The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Managing the comorbidity of schizophrenia and ADHD

Amy Gough, BA⪼ Jason Morrison, MD, MSc

A 19-year-old man was referred from the children's hospital for ongoing follow-up at an adult early intervention psychosis service. Despite 2 years of treatment for schizophrenia, his outcome has been poor owing to poor medication adherence and recurrent substance abuse. At age 16 he started treatment with stimulants for suspected attention-deficit/hyperactivity disorder (ADHD). Owing to concerns about overuse/abuse, the stimulant was discontinued during his recent hospital admission for psychosis. He insisted on restarting a stimulant, saying he was unable to function or recover without them.

The estimated prevalence of ADHD is 5.9%–7.1%[1] in children and adolescents and 2.5%–5% in adults.[1,2] It is associated with substantial childhood functional impairment and is a predictor of disadvantages extending into adulthood.[3] Despite no controlled epidemiological studies measuring comorbid ADHD and schizophrenia, evidence suggests that children and adolescents with ADHD[4] and their family members[5] are more likely to develop psychotic disorders.

Stimulants (e.g., methylphenidate and amphetamines) are the most common pharmacological treatment for ADHD.[6] As stimulants are often thought to work antagonistically to antipsychotics via opposing actions on dopamine (DA), clinicians may be wary of using stimulants in patients with or at-risk for psychosis. Unfortunately, few controlled studies have assessed whether stimulants worsen the course of illness in patients with psychosis, and there are no clear guidelines for clinicians.

Evidence opposing stimulant use in patients with psychosis includes the precipitation of acute psychosis in people with and without a history of psychosis with supra-therapeutic amphetamine doses and reversal with antipsychotics.[8] At therapeutic stimulant doses, several case reports describe psychosis as an adverse event in children, adults and older adults;[9] moreover, older review data demonstrate worsened psychotic symptoms in 40% of people with schizophrenia.[10]

Conversely, case reports[11,12] and systematic review data[13] show effective stimulant use without worsening positive symptoms and even improved negative symptoms. A nuanced understanding of antipsychotic and stimulant action on DA signalling suggests how these drugs may actually work synergistically.[14,15] Positive symptoms of schizophrenia are related to increased phasic DA signalling in the mesolimbic pathway.[15] Antipsychotics reduce this signalling by blocking postsynaptic DA D2 receptors. At therapeutic doses, stimulants also reduce phasic DA signalling by stimulating presynaptic DA autoreceptors. However, at supra-therapeutic doses, stimulants increase phasic DA signalling.[15] This may explain why high-dose stimulants can worsen psychosis, whereas therapeutic doses may not and may even prove beneficial.

Without clear risk data, clinicians should proceed carefully and empirically. The foundation of treatment starts with accurate ADHD diagnosis. Inattention is common during the prodromal phase of schizophrenia[16] and, without a comprehensive assessment, can be mistakenly attributed to the more common ADHD.[17] The diagnosis of ADHD requires symptoms starting before the age of 12 years,[18] therefore adolescent-onset inattention preceding psychosis suggests a prodromal etiology. Symptom history should be supported by collateral information from multiple caregivers and settings and ideally supported by results of cognitive or psychoeducational assessment.

If comorbidity is established, treat the psychosis first. This will clarify the contribution of treatable psychotic symptoms to the patient's cognitive and functional impairment and establish a baseline from which to judge whether ADHD treatments may be exacerbating or improving symptoms. If clinically significant inattention persists after psychosis treatment, consider nonstimulant treatment options, including atomoxetine[19] or bupropion,[7] and nonpharmacological interventions, like psychoeducation and cognitive behavioural therapy.[20,21]

If ADHD symptoms persist, consider a stimulant trial supported by psychoeducation for the patient and family on potential adverse events, including psychosis.[22] Pre–post patient and caregiver ratings of ADHD symptoms, or collaborating with a pharmacist on a blinded crossover placebo trial, can assess treatment efficacy. If stimulant misuse or diversion is a concern, daily medication pick-up/delivery can mitigate this risk. If psychosis worsens, discontinue the stimulant.[23,24] Symptoms typically resolve within 2–7 days.[24] Rechallenging can be successful[9] and considered in those with severe ADHD symptoms.[23]

ADHD is a common condition and likely a common comorbidity with schizophrenia. The above recommendations are based on limited available evidence. Controlled studies examining the risks of treating or not treating ADHD in those with psychosis are needed to help navigate this clinical challenge.

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