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Editorial

How can pharmacotherapy impact the quality of life of individuals with high functioning autism?

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1. Introduction

Considering how pharmacological interventions impact the lives of high functioning autistic (HFA) individuals is a matter of understanding the challenges faced by each individual. Given the heterogeneity of the disorder and the wide array of available treatments, this issue becomes complex. The effectiveness of the medication for the target symptoms and the potential for harmful side-effects must be considered.

Autism Spectrum Disorder (ASD) is a lifelong, neurodevelopmental disorder characterized by impairments in social interactions and restricted, repetitive behaviors and interests (RRBs). High functioning autism is a subset of autistic individuals with less severe symptoms and greater cognitive and language abilities than those on the lower end of the spectrum. These individuals may meet criteria for what was formerly known as Asperger’s Syndrome (AS) although evidence suggests that these are separate disorders [1].

The 5th edition of the Diagnostic and Statistical Manual of Mental Disorders made major changes to the classification and diagnostic criteria of ASD which previously included Autistic Disorder, Asperger’s Syndrome, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) among others. A notable change was removing the multiple diagnoses from the manual and using the umbrella term of ASD under which these previous diagnoses may fall in a continuum of severity. The 11th edition of the International Classification of Diseases (ICD-11) adopted this model and deleted the AS diagnosis. For the purposes of this editorial, HFA will be the primary focus, but studies of treatments for individuals across the autism spectrum including AS will be considered.

Despite having less severe symptoms, HFA persons still struggle with key issues such as core ASD symptoms, associated factors such as aggression and self-injurious behavior (SIB), and comorbid psychopathology. Individuals with HFA experience more core symptoms and more language impairments than those with AS [2] while those with AS still experience highly restrictive interests, severe difficulty in reciprocating social interactions, atypical speech content, and other impairments relating to core symptoms [1]. Heterogeneity of symptoms between each individual on the autism spectrum exists frequently and each individual may have completely different presenting problems to be addressed.

For HFA individuals with core ASD symptoms of social communication impairments and RRBs as the presenting problem, pharmacological interventions have not been shown to be effective. To date, no medication has been proven to effectively treat these core symptoms. However, some research has found a reduction in rates of RRBs as a secondary outcome of atypical antipsychotics in youth with ASD, although there is little evidence to support the effectiveness of this as a primary outcome [3]. Currently, attempting to treat these symptoms pharmacologically may only serve to subject the individual to unwanted side-effects.

The picture is quite different for HFA individuals with associated features of irritability (e.g., aggression, SIB) as the presenting problem. Research currently supports the use of aripiprazole and risperidone, the only FDA approved pharmacological interventions for ASD, to address irritability. These interventions have been shown to be effective in treating irritability in youth across the autism spectrum [3] and specifically in children and adolescents with AS [4]. Risks and benefits should be weighed before prescribing these medications, but they can ultimately be useful in short term treatment including acute hospitalization.

Common comorbid conditions in both HFA and AS include Obsessive-Compulsive Disorder (OCD), Attention Deficit Hyperactivity Disorder (ADHD), Bipolar Disorder (BDP) and Depression [5]. Psychotropic agents are poorly tolerated when used to treat comorbidities in individuals with ASD [6]. However, the utility of treating comorbid psychopathology pharmacologically varies by condition. Evidence suggests that treatment of BPD, OCD, and psychosis with psychotropic drugs resulted in poor responses in youth with HFA/AS [7]. Conversely, treatment of ADHD in individuals with ASD with methylphenidate, guanfacine, and atomoxetine has growing evidence and may hold promise [3]. Ameis and colleagues [3] also note that currently, no randomized control trials (RCTs) have been conducted to assess the effects of pharmacological treatments on mood disorders such as Depression in the ASD population, and this treatment is not supported by research at this time.

Several new areas of pharmacological research regarding the treatment of core symptoms are emerging. One such agent being developed is an extracellular signal-regulated kinases (ERK) inhibitor which targets the 16p11.2 microdeletion,
a chromosomal abnormality which is frequently linked to autism. The medication is proposed to be administered during a specific developmental period to halt the effects of the deletion and prevent autism from developing [8]. Novel treatments including Balovaptan, which has been designated as a ‘breakthrough’ therapy by the FDA, and L1-79, which has been given fast track approval by the FDA, have both been shown to improve social communication in ASD [9]. This evidence is still emerging, however. Other recent pharmacological research includes treatments focusing on oxytocin neuropeptides, which are tied to prosocial behavior in mammals [10].

Typical and atypical antipsychotics may both cause extra-pyramidal side-effects which may include symptoms such as tardive dyskinesia in typical antipsychotics, and sedation and weight gain in atypical antipsychotics [4]. These are unfortunate barriers to treatment of HFA individuals and care must be taken when prescribing medication. Further, although sufficient evidence for use of psychotropic agents in children and use of multiple agents has not been established, these practices are commonplace in the ASD population and are of concern due to risk of side-effects [11].

Parallels can be drawn between the treatment of HFA and other psychiatric conditions. For instance, ADHD is frequently treated with psychostimulant medications despite high attrition rates, problematic side-effects, and symptoms that cannot be treated with these medications, such as deficits in social interaction [12]. Considering the research literature, Schoenfelder and Sasser [12] go on to recommend that best practice for treating ADHD should focus on psychosocial interventions which can be used to address the unique symptoms of each person and can also be used in conjunction with medication, if appropriate. Given the current state of available autism interventions, this should be considered best practice for HFA treatment as well.

Effective, evidence based treatments for core autism symptoms include applied behavior analytic interventions (ABAIs) and group social skills interventions (GSSIs). Specifically, ABAIs have been shown to be effective in improving social communication deficits [13] as well as reducing RRBs [14]. GSSIs have been shown to be moderately effective in increasing social competence [15]. GSSIs may be of particular interest when treating individuals with HFA as these interventions specifically target social skills deficits and have less focus on cognitive impairments characteristic of individuals with ASD who are lower functioning.

2. Expert opinion

Whether an individual with HFA will benefit from pharmacotherapy depends on symptom presentation and medication tolerability. For maximum benefit, these agents must be carefully prescribed and monitored. Unfortunately, the majority of pharmacological studies focus on individuals with ASD and not HFA specifically, which may be a barrier to understanding which pharmacological interventions should be used in individuals with HFA. Still, if used properly, pharmacological interventions have the potential to improve the quality of life of HFA individuals.

Critical findings in pharmacological research literature include the emerging evidence of agents to address the core symptoms of ASD, where no medication has been shown to be effective thus far. However, there is a negligible evidence base for many common prescriptive practices (e.g., prescribing medications to young children) which warrants a need for more RCTs and more studies focusing on the HFA population in particular.

Pharmacotherapeutic research has an overall ambition to find effective treatments of core ASD symptoms and agents to fully prevent or reverse autism, and it is likely that the field will continue in this direction. Considering the neurodiversity movement, treatments such as these may cause concern for autistic self-advocates, many of whom are HFA/AS. While treatments that manage symptoms that impair life functions may be viewed as crucial, treatments that are proposed to fully prevent autism may be viewed as problematic. As treatment research progresses, these arguments may become more pervasive. Further, this research may be hindered due to ethical concerns of RCTs (e.g., withholding treatment from placebo groups), using medications in young children, the heterogeneity of ASD, and variable outcome measures. This emerging research in the development of new medications holds promise, but it is uncertain if efficacy and safety will be established before widespread use.

In light of current pharmacological advances, recently developing research concerning the neurodiversity movement and greater focus on acceptance and understanding of what should and should not be pathologized or medicated in individuals with ASD is of interest. This work may have the potential to facilitate a much-needed dialogue between autistic individuals and treatment providers to better inform treatment practices in the future.

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Reviewers Disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

References

Papers of special note have been highlighted as either of interest (∗) or of considerable interest (∗∗) to readers.

- Large review providing efficacy of many current pharmacotherapeutic treatments for ASD

- Examines BPD in AS while also reviewing medication use and side-effects.


- Best practice guide for deciding when to use pharmacotherapeutic interventions, psychosocial interventions, or both.

