He has also experienced an improvement in self-control, concentration, and visual, verbal, and social skills.

Ms B

Ms B is currently being treated with a combination of sedative antipsychotics (levomepromazine oral drops 25 mg/24 h) and low doses of an SSRI (citalopram 20 mg/24 h), which may be low to produce drastic changes but are enough for maintenance. The variations of her treatment are summarized in Table 3.

When Ms B first came to the clinic, she was being treated for depression with lamotrigine every 12 hours and

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gabapentin. Treatment with levomepromazine was initiated, aiming to improve her anxiety and sleep problems. The depressive state appeared only after the anxiety symptoms were gone, and, thus, we included citalopram 30 mg in her treatment. Once depressive symptoms subsided, lamotrigine treatment was stopped. Gabapentin has not yet been retired, as it maintains the strength of its effect with time and helps with anxiety (Ms B takes 1.8 g/d, 600 mg every 6 h). Ms B currently reports that she has experienced an improvement in self-control, irritability, and aggressiveness, and her mood has been stabilized. She feels happier than before, although she still has problems controlling her obsessions.

We conclude that the SSRI therapy seems to be the most adequate treatment to control mood variations and generalized anxiety disorder in individuals with Williams syndrome. However, treatment should be administered in lower doses than what is typically prescribed. The medication dose must be fine-tuned to each patient and supplemented with low doses of a typical, low-potency antipsychotic such as levomepromazine.

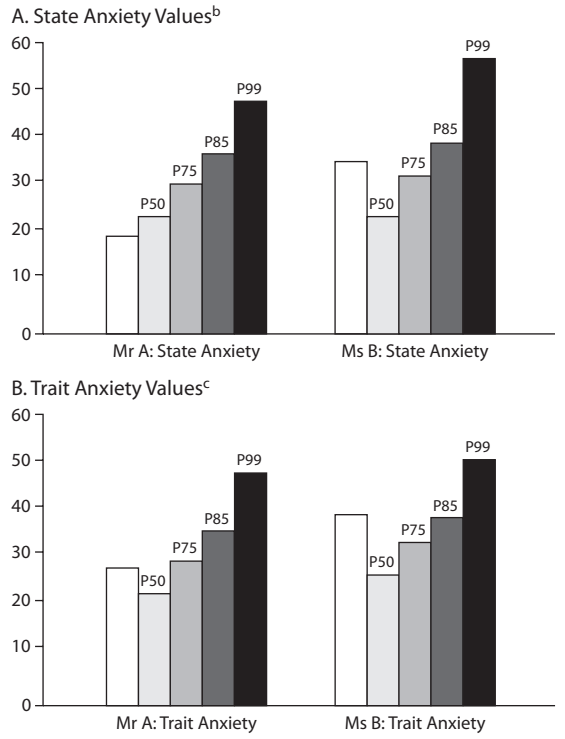
DISCUSSION

Williams Syndrome: Psychiatric Profile and Response to Antidepressants

The most common psychiatric disorders found in Williams syndrome have been reported mainly in children and encompass ADHD in 65%–84%,[10,41] specific phobia in 43%–54%,[41,42] and generalized anxiety disorders in 8%–24% of the cases.[41,42] Longitudinal trajectories of anxiety disorders in children with Williams syndrome have been evaluated, and it has been suggested that anxiety suffered by these children is most often chronic.[43]

Despite the difference in age and gender, both individuals with Williams syndrome presented here match in terms of strengths and weaknesses, and the neuropsychiatric profiles reveal a prefrontal cortex affliction in both subjects. A loss of prefrontal cortex abilities can give rise to an impulse control disinhibition. Interestingly, impulse control disorder has been described in individuals with Williams syndrome[17] (T.R.M., personal observation). Impulse control disorder is considered to be part of the OCD spectrum and has also been described as a trait in bipolar disorder. Thus, a common biological basis may be behind both OCD and bipolar disorder pathologies.[44,45] Patients with OCD tend to have an imbalance of serotonin and dopamine levels in the prefrontal cortex.[46] Drugs that increase serotonin output, such as SSRIs, reduce symptoms of OCD and are effective in bipolar disorder.[47–49] We postulate that it is likely that Williams syndrome neurologic pathologies stem from a similar biological basis as bipolar disorder, which is further validated by the finding that patients with Williams syndrome are highly responsive to SSRIs, as are patients with bipolar disorder.[49] In addition, an imbalance in serotonin receptors has been reported in the prefrontal cortex of a Williams syndrome mouse model[50] and has been linked to the pathogeny of bipolar disorder.[51]

Figure 2. State-Trait Anxiety Inventory (STAI) Profiles of 2 Adults With Williams Syndrome[a]



[a]The STAI was used to quantify anxiety.
[b]Scores show normal values for Mr A (left panel) and higher values for Ms B (right panel).
[c]Scores show a high trait anxiety for both individuals. P50 = 50th percentile, P75 = 75th percentile, P85 = 85th percentile, and P99 = 99th percentile. The first column of the graph refers to the scores obtained by each patient for every scale. Higher scores are positively correlated with higher levels of anxiety. For example, a score of P70 would mean that the anxiety levels of a given subject were higher than the anxiety levels of 70% of a given population.

Features involving the prefrontal cortex such as executive functions (planning and mental flexibility) have so far been poorly studied in Williams syndrome.[22,23] Here, we confirm and extend previous data on the executive functions as well as the decreased visual abilities. Furthermore, we have studied features such as delayed verbal recall; serial visual learning; sustained, divided, and selective attention and motor sequencing; intellectual index of processing speed; intellectual index of perceptive organization; and denomination and delayed memory for stories and found them to be in accordance with the intellectual level of the patients.

Williams Syndrome: Digestive System, Autoimmunity and Anxiety

Digestive problems including gastroesophageal reflux are well-known and encompassed in Williams syndrome.[19] Gastrointestinal problems might cause a deficiency in the immune system and could result in autoimmune problems in the long-term, as happens in other diseases such as Parkinson's disease.[52,53] Moreover, an inflammation in the digestive system could be potentiating a dysregulation in the hypothalamic pituitary system[52] that could in turn radicalize

Table 2. Medical Management and Effects of the Psychiatric Medication in a 26-Year-Old Man With Williams Syndrome[a]

Date	Medication and Dose	Medical History and Medication Adverse Effects
July 2009	Levomepromazine 12 mg	Mr A presents to the clinic for the first time with a mild depressive episode and general anxiety disorder according to *DSM-IV-TR* criteria; he is not taking any psychiatric medication Levomepromazine 12 mg is given as 3:1:8; to adjust the dose, Mr A receives variations of 1 drop every 15 d
May 2010	Levomepromazine 14 mg Sulpiride 100 mg	Levomepromazine is given as 1:0:13; Mr A reports to be depressive, irritable, impulsive, and aggressive; sulpiride is given as 1:0:1 for 3 wk combined with levomepromazine with no additional effect
June 2010	Lorazepam 1 mg Levomepromazine 14 mg	Lorazepam 1 mg is combined with levomepromazine 14 mg for 1 mo with no additional effect
July 2010	Citalopram 20 mg Levomepromazine 8 mg	Citalopram 20 mg is started with 1 tablet in the morning every 2 d for 3 wk; levomepromazine intake is 3:1:4 at this time
August 2010	Levomepromazine 25 mg	Mr A reports to have suffered a psychotic break produced by a corticosteroid injection; citalopram intake is suppressed for 1 mo, and the dose of levomepromazine is increased to 25 mg to control symptoms
September 2010	Citalopram 20 mg Levomepromazine 25 mg	Citalopram 20 mg is added to levomepromazine 25 mg
October 2010–April 2011	Citalopram 20 mg Levomepromazine 10–25 mg	Mr A reports an unstable mood and hyperactivity; a reduction in the dose of citalopram and a spaced intake of every 48 h are used to stabilize Mr A; in April, Mr A reports that he has started a biological treatment to control his symptomatology due to Behcet's syndrome
May 2011–June 2011	Citalopram 20 mg Levomepromazine 25 mg	Mr A reports an unstable mood (mania) that is controlled by increasing the dose of levomepromazine to 25 mg/d
July 2012–October 2012	Citalopram 15 mg Levomepromazine 22 mg	Citalopram is given as 15:0:0; Mr A reports that his mood is stable; he has experienced an improvement in concentration, visual abilities, and verbal and social skills; no depression, anxiety, or aggression are reported; levomepromazine is given as 10:0:12; self-control improvement is reported; Mr A is told that he has been taking glucocorticosteroids as part of his treatment to control his immune disease; glucocorticoid intake is suppressed and another similar treatment that contains no glucocorticoids is started
November 2012–present	Citalopram 10 mg Levomepromazine 21 mg	Levomepromazine is given as 9:0:12

[a]Only the combination of SSRI and antipsychotics is efficient in the control of generalized anxiety disorder and depressive symptoms. Dosing schedules represent the daily doses given in the morning, afternoon, and night.
Abbreviation: SSRI = selective serotonin reuptake inhibitor.

Table 3. Medical Management and Effects of the Psychiatric Medication in a 35-Year-Old Woman With Williams Syndrome[a]

Date	Daily Dose	Medical History and Medication Adverse Effects
January 2012–May 2012	Lamotrigine 100 mg Gabapentin 1.2 g Levomepromazine 46 mg	Ms B presents to the clinic for the first time and fulfills *DSM-IV-TR* criteria for general anxiety disorder, a mixed state with mild depressive symptoms and dysphoria, and mild obsessive-compulsive disorder; she had been treated for 2 y with lamotrigine 100 mg (1:0:1) and gabapentin 1.2 g (1:1:2) Levomepromazine 46 mg is added to her previous medications as 14:14:18 to control anxiety and sleep problems
June 2012–July 2012	Lamotrigine 75 mg Gabapentin 1.2 mg Levomepromazine 46 mg Citalopram 30 mg	Progressive removal of lamotrigine; lamotrigine is given as 1/2:0:1; Ms B reports an unstable mood; gabapentin is given as 1:1:2; levomepromazine is given as 14:14:18; mild obsessive-compulsive disorder is observed; due to depression, Ms B starts SSRI treatment with citalopram (1/2:0:1)
August 2012–November 2012	Lamotrigine suppressed Gabapentin 1.8 mg Levomepromazine 31 mg Citalopram 20 mg	Lamotrigine is suppressed once Ms B is asymptomatic; gabapentin is given as 2:2:2; lamotrigine is given as 5:10:16; Ms B's mood starts to stabilize, and she reports that stomach pain is decreased and self-control has improved; citalopram is given as 1:0:0
December 2012–present	Gabapentin 1.8 g Levomepromazine 25 mg Citalopram 20 mg	Gabapentin is given as 2:2:2; levomepromazine drops are given as 5:10:10; Ms B reports more self-control and less irritability and aggressiveness; citalopram is given as 1:0:0; depressive symptoms diminish and obsessive behavior improves

[a]Only the combination of SSRI and antipsychotics is efficient in the control of generalized anxiety disorder and depressive symptoms. Dosing schedules represent doses given in the morning, afternoon, and night.

anxiety and OCD in the long-term. A dysregulation in the hypothalamic pituitary axis has recently been described in Williams syndrome,[54] and to our knowledge, no studies describing the existence of autoimmune diseases in patients suffering from Williams syndrome are available. The above data, together with the higher frequency of celiac disease in patients with Williams syndrome[19] and previous data showing alterations in abnormal B-cell development,[55] suggest that a positive feedback might be occurring in Williams syndrome, ultimately enhancing the symptoms of anxiety. Untreated or mistreated anxiety could ultimately develop psychopathologic aspects in Williams syndrome in the long-term, and these neglected aspects have been described in those with Williams syndrome.[19]

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CONCLUSION

More detailed information with regard to treating and characterizing anxiety in Williams syndrome is needed for psychiatrists and neuropsychologists. Consideration of anxiety and frontal lobe affectations as basic symptoms in patients affected by Williams syndrome could help professionals and caregivers in the detection of these symptoms and would prevent treatments that potentiate psychopathologies in the long-term. Moreover, treating anxiety properly in Williams syndrome might allow these patients to develop adequate responses to social stimuli and neuropsychological strategies. The combination of SSRIs and low doses of antipsychotics to counteract SSRI side effects seems to be the most suitable medication to treat generalized anxiety disorder and related disorders in individuals with Williams syndrome.

Drug names: citalopram (Celexa and others), gabapentin (Neurontin and others), lamotrigine (Lamictal and others), lorazepam (Ativan and others), methylprednisolone (Depo-Medrol, A-Methapred, and others).

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