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Minimally Verbal Individuals with Autism Spectrum Disorders/Intellectual Disability and Challenging Behaviors: Can Strategic Psychiatric Treatment Help?

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Abstract: (1) *Background*: Psychiatrists are increasingly required to treat minimally verbal (MV) individuals with autism spectrum disorder (ASD), intellectual disability (ID) and behavior problems without much published guidance. (2) *Methods*: We reviewed 80 charts of MV patients managed strategically for challenging behaviors, following IRB approval. Data extracted included demographics, ASD/ID level, diagnoses, epilepsy and medications. In this descriptive study, we examined the course of assessment and treatment and made recommendations for a strategic, person-centered approach. (3) *Results*: Of 53 males and 27 females, mean age 34 years (range 7–76), all had ID; 75 had ASD (94%). Diagnoses included seizures in 40/80 (50%), frequent aggression (89%), self-injury (80%), attention-deficit hyperactivity disorder (ADHD) (64%) and obsessive compulsive disorder (OCD) (34%). The commonest medication classes adjusted were antiseizure medications, antipsychotics, and non-stimulant ADHD medications. (4) *Conclusions*: Clinical impressions suggested that this strategic psychiatric approach was beneficial, notably a review of antiseizure and all other medications for polypharmacy, behavioral and other side effects, followed by a review of possible childhood/current ADHD and a trial of low-dose non-stimulant ADHD medications if warranted. Low-dose risperidone was often effective and tolerable for irritability and self-injury.

Keywords: minimally verbal; epilepsy; psychiatric diagnosis; strategic approach; treatments

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1. Introduction

Minimally verbal (MV) individuals, notably those with fewer than 20 words of expressive language, with autism spectrum disorders (ASD), intellectual disability (ID) or neuropsychiatric illness represent the most vulnerable and underserved of the rapidly growing spectrum of individuals with neurodevelopmental disabilities [1]. This applies to school-aged children older than 5 years, adolescents and adults. Based on most definitions of MV, it is not required that co-occurring ID is present together with an ASD diagnosis. Minimally verbal status has been defined differently by different research groups [2], and for the purposes of this study also includes individuals with absent speech. A significant proportion, notably 25% to 30% of all individuals with ASD, are MV [3]. Clinically, they have higher rates of brain malformations, birth injuries, genetic disorders, hydrocephalus and epilepsy, compared with individuals with ASD/ID who are not MV, although studies are needed. Brain lesions of the frontal lobe in the primary motor cortex in the relatively large area controlling the tongue and larynx affect the motor activity of the tongue and larynx, as well as important aspects of cognitive function, and such lesions may cause seizures [4]. Broca's area, another brain region located in front of the motor cortex of the

dominant hemisphere, normally interacts with the temporal lobe cortex to process sensory information and control mouth movements and thus speech [5].

MV individuals are more likely also to suffer physical disabilities, including cerebral palsy, hemiparesis and quadriplegia, which render them more disabled and susceptible to illnesses and medication treatment side effects. Such medical issues complicate community integration due to increased nursing needs; however, when accompanied by aggression, self-injury, seizures and other challenging behaviors, the urgency for appropriate behavioral and psychiatric interventions becomes even greater.

Along with such increased needs, individuals who are MV often experience serious difficulty tolerating in-person clinic visits, as well as electroencephalograms (EEGs) and other procedures such as blood draws, even with oral sedation attempts. They have the highest seizure rates of all individuals with developmental disability (DD). EEG studies are estimated to diagnose only about 35% of actual seizures, even with optimal tracings. Sedation efforts for EEG in those with severe behavior problems often fail, and may mask seizure activity. While 72 h EEG monitoring is most helpful, many individuals with behavior problems and sensory issues will not keep the EEG head cap on. All of these problems magnify the barriers that such people face in achieving optimal health and well-being [6].

As with individuals on the ASD spectrum in general, the hypothesized causes of such severe disabilities are extremely heterogeneous, including genetic abnormalities [7] and environmental factors such as prenatal infections, toxins and birth injuries [4]. There are still no known medication treatments for the core symptoms of ASD in general, including in those with ASD and co-occurring ID. The treatment of cerebral folate deficiency in cases of central folate receptor autoantibodies by administration of folinic acid shows promise but requires more studies [8]. Furthermore, until the different anatomical, electrophysiological and molecular abnormalities underlying MV status are better elucidated, interventions may remain challenging for improving functional language in the majority of these individuals.

Along with targeting improvements in language, management should also focus on improving functional communication from an early age. Being MV itself sets the stage for communication breakdowns that contribute to challenging behaviors, although with appropriate functional communication and behavioral supports, this can be avoided. Instead of persisting with natural speech training, interventions should focus on developing functional communication, which includes attention to both receptive and expressive components of language [9]. This relies on alternative communication modalities, such as the use of tangible or visual symbols, and manual signs for communication, given that auditory comprehension of natural speech is typically severely impaired. Others serving the individual should also participate in the training. Thus, being MV does not preclude learning functional communication via another modality [10].

Lack of expressive language by the age of 5 years is a general indicator of greater risk for future MV status, although there are exceptions [1]. Many children who are MV may be unable to attend speech/communication therapy if they manifest accompanying behavior problems unless these are treated. In addition, a longitudinal cohort study examined the proportion of children with ASD and MV status before and after a specific early language intervention community program. More than half left the program with significant remaining communication deficits [3]. A prospective, longitudinal study focusing on language trajectories confirms such findings, based on outcomes in 192 children between the ages of 2 and 19 years assessed for possible ASD [11]. Thus, a notable proportion of children who are MV will likely continue to lack expressive language into adulthood, in spite of early childhood speech and language interventions. In addition, a more uniform speech and language assessment protocol is needed to clearly delineate the group's heterogeneity so that research findings in children who are nonverbal/MV can be replicated. A recent review of the clinical and neurobiological features of children who were MV with ASD described psychiatric comorbidities of attention deficit hyperactivity disorder (ADHD), spe-

cific phobias and compulsions, along with aggression, self-injury and property destruction, but also emphasized the lack of an evidence base and the need for further studies [12].

Studies report a significant increase in antipsychotic prescribing in DD, not only due to increased rates of mental disorders, but also for high rates of behavior problems such as aggression in this population with severe DD [13]. Overall polypharmacy rates were higher in a study of adults with cerebral palsy (CP) only, and in those with CP together with other neurodevelopmental disabilities, in comparison with general population rates [14]. Those authors emphasize that clinical care and care coordination are suboptimal for those with cerebral palsy. Since polypharmacy in general has been shown to be potentially harmful, and MV individuals are unable to voice side effects, extra communications with other providers and medication side effect scrutiny are needed. Polypharmacy definitions vary, but generally the term refers to concomitant use of several medications for the same purpose or diagnosis, implying that some of the medications are clinically unnecessary [15]. In addition, antipsychotic polypharmacy, as defined by the use of two or more antipsychotics at the same time, in psychiatric inpatients is associated with increases in significant adverse effects, including falls, hypotension, respiratory depression and extrapyramidal symptoms. Few studies are published regarding the risks and adverse events associated with outpatient antipsychotic polypharmacy in those with DD.

Randomized clinical trials of medications usually exclude individuals with severe developmental disabilities. As a consequence, their treatment often consists of extrapolations made from general population studies; for example, studies of schizophrenia and bipolar disorder, without much consideration of ADHD as a contributor to impulsive aggression and self-injury [16]. Polypharmacy is common in those with severe DD, not only of antipsychotics and other psychotropic medications such as mood stabilizers and antidepressants, but also of other medications, including those for constipation, seasonal allergies, hypertension and dyslipidemia. Especially challenging to clinicians is the common presentation of severe aggression, self-injury and property destruction in a person often already receiving much medication polypharmacy.

Furthermore, the general approach when treating individuals with all levels of DD is slow, and requires the use of collateral information to build a longitudinal profile while getting to know the patient in order to understand their experiences. By the time they are adults, they often receive far more medications, both psychotropic and medical, than the average psychiatric patient in the general population. Stressors including moves, losses, illnesses and medication changes that occurred in their lives around the time of behavioral worsening are key [17]. MV individuals are unable to convey such stresses verbally but may be doing so using self-injury and aggression as a communication or protest behavior. This requires that the clinician use a comprehensive approach to cover all such important factors that may hold the key to their recovery. This includes gathering collateral information on when the person was last doing well, and what has changed since that time. This study examines real-world psychiatry patients who are MV for their diagnoses, treatments and outcomes using an individualized but overall strategic approach based on these factors.

2. Materials and Methods

This study describes 80 patients who are MV with severe behavior problems assessed and treated using a person-centered psychiatric approach and medication adjustments (if indicated) based on a detailed, strategic approach (see Table 1). This approach involves first advocating for behavioral consultation, along with assessing and adjusting antiseizure and all other medications being prescribed that may adversely affect behavior and well-being. Polypharmacy reduction and medication rationalization is a key focus, and requires networking with other providers, including neurologists and primary care clinicians. Another consideration includes treating self-injury and aggression, with consideration of low-dose risperidone if appropriate, as the antipsychotic of choice, especially for self-injury, based on research and clinical experience [16].

Table 1. Treatment strategy for challenging behaviors and polypharmacy.

Clinician Strategy	Intervention
Address functions of challenging behaviors	Order behavioral consultation
Review antiseizure medication behavioral S/Es	Ask neurologists for changes
Review for medical causes or untreated seizures	Review medication needs
Review all medications for side effects	Reduce polypharmacy *
Treat self-injury and aggression	Consider low -dose risperidone
Review childhood ADHD, prior treatment	Consider non-stimulant ADHD med
Minimize antipsychotic polypharmacy	Try taper of other AP meds **

* Examples include duplication of allergy medications, antihypertensives, and taper of psychotropic medications possibly worsening behavior (SSRIs, BZPs). ** Once behavior is improved, try gradual taper of presenting antipsychotics; must be very slow, such as by smallest possible dose per month, to avoid rebound worsening of behavior. ADHD: attention-deficit hyperactivity disorder.

Thereafter, the strategy includes assessing for childhood and current ADHD as an overlooked but common cause of impulsive aggression and self-injury, and treating that if warranted. Improvements in behavior are followed by strategic attempts at a very gradual taper of other antipsychotics and other psychotropic medications that were less effective for that individual. At the same time, vigilance is needed for any untoward effects of medications that are started, given the inability of the individual to communicate these, as well as their increased susceptibility to side effects. Since most responses based on the principle "start low and go slow" may take weeks or even months to produce significant improvements after adjustments in medications are made, overall the goal is to establish a positive trend in behavior, emotional and medical health.

The outpatients in the study were served by the same psychiatrist (author JH) on an ongoing basis, long-term. Referrals were made by parents, guardians, residential facilities and other community providers, due most often to treatment resistance together with severe behavior problems. The university-affiliated outpatient clinic serves patients aged 5 years and older with developmental disabilities and behavior problems. Baseline information used in the study refers to that pertaining to the first consultation.

The study began with a thorough chart review and extraction of data from 80 charts of patients meeting MV criteria (<20 words of expressive language) in our IRB-approved Neuropsychiatry Clinical Database. Data extracted included age, gender, race, ASD diagnosis if present, ID and any other psychiatric diagnoses, baseline aggression and self-injury, seizure status and medications at the time of chart review. Developmental history, prior treatments and possible childhood history of ADHD were elucidated with a parent or close relative who knew the patient well if possible, and by review of available prior medical records.

All psychiatric diagnoses were made based on Diagnostic and Statistical Manual (5th Ed.) (DSM-5) criteria, excluding verbal items [18] and Diagnostic Manual—Intellectual Disability 2 (DMID-2) criteria [19], which is a cross-walk for DSM-5 diagnoses in individuals with DD. In the state of Missouri, in which the clinic operates, all ADHD medication prescriptions for adults except for tricyclic antidepressants required prior authorization involving a detailed review of patient clinical notes by a psychopharmacology expert at the state level. Obsessive compulsive disorder (OCD) was diagnosed based on the presence of compulsive behaviors that interfered with daily functioning, rather than obsessive thoughts, since the latter could not be elicited due to their MV status [20]. Other DSM-5-based diagnoses were less common, but all may be made in MV individuals by excluding verbal criteria.

The clinician, while following the general strategic approach, made mostly recommendations and changes to medications involving small doses, based on the principle of "start low and go slow" while looking for a trend towards improvement. Improvement included longer and more frequent intervals of improved behaviors and quality of life.

3. Results

A total of 53 males and 27 females, with a mean age of 34 years (range 7 to 76 years), were involved in this study (see Table 2). Eight were children or adolescents aged 7 to 17 years, and seventy-two were adults. Overall, 63 were Caucasian, 11 African American, 3 Hispanic, 2 Asian and 1 mixed-race. Four individuals had Down syndrome, 2 Fragile-X, 1 Prader–Willi, 1 Sturge–Weber, and 1 Bannayan–Riley–Rivulcaba syndrome. Three others were legally blind, one was deaf–blind and three had spastic quadriplegia. All had ID; 75 of 80 had ASD (94%), mostly diagnosed at a young age in other specialty child development clinics, and still met current DSM-5 ASD diagnostic criteria. Seizure disorders were already diagnosed and treated by neurologists in half of the sample (40/80, 50%), along with self-injury in four-fifths (64/80, 80%), and aggression in almost all (71/80, 89%). Attention deficit hyperactivity disorder (ADHD) diagnostic criteria were met in 51/80 (64%), which often had been diagnosed along with ASD in early childhood, and OCD rates were lower (27/80, 34%). Bipolar disorder was rare; notably, relatively clear-cut diagnoses were made in 5/80 (6%), and bipolar disorder was a rule-out (possible) diagnosis in 1 case.

Table 2. Demographics.

Gender	Males	53/80
	Females	27/80
Race	Caucasian	63/80
	Black	11/80
	Hispanic	3/80
	Asian	2/80
	Mixed-race	1/80
Mean Age (years)		34
Age Range (years)		7–76
Syndromes/Physical	Down	3/80
	Fragile X	2/80
	Sturge–Weber	1/80
	B-R-R *	1/80
	Legally blind	1/80
	Spasticity	3/80
Autism Spectrum disorder		75/80
Aggression		71/80
Self-injury		64/80
Comorbidities	Epilepsy	40/80
	ADHD	51/80
	OCD	27/80
	Bipolar Disorder:	5/80
	R/O Bipolar Disorder	1/80

* Bannayan–Riley–Ruvalcaba syndrome. OCD: obsessive compulsive disorder.

Treatment resistance, defined as prior treatment with more than three psychotropic medications, was found in over two-thirds of patients, notably 54 of 80 (68%). Using the strategic approach described, the rated outcomes showed a positive treatment response in the majority of the patients treated, using the Clinical Global Impressions-Improvement subscale [21] purely for clinical response tracking, and not research purposes [22]. (For outcome studies, this would require independent validation). Mean treatment duration was 28 months (range 0.5 months to 52.5 months); one child was seen for one visit only.

The three most common medication classes used were antiseizure medications, antipsychotics and ADHD medications. Selective serotonin reuptake inhibitors were seldom used. A total of 40/80 (50%) received antiseizure medications for seizure disorders, managed by neurologists. Seizure medications were changed in collaboration with treating

neurologists at our request in four individuals due to behavioral side effects, with good results. Three of the four were tapered gradually off phenytoin after the initiation and increase of other antiseizure medications to achieve therapeutic doses of the latter (see Table 3). Another patient was tapered off carbamazepine-extended release and lacosamide and onto divalproex in therapeutic doses with good results. In an additional 11/80 (14%) in this sample, antiseizure medications were used for irritability or mood-stabilizing properties. Bipolar disorder diagnoses were rare in this series, as noted above.

Table 3. Changes in antiseizure medications followed by behavioral improvements.

Age, Race, Gender	Medications Tapered Off	Substitute	End CGI-I
28 yr AF	CBZ-ER, lacosamide	divalproex	2
32 yr WM	phenytoin, levetiracetam	clobazam	2
46 yr WM	phenytoin	divalproex	1
67 yr WF	phenytoin	lamotrigine	2

CGI-I: Clinical Global Impressions-Improvement scale. 1 = Very Much Improved, 2 = Much Improved. CBZ-ER: carbamazepine-extended release.

Antipsychotics were the most common class of drug prescribed, of which risperidone was most commonly added, or doses adjusted, in 45/80 or 56% of patients. Target doses employed were most often 0.5 mg up to four times a day, although some patients received higher doses. If behavior improved, the strategy was to gradually attempt taper off of other antipsychotics that had been less effective, including long-acting injectable types. The classical antipsychotic loxapine was prescribed less often and in low doses, mostly 5 to 10 mg/day, in 22/80 or 28% of patients, based on good response and tolerability, and promising weight-sparing preliminary data [16,23]. Dysphagia and constipation, potentially leading to aspiration pneumonia and bowel obstruction, are side effects requiring close monitoring in MV individuals receiving all antipsychotics, especially in high doses or together with SSRIs that inhibit cytochrome P450 CYP2D6 [24]. Other antipsychotics were less commonly used.

ADHD medications, mostly of the non-stimulant subgroup, were used in a majority of patients, often together with antiseizure medications and antipsychotics. Thirty-four of eighty patients (43%) received low-dose amitriptyline, with a mean dose of 64 mg/day (range 10 mg to 150 mg daily). Amitriptyline was used for ADHD, impulsive aggression and self-injury in addition to anxiety, sleep and mood [16]. Seven others received atomoxetine, most often in low doses (range 10 mg to 80 mg daily), while others with ADHD received other ADHD medications (guanfacine, clonidine, or dextroamphetamine in low doses).

4. Discussion

Psychiatrists are increasingly required to treat individuals of all ages who are MV, largely based on their own experience due to inadequate training and minimal published guidance. Prescribing for behavior problems is often required when more suitable behavior management is lacking. At the same time, inappropriate medication adjustments can worsen the problems they aim to treat. Appropriate interventions using the approach we describe can, however, bridge the gap until behavior programming can be established. Detailed functional analysis of behavior, communication strategies and behavioral programming are also important for severe behavior problems, but may take months to establish. Behavior analysis often helps to identify a mismatch between the individual and their circumstances. Stressors that worsen aggression and self-injury include communication breakdowns and demands on the individual that exceed their capacity to handle.

Of 173 empirical studies that used functional assessment to identify causes of challenging behavior, most were identified as able to achieve this [25]. Rating scales such as the Motivation Assessment Scale [26] are designed to address basic motivators for challenging behaviors, including attention, escape from demands, and others. Behavioral interventions are overall extremely effective and beneficial, but they require extensive resources, per-

sonnel training and adherence to specific protocols. Frequent staff turnover and patient moves disrupt such programs even after they have been established. In such situations, psychiatrists may be consulted to prescribe medications for challenging behaviors.

Clinicians rely out of necessity on the direct observation of psychiatric symptoms, behavioral data collection and collateral information. The use of an informant that knows the person well is essential. Providers not routinely serving such severely disabled individuals may feel challenged by the severity and complexity of the multitude of presenting behavioral issues along with higher rates of epilepsy and medication polypharmacy. More published research and improvements in clinical training to serve individuals who are MV and others with severe developmental disabilities are urgently needed. The present undertraining of psychiatrists for this challenging task requires attention globally, including in the USA [27].

Recent large-scale use of in-home televideo platforms for psychiatric and medical visits in the USA, first adopted during the coronavirus pandemic, may ease the severe discomfort felt by patients who are MV during in-office medical visits [28]. Many visits of patients in this series were conducted by televideo, as well as in person. Televideo affords clinicians a safer and more accurate observation of such patients' behavior and mental status in their own environments. However, such patients' difficulties tolerating physical examinations and medical tests remain. The use of techniques to desensitize the person to each step of the visit process may be helpful [29], while giving positive encouragement and preferred food items along with favored object or handheld screen availability if appropriate. In clinical experience, pre-visit or pre-procedure sedation may be helpful, notably using 1 mg each of risperidone and alprazolam an hour before the visit, with repeat doses of each at procedure time if needed for agitation.

Our descriptive study focuses on a real-world cohort of 80 consecutive MV psychiatric patients with ASD and ID in order to review presenting symptoms, diagnoses made and types of treatments prescribed. The strategic approach aims to treat the whole patient. Key areas of focus include ruling out medical or dental problems causing self-injury and aggression such as pain or discomfort from any source, attention to reducing polypharmacy and examining all medications for side effects affecting behavior and well-being. This is ideally performed before adding other medications if necessary, while getting to know the patient and making diagnostic clarifications. Although a similar general approach may already be employed by experts serving this population, our description of the structured approach aims to encourage psychiatrists and other clinicians who may be less familiar with this population to serve them with greater treatment success. Prospective, more detailed studies based on this approach are needed.

The individuals in this study had high rates of ASD, ID, aggression, self-injury, ADHD and diagnosed epilepsy. Very few were diagnosed with bipolar disorder or rule- out (possible) bipolar disorder. Seizure disorder rates were high, with 50% receiving antiseizure medications prescribed by neurologists. One additional individual had not yet been stabilized on medications for his seizures, and another received topiramate for prophylaxis of possible headaches related to his self-injurious behavior of head-hitting. Of note also is a male in the sample with Prader–Willi syndrome and bizarre aggressive and self-injurious behaviors associated with staring spells. He responded well to lamotrigine, which was gradually increased to therapeutic doses along with the addition of guanfacine based on a history of ADHD. He would likely not have cooperated with EEG even with prior sedation attempts as judged by his guardian and clinicians. Of note is that smartphone videos may be important tools for diagnosing seizures, although video recording is not allowed in residential facilities.

Changing from antiseizure medications that likely worsened behavior to more beneficial ones was effective in the cases shown in Table 3. This involved tapering off phenytoin, but only after establishing treatment with another antiseizure medication in therapeutic doses. In turn, that allowed for subsequent psychotropic medication taper due to the improved behavior. Vigilance for behavioral worsening associated with antiseizure medica-

tions is important when working with individuals with developmental disabilities [30,31]. Phenytoin is well known to cause hyperactivity and behavioral worsening, as well as osteoporosis and gingival hypertrophy [32].

Two classes of antiseizure medications linked with behavioral worsening are the barbiturate-based and benzodiazepine-based preparations. Barbiturate-related drugs include phenobarbital and phenytoin; guidelines advise avoiding their use except in special circumstances [33]. However, many other antiseizure medications may worsen behavior, including carbamazepine, oxcarbazepine, topiramate and levetiracetam. Lamotrigine as an anticonvulsant may have antidepressant and anti-aggressive effects, but requires very gradual tapering up and early close monitoring for skin rash in order to prevent life-threatening Stevens–Johnson syndrome. Treatment of seizures may also improve cognition, whereas topiramate may cause cognitive dulling.

In a minority (14%), antiseizure medications were prescribed for irritability and mood stabilization. Bipolar disorder and rule-out bipolar disorder were rare in this series, but can be associated with severe aggression and treatment resistance. Rapid cycling bipolar disorder was found in 10% of long-term residents with developmental disabilities in a psychiatric hospital in one study [34]. Study results are mixed for valproate in ASD for aggression [35]. One study found good results of divalproex for repetitive behaviors in ASD, but lacks replication [36]. A controlled clinical trial of gabapentin in individuals without ASD/ID found good efficacy when used as adjunctive treatment with lithium in patients with bipolar disorder and acute mania [37]. Gabapentin combination treatment with divalproex however avoids the common lithium side effects of thirst, wetting and tremor, and risks of lithium toxicity. Like lithium, gabapentin is renally excreted but has a higher therapeutic index, and it is important to monitor renal function. Prospective studies of gabapentin in addition to divalproex are warranted in individuals with ASD/ID and bipolar disorder.

Antipsychotics, primarily risperidone, were commonly used for self-injury and aggression not responding to other intervention strategies. Based on our clinical and research experience, risperidone has shown the best efficacy of the available antipsychotics for self-injury in low divided doses totaling approximately 2 mg per day. Risperidone is usually given in divided doses to minimize side effects [38]. Risperidone is the best studied of the antipsychotics used in ASD/ID; however, minimally verbal individuals were excluded from those studies. Following the addition of low-dose risperidone, the patient may become less irritable, with reductions in aggression and self-injury, quite rapidly if the risperidone is effective and tolerated. Weight gain and metabolic side effects require monitoring [39] as is needed with all atypical antipsychotic drugs. Another strategy used clinically in this series was to try low-dose loxapine if deemed tolerable, due to the promising weight-sparing properties observed thus far with loxapine at doses of 5–10 mg daily. In these low doses, loxapine resembles an atypical antipsychotic on brain PET studies [40]. The addition of loxapine 5 mg at bedtime if indicated, for the adolescent or adult patient, may reduce irritability and aggression while improving the flexibility of behaviors fairly rapidly if the loxapine is effective and tolerated. Loxapine may, however, be intolerable in some MV individuals with spasticity or swallowing difficulties due to its potent dopamine-blocking properties, in which case risperidone may be preferable.

Dysphagia is a potentially dangerous side effect listed for olanzapine and other antipsychotics, to which individuals who are MV are more susceptible. Gradual olanzapine taper helped reverse dysphagia in some cases in this series, and enabled reintroduction of food by mouth, as described in a separately published study [24]. However, all antipsychotics may produce dysphagia, aspiration pneumonia, constipation and bowel obstruction when used in high doses in all ages, including in the general population. Along with risperidone, loxapine or other antipsychotics, ADHD medications were used in many cases for impulsive aggression and self-injury in individuals with a childhood ADHD history and meeting criteria for ADHD as adults. Differential diagnoses for hyperactivity include medication side effects and akathisia due to antipsychotics.

High rates of ADHD diagnoses were identified, notably 64% or almost two-thirds, and treated with good results. This rate aligns with the high ADHD rates in children and adolescents with ASD/ID, approximately 50% to 80%. ADHD is also four times more common in individuals with epilepsy [41]. Childhood hyperactivity and impulsivity, as well as other ADHD symptoms, are less likely to improve in individuals with more severe developmental disabilities as they age, in comparison with ADHD symptoms in otherwise typically-developed individuals [42]. In individuals with DD, an ADHD history may be overlooked, especially in the transition to adult care, since individuals with state-appointed guardians switch guardianship systems after reaching the age of 18 years. In addition, ADHD is likely underdiagnosed in adults overall.

A study of hospitalized adults with severe or profound ID found that ADHD criteria were met in 55%, although the ADHD identified was of the predominantly inattentive type [43]. Many individuals with MV disability manifest self-injury, which is often worsened by stimulant medications [44], resulting in the preferential use of non-stimulant ADHD medications for them. There are no controlled studies available of ADHD treatments in adults with ASD/ID and MV, and treatments are therefore extrapolated from studies in children. Similarly, studies of adults with ASD/ID and ADHD treated with atomoxetine, guanfacine or amitriptyline are still needed.

All ADHD medications in the current series were used in combination with other psychotropic medications, most often antipsychotics and antiseizure medications. Treatment resistance, especially to antipsychotics, could possibly relate to missed/untreated ADHD in cases with impulsive aggression and self-injury. Aggression and self-injury correlated significantly with hyperactivity and impulsivity in individuals with developmental disabilities, in a large study of 755 individuals with ID [45], as did restrictive and repetitive behaviors. Of those studied, 156 were nonverbal, and another 106 were immobile and either verbal or nonverbal. Most individuals treated for ADHD as adults in the current study had a confirmed childhood history of ADHD, but were not on ADHD medications at presentation. Clinical experience suggests that addition of a low-dose non-stimulant ADHD medication may produce a trend towards reductions in unpredictable and impulsive behaviors, including aggression, with improved self-regulation also of mood.

While clomipramine has been studied in ASD [46], in the author's experience, amitriptyline may produce greater benefits in terms of behavioral outcomes. A published chart review of 50 children and adolescents with ASD and ADHD accompanied by aggression and self-injury found that most benefited from amitriptyline in low doses, often in combination with risperidone, aripiprazole and/or stimulant medications [47] Amitriptyline was the most commonly prescribed of the ADHD medications in this current series, in low doses. Benefits of amitriptyline in ASD may include improvements in sleep, anxiety, irritability, impulsive aggression and self-injury, as well as in headaches, enuresis and gastrointestinal pains. Tricyclic antidepressants remain second only to stimulants in potency for treating ADHD. Safety precautions are needed to prevent overdose toxicity, cardiac side effects and drug interactions, by having all medications locked away to prevent overdose as well as taking a careful cardiac history. Most individuals with DDs living in residential facilities do not have direct access to their medications.

In our current sample, good overall response occurred to low doses of amitriptyline, usually at 25–100 mg daily, at a low mean dose of 64 mg daily, often together with antiseizure medications and risperidone or other antipsychotics. While atomoxetine is a tricyclic derivative, side effects of gastrointestinal pain and headache may be reasons to try low-dose amitriptyline instead. Another non-stimulant ADHD medication used in this series was atomoxetine, most often with twice-daily dosing, morning and night, to improve efficacy and minimize side effects. In a study of youth with ASD, atomoxetine also showed a trend toward reductions in repetitive behaviors, though this requires confirmation in more studies [48].

The weaknesses of the present study include the retrospective nature of the study, involving tertiary referral patients who were thus more likely to be treatment-resistant

and thus possibly less representative of other community patients. Nevertheless, these are the patients that would most likely be referred for treatment in tertiary referral settings such as university clinic training programs. Blinded outcome ratings and standardized questionnaires were not used; however, a prospective study could incorporate these. We examine and describe principal medication classes and highlight the main medications used in each class in this strategic approach, rather than exact medication tapers or additions, the details of which could be overwhelming. However, this could be achieved in a detailed prospective study. While all patients in this series were treated by one psychiatrist, the author JH, other clinicians may have different prescribing approaches in individuals who are MV than documented in this series. While amitriptyline use in ASD/ID requires controlled studies, low doses are commonly prescribed by neurologists for headaches, and by gastroenterologists for functional abdominal pain, which has been a practice for many decades with good results overall. Randomized controlled trials of all important medications are still lacking in those with severe DD and ASD/ID.

Our goal is to provide an overall, holistic strategic approach to encourage clinicians less familiar with individuals who are MV to treat them and help these vulnerable individuals achieve better, more accessible clinical care and improved coordination of care. Individuals who are MV comprise 25–30% of all those with ASD yet are often unable to access mental health services. Specialty inpatient psychiatry units for such cases with DD are also extremely limited [49]. Global deficits in formal training of psychiatrists to serve this vulnerable population, as well as the exclusion of individuals who are MV from studies, renders them at a serious disadvantage for obtaining optimal help, which in turn affects community integration efforts. The rapidly rising incidence of ASD highlights the immediate need to improve the availability of psychiatric assessment and treatment, as well as the inclusion of studies designed to accommodate and treat the problems of MV individuals in psychopharmacologic research. Planning controlled, prospective studies of medications that show great promise in the real world for individuals who are MV with severe disabilities is surely a justifiable strategy.

5. Conclusions

Functional, non-speech communication strategies often help MV individuals and their caregivers, along with behavior analysis to remedy mismatch between the demands placed on the person and their capabilities. Such strategies can significantly reduce behavior problems including self-injury and aggression; however, these interventions are not usually available at short notice, and often take months to obtain. In such settings, psychiatrists are called upon to treat these vulnerable individuals with complex medical, neurological and psychiatric comorbidities. Collateral information and a detailed, person-centered approach are essential.

Based on this 80-patient MV case series, we describe a strategic approach aimed at guiding the clinicians serving them. The major classes of medications prescribed in this case series were antiseizure medications, antipsychotics and non-stimulant ADHD medications. Prospective, systematic studies focusing on individuals who are MV, and targeting antiseizure medication side effects, polypharmacy reduction and systematically examining diagnoses, interventions, side effects and outcomes are urgently needed.

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Data Availability Statement: Data used in the study will be made available upon request to the corresponding author.

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