Schizotypal personality disorder: Treatment overview

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INTRODUCTION

Schizotypal personality disorder is a chronic disorder with manifestations beginning in childhood and adolescence. Phenomenologic characteristics of the disorder include cognitive-perceptual problems (eg, magical thinking and paranoia), oddness (eg, odd rapport, affect, and speech), and interpersonal problems (eg, social anxiety and a lack of close friends).

Schizotypal personality disorder is underrecognized, and its treatment is understudied. The lifetime prevalence of schizotypal personality disorder in the general United States population has been estimated at just under 4 percent. The disorder is associated with significant disability, as well as a wide range of psychiatric comorbidities. Schizotypal personality disorder is challenging to treat.

This topic reviews our approach to selecting treatments for schizotypal personality disorder, as well as pharmacotherapy for the disorder. The epidemiology, pathogenesis, clinical manifestations, course, and diagnosis of schizotypal personality disorder, as well as psychotherapy for the disorder, are reviewed separately. Establishing and maintaining a therapeutic relationship in patients with personality disorders are also reviewed separately. (See "Schizotypal personality disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis" and "Schizotypal personality disorder: Psychotherapy" and "Overview of personality disorders" and "Approaches to the therapeutic relationship in patients with personality disorders".)

INITIATING TREATMENT

The priorities of the initial treatment visits for individuals with schizotypal personality disorder include establishing an alliance, reviewing the individuals symptoms and level of functioning, assessing the individuals capacity to critically examine thoughts, and establishing treatment plan and goals. (See "Schizotypal personality disorder: Psychotherapy", section on 'Initiating a psychotherapeutic relationship'.)

PSYCHOTHERAPY AS THE PRIMARY INTERVENTION

For individuals with schizotypal personality disorder, we suggest first-line treatment with a long-term, psychodynamically informed psychotherapy. We prefer to use pharmacologic treatment for targeted symptom relief in the context of psychotherapy. (See 'As needed symptom-targeted pharmacotherapy' below.)

Selection of psychotherapy — There are limited data to support the use of a specific type of psychotherapy in the treatment of schizotypal personality disorder [1]. Our choice is based on our clinical experience. We favor the use of supportive, supportive-expressive, or exploratory/insight-oriented psychotherapies.

We base our specific choice of psychotherapy on the individual's level of impairment, ability to critically examine thoughts, and capacity to tolerate negative emotions. As examples:

- **Lower functioning, less introspective** – For these individuals, we favor a supportive psychotherapy that maintains stability and mitigates symptomatic exacerbation. These individuals are typically highly impaired and have chronic symptoms and are less able to critically examine thoughts. Technique and goals of this therapy and further description of individuals it is best suited to are discussed elsewhere. (See "Schizotypal personality disorder: Psychotherapy", section on 'Less introspective, lower functioning individuals'.)

- **Intermediate level of functioning and introspection** – For these individuals, we favor supportive-expressive therapy. These individuals are typically superficially well adjusted, able to live independently and often sustain gainful employment. Technique and goals of this therapy and further description of individuals it is best suited to are discussed elsewhere. (See "Schizotypal personality disorder: Psychotherapy", section on 'Intermediate introspection and functioning'.)

- **Higher functioning, more introspective** – For these individuals, we favor exploratory, insight-oriented psychotherapy. These individuals are generally able to critically examine thoughts and may be able to explore unconscious thoughts. These individuals are typically able to maintain a job and live independently. The techniques and goals of this therapy and further description of individuals it is best suited to are discussed elsewhere. (See "Schizotypal personality disorder: Psychotherapy", section on 'More introspective, higher functioning individuals'.)

Rationale for psychotherapy — In our clinical experience, a psychodynamically informed, supportive, supportive-expressive or exploratory/insight-oriented psychotherapy is critical for patient stabilization and engagement in treatment.

Our recommendation is based primary on our clinical experience, which is consistent with the recommendations of others with expertise in the treatment of the disorder [2,3]. Our approach is also consistent with that of others who have described metacognitively oriented psychotherapeutic approaches (ie, approaches that focus on enhancing the development of more flexible and nuanced interpretations of thoughts, feelings, and intentions) to schizotypal personality disorder [4,5].

While there are theoretical and technical differences between psychodynamically informed and metacognitive psychotherapies, each places an emphasis on developing the ability to form complex and integrated ideas of self and others. These are then used in regulating distress and guiding responses to psychosocial challenges [5]. Both allow for the treatment to be tailored according to level of personality function.

There are no controlled clinical trials on the efficacy of psychotherapy for the disorder. Case series and reports have supported the use of metacognitively oriented therapy in the treatment of schizotypal personality disorder [4,5]. Techniques, goals, and choice of psychotherapy for individuals with schizotypal personality disorder are discussed elsewhere. (See "Schizotypal personality disorder: Psychotherapy", section on 'Efficacy' and "Schizotypal personality disorder: Psychotherapy", section on 'Choosing psychotherapy'.)

AS NEEDED SYMPTOM-TARGETED PHARMACOTHERAPY

In our clinical experience, pharmacotherapy targeting certain core symptoms of schizotypal personality disorder can be a helpful adjunct to psychotherapy and can partially attenuate symptomatic manifestations. These core symptoms include cognitive-perceptual/psychotic

symptoms, cognitive deficits, and social anxiety. (See 'Cognitive-perceptual and psychotic symptoms' below and 'Cognitive deficits' below and 'Social anxiety' below.)

Counseling on medication use — Individuals with schizotypal personality disorder can be highly ambivalent about medication. This can be exacerbated if the symptoms a psychiatrist recommends treating pharmacologically do not bother the patient. We use the following guidelines in the pharmacological management of individuals with schizotypal disorder.

- **Empathic clarification of false beliefs** – We support empathic clarification and tactful confrontation of odd/magical or paranoid beliefs concerning medication. While a medication may be helpful, psychotherapeutically addressing ambivalence about the medication may be the more pressing issue.

- **Avoid excessive reliance on medication** – We typically avoid excessive reliance on medications in treating schizotypal personality disorder. This is in part because the symptomatic manifestations (eg, social anxiety, attenuated emotional reactivity, and cognitive-perceptual symptoms) can be mistaken for other mental disorders that are more responsive to medication (eg, social anxiety disorder, major depression, psychotic disorders). The relatively indolent course of schizotypal personality disorder symptoms in general may also encourage an undue reliance on medication rather than psychotherapy. (See "Schizotypal personality disorder: Psychotherapy", section on 'Chronicity of symptoms, indolent course'.)

Rationale for symptom-targeted pharmacotherapy — There are no clinical trials comparing various pharmacologic approaches for symptoms of any of the domains. A handful of small clinical trials suggest that judicious, adjunctive use of medications for certain targeted symptoms of the disorder may partially reduce their severity. As an example, in a clinical trial, treatment with cognitive remediation, social skills training and guanfacine led to greater improvement in reasoning, problem solving, and social cognition than treatment with cognitive remediation, social skills training, and placebo [6].

Cognitive-perceptual and psychotic symptoms — We suggest adjunctive medication with an antipsychotic medication for individuals with schizotypal personality disorder with cognitive-perceptual symptoms that cause significant impairment and/or are highly ego-dystonic. (See 'Antipsychotic medication' below.)

Target symptoms in this domain include odd beliefs/magical thinking, unusual perceptual experiences, ideas of reference, and paranoia. They are generally chronic but can become more pronounced (eg, to a psychotic degree) under stress. (See "Schizotypal personality disorder:

Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis", section on 'Cognitive-perceptual'.)

Antipsychotic medication — In our clinical experience, low-dose atypical antipsychotics can attenuate clinically significant and ego-dystonic cognitive-perceptual symptoms and acute exacerbations of cognitive-perceptual symptoms. However, the presence of cognitive-perceptual symptoms in and of itself is not an indication for antipsychotic treatment. (See 'Choice and administration of antipsychotic' below.)

We prefer using antipsychotic treatment used within the context of treatment with psychotherapy. We focus on understanding how the patient makes sense of their symptoms, their thoughts, fears, and expectations about medication, as well as on processing of salient psychosocial events that may be precipitating these symptoms.

Choice and administration of antipsychotic — As there do not appear to be significant differences in efficacy among antipsychotics (see 'Efficacy' below), we typically base our choice of antipsychotic medication on comorbid conditions, the patient's risk factors for side effects, and the medication's side effect profile. We generally use aripiprazole, quetiapine, risperidone, or olanzapine, which have lower rates of extrapyramidal symptoms compared with first-generation antipsychotics, and have been studied in schizotypal personality disorder or have indications for comorbidities common to schizotypal personality disorder. (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects", section on 'Adverse effects'.)

Individuals with schizotypal personality disorder may be particularly sensitive to side effects. We often begin with a dose towards the lower end of the starting dose range. This is typically lower than dosing for acute psychosis and psychotic disorders (table 1). We typically titrate in slowly (eg, increase the medication every two to three weeks), unless a more rapid pace is necessary due to the acuity and severity of co-occurring symptom. It is essential to engage patients in the process of titration.

As an example, risperidone can be started at 0.25 mg daily (at bedtime if insomnia is present) for at least two weeks, and increased to 0.5 mg daily if clinically indicated. Further dose changes should be determined on a case-by-case basis. Starting and therapeutic doses of other antipsychotic drugs for the disorder include:

- Aripiprazole – 2 mg and 5 to 10 mg
- Quetiapine – 25 mg and 50 to 100 mg
- Olanzapine – 1.25 mg and 5 to 7.5 mg

We often continue antipsychotics medications for weeks to months if a transient exacerbation is targeted, or longer if chronic symptoms respond to treatment. The need for ongoing use should be reviewed with the patient approximately every three months and weighed against the side effects. (See 'Side effects' below.)

Side effects — Common side effects associated with second-generation antipsychotics include weight gain and related metabolic effects, extrapyramidal symptoms, hypotension, sedation, anticholinergic symptoms, hyperprolactinemia, cardiac effects, cardiomyopathies, cataracts, and sexual dysfunction. The rate and severity of these side effects and their treatment is discussed elsewhere. (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects", section on 'Adverse effects' and "Schizophrenia in adults: Maintenance therapy and side effect management".)

The potential morbidity of metabolic effects has led to recommendations for routine short- and long-term monitoring of weight, waist circumference, blood pressure, fasting glucose, and lipid profile of patients taking any of the antipsychotic drugs (table 2) [7]. (See "Schizophrenia in adults: Maintenance therapy and side effect management".)

Efficacy — Limited clinical trial data suggest that antipsychotic medication may be useful as an adjunct to psychotherapy in schizotypal personality disorder.

Two small trials provide limited evidence that second-generation antipsychotics may be efficacious for symptoms of schizotypal personality.

- In a clinical trial, 25 individuals with schizotypal personality disorder were randomly assigned to receive risperidone (2 mg/day) or placebo for nine weeks [8]. Risperidone was titrated to 2 mg/day over seven weeks. Mean total scores on the Positive and Negative Symptoms Scale (PANSS) improved in the risperidone treated group compared with placebo. The negative and general PANSS subscales improved more quickly and/or at a lower antipsychotic dose (0.25 to 0.5 mg/day) compared with the positive-symptom subscale (1 to 2 mg/day).

- An uncontrolled, open-label trial tested the efficacy of olanzapine (average dose 9.32 mg/day) on a range of psychiatric symptoms in 11 patients with schizotypal personality disorder [9]. After 26 weeks of treatment, mean scores on the Brief Psychiatric Rating scale and the Global Assessment Scale of overall patient functioning improved in 7 of the 11 individuals. Olanzapine was generally well tolerated; however, close to half of patients experienced more than a 7 percent increase in body weight.

Cognitive deficits — Cognitive deficits are very common in schizotypal personality disorder and are typically a function of deficits in working memory, executive function, and verbal memory. Cognitive deficits clinically manifest as absent mindedness, daydreaming, losing one's train of thought, forgetfulness, losing/misplacing everyday items, poor time management, difficulty with organizing complex tasks, and trouble remembering verbally processed information. (See "Schizotypal personality disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis", section on 'Cognitive deficits'.)

Stimulants as preferred option — Our first choice of medication to treat cognitive deficits in individuals with schizotypal disorder is a stimulant. However, because of the risks of misuse and addiction, stimulants are not recommended in patients with an active substance use disorder or history of a stimulant use disorder.

In our clinical experience, the cognitive deficits of schizotypal personality disorder can be treated effectively with stimulants at doses used for attention deficit hyperactivity disorder (ADHD).

A small, uncontrolled trial and our clinical experience suggest that stimulants may be effective in the treatment of cognitive deficits in patients with schizotypal personality disorder. As an example, a single dose of 30 mg of amphetamine was found to decrease perseverative errors on the Wisconsin Card Sorting Testing in nine patients [10].

Administration — We suggest starting with a low dose of a stimulant and titrating relatively slowly to allow for close clinical monitoring of efficacy and potential adverse reactions. As an example, long-acting methylphenidate (eg, Concerta or generic equivalents) can be started at 18 or 27 mg once per day in morning and increased by 18 mg/day at weekly intervals to a therapeutic range of 54 to 72 mg.

Due to risks of adverse cardiac events, prior to treatment with stimulants, patients should receive an evaluation for cardiovascular symptoms (eg, chest pain, palpitations and syncope), and measurement of blood pressure and pulse are recommended [11]. When findings outside of normal limits are seen, consultation with an internist or cardiologist is recommended to determine whether the findings are sufficiently severe to avoid these medications. Blood pressure and pulse should be monitored at regular intervals (eg, initially weekly, then monthly or bimonthly) over the course of stimulant treatment. (See "Cardiac evaluation of patients receiving pharmacotherapy for attention deficit hyperactivity disorder", section on 'Pretreatment clinical evaluation'.)

Side effects — Patients with schizotypal personality disorder theoretically have an increased risk of psychosis when treated with stimulants; cases have been reported in

schizotypal personality disorder patients treated with a stimulant for co-occurring ADHD [12], but appear to be relatively rare. A neurobiological study in which patients with schizotypal personality disorder received an amphetamine challenge did not find the medication to be associated with psychotic reactions [13-15].

Side effects of stimulants reported in adults treated for ADHD include dry mouth, insomnia, edginess/irritability, dysphoria, diminished appetite, weight loss, and headaches [16]. (See "Attention deficit hyperactivity disorder in adults: Treatment overview", section on 'Adverse effects'.)

Other serious, less common adverse effects seen in adults treated with stimulants for ADHD include cardiovascular events [11,17], priapism [18-20], and congenital cardiac malformations in children born to women treated with methylphenidate during pregnancy [21].

Prescription stimulants are subject to misuse, addiction, and/or diversion in some patients. Patients with a recent or current substance use disorder are believed to be as higher risk. Misuse of prescription drugs, including stimulants, is discussed in detail separately. (See "Prescription drug misuse: Epidemiology, prevention, identification, and management", section on 'Stimulants'.)

Guanfacine as alternative — Extended-release guanfacine, an alpha-2a adrenergic agonist used in the treatment of ADHD, is an option, particularly for patients with a contraindication to a stimulant or who fail to respond to initial trial of a stimulant.

Guanfacine can be started at 0.5 mg twice daily, and increased to 1.5 to 2 mg twice as tolerated, if needed, at a rate of 0.5 mg twice daily per week; guanfacine extended release is started at 1 mg/day (usually in the evening), advancing after one to two weeks in 1 mg increments, up to a maximum of 4 mg/day as needed and tolerated. To enhance tolerability, dosing of guanfacine extended release can be twice daily. (See "Attention deficit hyperactivity disorder in adults: Treatment overview", section on 'Treatments with limited supporting data in adult ADHD'.)

Side effects of guanfacine included hypotension, tachycardia, headache, fatigue, abdominal pain, constipation, and sedation [22].

In individuals with schizotypal personality disorder, guanfacine may be helpful in improving working memory, as well as lead to improvements in reasoning, problem solving and social cognition. As examples:

- In a randomized clinical trial of 29 patients with schizotypal personality disorder, treatment with 2 mg/day of guanfacine (an alpha-2a adrenergic receptor agonist) was shown to

improve performance on a context processing task, which reflects working memory ability [23].

- In a randomized clinical trial of 28 patients with schizotypal personality disorder receiving an eight-week course of computerized cognitive remediation and social skills training, the addition of 2 mg/day of guanfacine led to improved reasoning, problem solving scores, and measures of social cognition as compared to individuals receiving similar treatment combined with placebo [6].

Social anxiety — Social anxiety, a prominent and difficult to treat feature of schizotypal personality disorder, has not been subject to clinical trials of medication efficacy in schizotypal personality disorder patients.

For most patients with schizotypal personality disorder and prominent social anxiety, we suggest adjunctive treatment with a long-acting benzodiazepine. In our clinical experience, social anxiety in patients with schizotypal personality disorder does not appear to respond robustly to a selective serotonin reuptake inhibitor (SSRI), the first-line medication treatment for social anxiety disorder. However, an SSRI or serotonin-norepinephrine reuptake inhibitor is a reasonable alternative in patients with an active substance use disorder or history of a benzodiazepine use disorder or in patients with coexisting depression or anxiety disorder. Gabapentin is another potential option.

In our experience, a long-acting benzodiazepine such as clonazepam appears to be effective, albeit partially, when taken as a standing daily dose (rather than as needed) for social anxiety in schizotypal personality disorder. As an example, clonazepam can be started at 0.25 mg twice daily, and titrated at a rate of 0.25 to 0.5 mg day or week according to efficacy and tolerability, to a maximum dose of 3 to 4 mg/day.

Side effects of benzodiazepines include impairment of psychomotor performance, amnesia, addiction, and withdrawal symptoms after long-term treatment, and rebound anxiety after short-term treatment. Benzodiazepines should not be used in those with an active substance use disorder or a history of benzodiazepine use disorder.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Psychotic disorders" and "Society guideline links: Personality disorders".)

SUMMARY AND RECOMMENDATIONS

- **Psychotherapy** – For individuals with schizotypal personality disorder, we suggest first-line treatment with a long-term psychodynamically informed psychotherapy rather than pharmacotherapy alone (**Grade 2C**). (See 'Psychotherapy as the primary intervention' above.)

- **Selection of psychotherapy** – We base our choice of psychotherapy for individuals with schizotypal personality disorder on the individual's level of impairment, ability to critically examine thoughts, and capacity to tolerate negative emotions. There are no trials comparing different psychotherapeutic approaches in patients with schizotypal personality disorder. (See 'Selection of psychotherapy' above.)

  - For individuals who have limited capacity to critically exam thoughts and are poorly functioning we favor treatment with supportive psychotherapy. (See 'Selection of psychotherapy' above.)

  - For individuals who have a modest ability to critically examine thoughts, emotions or behaviors, we favor supportive-expressive psychotherapy. (See 'Selection of psychotherapy' above.)

  - For individuals who have greater ability to critically examine thoughts and are higher functioning, we favor a modified exploratory/insight-oriented approach. (See 'Selection of psychotherapy' above.)

- **Symptom-targeted pharmacotherapy** – In our clinical experience, pharmacotherapy targeting certain core symptoms of schizotypal personality disorder can be a helpful adjunct to psychotherapy. Pharmacologic management can partially attenuate symptomatic manifestations of schizotypal personality disorder. (See 'As needed symptom-targeted pharmacotherapy' above.)

  Individuals with schizotypal personality disorder can be highly ambivalent about medication. This can be exacerbated if the symptoms that being addressed pharmacologically are not particularly bothersome to the individual. In order to minimize this we clarify the reason we are choosing to use medications, address odd/magical or paranoid beliefs about medications, and avoid excessive reliance on medication.

  - For individuals with schizotypal personality disorder with cognitive-perceptual symptoms that cause significant impairment or distress, and/or are highly ego-

dystonic, we suggest adjunctive treatment with low dose atypical antipsychotic medication rather than other medications (**Grade 2C**). (See 'Cognitive-perceptual and psychotic symptoms' above.)

- For most individuals with schizotypal personality disorder with prominent cognitive deficits, we suggest adjunctive treatment with a stimulant medication (eg, long-acting methylphenidate) rather than other medications (**Grade 2C**). Guanfacine is a reasonable alternative for patients with an active substance use disorder or a history of a stimulant use disorder, or who did not respond to a stimulant. (See 'Cognitive deficits' above.)

- For most individuals with schizotypal personality disorder with prominent social anxiety, we suggest adjunctive treatment with a standing (rather than "as needed") dose of the benzodiazepine, clonazepam (**Grade 2C**). A selective serotonin reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor is a reasonable alternative in patients with an active substance use disorder or history of a benzodiazepine use disorder. (See 'Social anxiety' above.)

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