Psychotropic (psychiatric) drugs prescribed to those with autism spectrum disorder and intellectual disabilities: reasons, prevalence, adverse effects and potential for deprescribing.

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Many people with autism spectrum disorder (ASD) and intellectual disabilities are prescribed psychotropic (psychiatric drugs) such as antipsychotics even though they have never been diagnosed with a mental health condition. These drugs are associated with many adverse effects, including behavioural issues, irritability, aggression, restlessness, anxiety, tremors, sleep problems and many others. The majority of the drugs prescribed to this population are prescribed off-label, that is they are primarily approved for mental health conditions such as schizophrenia and psychosis. Many people in this group are prescribed more than one psychiatric drug, leading to additional adverse effects (this is called the prescribing cascade).

This overview was developed for those belonging to or working with the ASD and intellectually disabled community. It provides current thinking on potential risks of the drugs, the ways they can affect thinking, mood and behavior, whether deprescribing works and what we know about best practices.

This paper provides a brief overview of the use and adverse effects (side effects) of psychotropic drugs when they are prescribed to those diagnosed with autism spectrum disorder (ASD) and/or intellectual disabilities (ID). I also discuss how effective these drugs appear to be for managing challenging behaviours and whether they can be withdrawn or reduced safely if they are causing health problems.

This paper is not a comprehensive review of the medical literature on this issue. It is meant to provide family members, patients, caregivers and healthcare providers with a basic understanding of these issues and what many medical experts are saying on these subjects. The papers I consulted are listed below and provide additional sources of information.

What are psychotropic drugs and what do they do in the body?

Psychotropic drugs, (sometimes also called psychiatric drugs), are any drugs that affect a person's mind or mood. There are dozens of psychotropic drugs that generally fall into different categories. Table 1 lists these broad categories and gives examples of the types of drugs found in them. All of these drugs are frequently prescribed to people with ASD and ID.

Table 1: Classes and examples of psychotropic drugs prescribed to ID and ASD community

CLASS OF DRUG	EXAMPLES OF DRUGS IN THIS CLASS
Anti-anxiety pills (benzodiazepines)	There are many different benzodiazepines prescribed in Canada. e.g., Ativan (lorazepam). Some are used as sleeping pills
Antidepressants	There dozens of types of antidepressants prescribed in Canada. Examples are escitalopram (Cipralex); venlafaxine (Effexor)

Stimulants	Prescribed for ADHD – (attention deficit hyperactivity disorder). Examples are methylphenidate (Concerta, Ritalin)
Antipsychotics	There are many antipsychotics prescribed in Canada. They are mainly approved for people who have been diagnosed with psychosis or schizophrenia but are prescribed for many unapproved uses, for example, to manage "challenging behaviours." Examples are: quetiapine (Seroquel) and risperidone (Risperdal)
Mood stabilizers	valproic acid (Depakote)
Sleeping pills or hypnotics	Zopiclone – a common sleeping pill. Very similar to benzodiazepines with the same adverse effects
Drugs for bipolar disorder	Lithium

All psychotropic drugs appear to work by acting on specific neurotransmitters which are the chemicals in the body and brain that help send messages between the neurons (nerve cells). For example, most antidepressants act on the neurotransmitter serotonin. However, because the brain is very complex the exact ways these different drugs work on neurotransmitters or how neurotransmitters interact with each other is not well understood. There are at least 100 different neurotransmitters, and we don't know much about most of them.

Although drug companies often say that psychotropic drugs restore the "chemical balance in the brain," there is no evidence to show this is the case. There is no way of measuring the "balance of chemicals" in the brain or to determine exactly how drugs affect neurotransmitters or whether deficiencies in these chemicals cause mental illnesses. For example, it was once thought that depression was caused by a lack of the neurotransmitter serotonin in the brain, but it was found that many people who are depressed have normal levels of serotonin.

We know that neurotransmitters play a role in almost every body function. This includes functions such as breathing, digestion, heart rate, sleep, mood, muscles/movement and hormones. This means that people who take psychotropic drugs, which act on these neurotransmitters, can experience many adverse effects (side effects) related to these important functions. For example, adverse effects from taking psychotropic drugs can include stomach problems or constipation, movement disorders, tremors, depression and anxiety, sexual problems, poor concentration and memory problems, weight gain, growth of breast tissue in men, pre-disposition to diabetes, insomnia, emotional instability, irritability and sometimes aggression.

Nobody can predict the number and type of adverse effects a person may have when taking a psychotropic drug. This depends on the type of drug being used, the characteristics of the person, whether they have other health conditions and whether they are taking other drugs. People who take multiple drugs (of any type) are at increased risk of having many more drug interactions.

If a person uses psychotropic drugs for a longer term (more than a few weeks or months) they are likely to become tolerant to them. If they try to stop using them or reduce or change their dose, they may experience more severe adverse effects. These symptoms, which are caused by the drug, can be mistaken for a worsening of someone's mental health condition. A

psychotropic drug should never be reduced or withdrawn suddenly but must be slowly tapered over a weeks or months.

How frequently are psychotropic drugs prescribed to those with ASD or ID? What drugs are most commonly prescribed?

Psychotropic drugs are very frequently prescribed to youth and adults with ASD and ID, compared to those in the general population (2,4,8,12,13,14). Research indicates that 30–50% of those experiencing these conditions are likely to be using at least one psychiatric drug; with some studies showing rates as high as 60%. Despite some attempts to reduce the use of psychotropic drugs in this population, rates of prescribing have continued to increase (3).

One study has found that 90% of the psychotropic drugs that are prescribed to this group are being prescribed off-label, that is, the drugs are not being used for uses that are approved by health regulators. Many antipsychotics are prescribed off-label (13). These drugs are mainly approved to treat psychosis and schizophrenia but are being prescribed to treat challenging behaviours which are sometimes seen in this population. This is an unapproved use and there is no clear evidence that antipsychotics are effective for this purpose.

Another study found that rates of prescribing to females are higher than that for males even though more males are diagnosed with ASD and ID. Females were most commonly prescribed antidepressants, sleeping pills and antipsychotics while males were most commonly prescribed sleeping pills, antidepressants and stimulants such as methylphenate. Mood stabilizers and anti-seizure drugs are also regularly prescribed. When antipsychotics are prescribed to those with ASD and ID about a third of them remain on them for over one year (8).

Why are people with ASD and ID prescribed so many psychotropic drugs?

Although depression and anxiety are some of the most common reasons why people with ASD and ID receive psychotropic drugs (4), anti-seizure drugs and antipsychotics are often used for what are considered to be "problem or challenging behaviours." Challenging behaviours are described as behaviours that are aggressive, self-injurious, characterized by irritability, tantrums, sometimes property destruction and inappropriate sexual conduct. Challenging behaviours can be triggered by physical symptoms such as pain, visual problems, sleep problems, incontinence and existing mental health problems. Other triggers include distressing life events and changes in a patient's socio-demographic conditions like changes in housing and caregivers.

Adverse effects, which occur with all psychotropic drugs, can contribute to or mimic challenging behaviours such as aggression, irritability, rage, poor focus, pain and restlessness. (9,13,14). For example, antipsychotics, antidepressants and anti-anxiety drugs can make anxiety and agitation worse. It is often difficult to determine the exact cause of challenging behaviours if a person is taking psychotropic drugs, especially if they are taking more than one.

Because challenging behaviours can be persistent, a patient can remain on psychotropic drugs for a long period of time, especially if they do not have access to non-drug alternatives such as behaviour modification interventions.

The dangers of a prescribing cascade

As described above, psychotropic drugs can have many adverse or side effects affecting many functions in the body. People with ASD and ID can also be taking drugs that are not psychotropic for other physical problems which can also cause adverse effects (13).

The more drugs a person is taking, the more likely they will become victims of a **prescribing cascade** (10,13). A prescribing cascade is when a drug prescribed to a patient causes adverse effects, but this is misinterpreted by the doctor to be caused by a new health condition (rather than by the drug). Instead of discontinuing or reducing the drug causing the symptoms, the doctor may prescribe a new drug or increase the dose of an existing drug.

Prescribing cascades are a serious medical problem and account for many adverse effects. They can go on for many years and involve many different drugs. Adverse effects caused by drugs may not be identified by physicians who sometimes lack this knowledge.

Adverse drug reactions, particularly the effects of a prescribing cascade, should always be considered if someone is experiencing new or worsening symptoms or behaviours.

Do psychotropic drugs reduce or control challenging behaviours?

None of the drugs regularly prescribed to those with ASD and ID are approved by Health Canada to treat challenging behaviours. Shankar et al. note that, in the absence of an existing mental illness, no psychotropic drug has been found to improve these behaviours.

Some experts suggest that a clearer understanding and diagnosis of challenging behaviours, better training of healthcare providers and caregivers, more rational prescribing, acceptance of neurodiversity and using non-pharmacological solutions are more effective in addressing these behaviours (4). There is a view among experts in the field that psycho-social interventions should be the first line of treatment for challenging behaviours, rather than pharmaceuticals (4,6,14).

Better management of challenging behaviour also requires carrying out regular medication reviews to determine drug related symptoms and initiating deprescribing or reducing the drug(s) if called for.

Can psychotropic drugs be safely reduced or withdrawn among those with ASD and ID?

One systematic review involving 21 studies concluded that withdrawal could take place with substantial benefits if concerted efforts are made. However, there was a lack of consistency in the studies included in this review. The studies were small, the types of program interventions were different, the quality of the studies was problematic and there were short periods of follow-up (14). There is a lack of research that examines the optimum speed of withdrawal from psychotropic drugs, the consideration and support needed by individuals undergoing withdrawal and the use of other interventions associated with better withdrawal outcomes (4,5,14).

This systematic review (14) included ten studies that looked at the outcomes of reduction or discontinuation from antipsychotics. The proportion of patients in the studies who discontinued

antipsychotics ranged from 4 to 74% and the proportion who maintained antipsychotic reductions was between 19–83%. There was a high rate of represcribing in some of the studies after the deterioration in behaviour of some subjects.

In terms of health outcomes, some of the studies found that there was an increased dyskinesia among subjects who attempted withdrawal in some studies, but this was reduced when smaller reductions of the drug took place. Transient withdrawal dyskinesia occurred in three studies at a peak withdrawal period but returned to baseline at follow-up. One study reported improvements in weight, BMI and some metabolic indicators.

In terms of cognitive function, one study showed cognitive improvements as seen on a standardized computer test among those who underwent reductions or deprescribing. In another study cognitive function which suggested dementia was improved so that this diagnosis was withdrawn. Level of engagement in activities was increased among those discontinued or who reduced their dose by 50%.

Studies reported in the systematic review which looked at the effect of antipsychotic withdrawal on behaviour appear to be inconclusive. While several studies indicated improvement or no deterioration, several others indicated that 40–90% of their subjects had behavioural deterioration. Although some aberrant behaviour increased in almost half the population which wasn't able to withdraw successfully, 40% were able to withdraw with no worsening of behaviour. (14)

Despite the variable results included in the systematic review, the authors concluded that reduction of antipsychotics, where possible, is desirable, citing the positive effect of withdrawal found in other research.

In a more recent study of a program to withdraw antipsychotics among adults with ID, Shankar et al. achieved successful antidepressant withdrawal totally among 46% of these adults and reduced dosage in another 11.3%. At three months follow-up no one required hospital admission or changes in placement. In another study by de Kuiper, 61% of the study population completed withdrawal at 16 weeks but subsequent represcribing reduced this outcome to 46% at 28 and 40% at 40 weeks. (6)

These more recent studies suggest that antipsychotics can be reduced or deprescribed safely in 40–60% of subjects if a well-managed plan is in place, however, evidence is still lacking on the best way to succeed (13). There appears to be limited detailed advice on how to withdraw and how to manage behavioural challenges in withdrawal considering many patients have been taking the drugs for many years.

Ritter (12) examined psychotropic pharmacology among children and youth by reviewing sixteen studies comprising over 300,000 youth with autism. Rates of polypharmacy (taking multiple psychotropic drugs) ranged from 6.8–87% of autistic youth. However, the research concluded that although rates of psychotropic use in this population are high, there is little empirical evidence to support polypharmacy as a way of improving the behaviour of children and youth with autism. There is also insufficient information on all the impacts of these drugs on this group (12).

Whether and what degree those who are withdrawing or reducing psychotropic drugs receive other interventions while undergoing withdrawal has not been fully explored. McLennan (9) presents a case study of a 15-year-old boy with ASD and ID who was on five psychotropic medications, including two antipsychotics. He was referred for a psychiatric consultation due to behavioural problems including physical aggression, property destruction and various repetitive behaviours as well as having severe obesity. While the withdrawal was underway, a behavioural consultant worked with group home staff to institute behavioural modification strategies. Four of the drugs (sertraline, clonidine, quetiapine and lamotrigine) were discontinued with no apparent behavioural deterioration. Olanzapine was replaced with ziprasidone and another drug was also added (trazodone). Behavioural problems did not reoccur under the new regime but commenced when attempts were made to reduce the ziprasidone, (this drug has many adverse effects). The study notes the that although behavioural modifications are the first line of treatment for behavioural challenges in this population there is often poor access to timely interventions. According to the author, "This likely contributes to physicians wanting to 'do something' (i.e., medicate) while waiting for access to quality behavioural interventions, as well as the provision of other services." (P.144). This case study also illustrates some of the issues with drug substitution which may, in the long-term, be counter productive.

De Kuiper (6) notes that withdrawal often fails because of worsening behaviour even though the specific causes of these behavioural changes are not identified. There is concern that problems when a subject is undergoing withdrawal are often attributed to the withdrawal process when many factors can lead to challenging behaviours. There is also poor monitoring of withdrawal by the school and home

What concerns do patients, family members and caregivers have about withdrawal from psychotropic drugs?

In one study (13), that looked at this question, caregivers and people with ASD and ID themselves expressed concern about the withdrawal of antipsychotics because they were afraid of upsetting the status quo. The literature suggests that those proposing withdrawal or reductions in dose need to be transparent with caregivers, family and patients about the pros and cons of reduction/withdrawal and the types of symptoms that might be encountered. People also need to be told that some symptoms may worsen during periods of the withdrawal but that they will diminish over time and fewer drugs will lead to a better quality of life and lessen behavioural challenges.

What factors are associated with withdrawal success?

Enough research has now been done on efforts to reduce or withdraw psychotropic drugs in the ASD and ID population to identify some broad approaches that are effective. Many of these initiatives have focused on antipsychotic withdrawal but the guidelines for withdrawal would apply to many psychotropic drugs (benzodiazepines and sleeping pills are somewhat different and may require a longer-acting benzodiazepine substitution).

Some of the factors that are associated with withdrawal success are listed below:

Predictors of withdrawal success related to planning and implementation

- Use of a structured pathway and withdrawal plan for each person based on their characteristics and the drug(s) being taken
- Withdrawing only one drug at a time
- Taking a complete patient history
- Educating/informing physicians, patients, (where feasible), family members and other caregivers on the pros and cons and process of withdrawal
- Developing and delivering staff training to those involved in the reduction/withdrawal process. This would involve how to respond to challenging behaviours
- Discussing the concerns of the patient, family members and caregivers
- Incorporating a behavioural modification expert and approaches in the planning
- Developing a crisis response element in the withdrawal plan
- Monitoring and documenting the withdrawal including changes in symptoms and behaviour
- Using non-drug approaches to address withdrawal symptoms
- Avoiding drug substitutions
- Being willing to temporarily stop or slow down the taper if symptoms intensify
- Slowing down the taper in its last phase, if required
- Ruling out comorbidities that may affect the taper
- Involving all team members – using a multidisciplinary approach
- Everyone having a realistic view of tapering/withdrawal symptoms, for example, dyskinesia can increase during the peak of the taper
- Using experienced and stable staffing in regular employment in significant roles

Predictors of withdrawal success related to the individual and caregivers

- Maintaining a stable living situation and environment for the person who is withdrawing
- Encouragement of caregivers to reduce environmental restrictions
- Involvement in and support for the plan by caregivers and family members (based on education and transparency)
- Being careful to not misinterpret symptoms arising from the withdrawal as always being related to the withdrawal. They could also be due to pain, infection, psychological issues such as bereavement, and social issues like changes in caregivers and in the environment
- Handling upsurges of withdrawal symptoms by support, education and slower titration.
- Female gender, low baseline dosage and lower level of problem behaviours appear to contribute to a highly likelihood of successful withdrawal
- Subjects taking multiple drugs and having a higher baseline dose of antipsychotics appear to have a lower likelihood of withdrawal

What we still need to know about withdrawal of psychotropic drugs and the management of challenging behaviour?

- We still lack detailed evidence on how to effectively reduce or stop antipsychotics, for example, determining the best pace of withdrawal, the level of reductions and best ways to manage symptoms

- What are the best methods for handling the withdrawal of other psychotropic drugs? (e.g., benzodiazepines, sleeping pills, antidepressants and stimulants)
- What are the best non-drug methods for managing sleep problems in this population?
- We haven't fully assessed the value of other interventions in handling challenging behaviours such as anger management and CBT
- We still need more data on how long withdrawal should take, especially for people on drugs for many years. What kind and length of follow-up is needed?
- We don't know the extent to which withdrawal can unmask unrecognized mental illness?
- How do we separate mental health symptoms or challenging behaviours from adverse drug effects? Sleep medications can also cause serious adverse effects such as anxiety, balance, memory and cognitive problems and insomnia. After a period of use (sometimes only a few weeks or months), benzodiazepines and sleeping pills can cause rebound insomnia.

DESCRIPTION OF THE STOMP PROGRAM

The Stopping Overuse of Medication in People with Learning Disabilities and/or Autism (STOMP) (Shankar et al.)

The STOMP campaign is part of England's National Health Service and aims to reduce inappropriate antipsychotic prescribing of people with ID or autism.

The campaign states that non-pharmacological interventions to address challenging behaviour such as positive behavioural support or cognitive therapy and responses to environmental triggers are preferred to psychotropic medications but that antipsychotics are often prescribed for challenging behaviour in the absence of severe mental illness without evidence of their effectiveness.

The campaign has identified many issues related to the prescribing of psychotropic medication to adults with ID and ASD. These include a lack of ability for patients to consent to treatment, increased exposure to drug/drug interactions and potential for drug disease. The campaign states that those with ASD and ID are more sensitive to adverse drug effects and may have atypical responses to drug treatment.

Despite these issues the campaign report notes that there is an absence of robust evidence on approaches to withdrawal which means that a pragmatic and individualized approach is needed. The campaign recommends a multidisciplinary approach, consideration of co-morbidities and consultation/involvement with patients and their caregivers. More detail on these approaches, further references, key steps in antipsychotic reduction and good practice principles are available on this website. Most of these have been incorporated into the list of factors associated with successful withdrawal (see above).

https://www.england.nhs.uk/learning-disabilities/improving-health/stomp/

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