

Recognition and treatment of mood dysregulation in adults with intellectual disability

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Abstract

Mood dysregulation is a common feature in the psychopathology of people with intellectual disability (ID) and co-occurring behavioral/psychiatric disorders. It can present with a host of dangerous behaviors, including aggression, self-injury, and property damage. There are special techniques that are used to assess these behaviors in people with ID, that can eventually inform an appropriate approach to pharmacologic and nonpharmacologic treatment. Two case studies are presented that illustrate the elements in the assessment and treatment of mood dysregulation in ID.

Keywords: mood dysregulation, autism, intellectual disability

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Introduction

The ability to appropriately monitor and regulate one's own emotional responses to stimuli in the environment is an important part of maintaining mental wellness. Emotions, such as anger, fear, and sadness, may develop in situations that an individual perceives as relevant. The responses to these situations are not just emotional, but can be physiologic and behavioral as well. Well-regulated moods and emotions should serve to produce productive and contextually appropriate action.^{1,2}

Difficulties in mood regulation have been recognized as key features contributing to psychopathology in a wide

range of psychiatric disorders,^{3,4} including affective disorders,⁵ anxiety disorders,⁶ substance use disorders,⁷ eating disorders,⁶ and borderline personality disorder.⁸ Likewise, mood dysregulation is seen as a key feature in psychopathology among individuals with intellectual disability (ID).⁹

The term *intellectual disability* has been adopted by the World Health Organization, the US federal government, and advocacy and professional organizations to replace the term *mental retardation*.⁹ Intellectual disability encompasses a wide variety of conditions arising from genetic, perinatal, developmental, or idiopathic causes that are associated with below-average intelligence and corresponding deficiencies in adaptive behavior. Adaptive behavior includes the conceptual, social, and practical skills that allows people to function in their daily lives. About 1% of the population has an ID.⁹ Intellectual disability is categorized as mild, moderate, severe, or profound based on measured intellectual functioning and associated levels of functional impairment.

Mood dysregulation (also widely referred to in the literature as *emotion dysregulation* or *affect dysregulation*) can vary widely in its clinical presentation, particularly in those with ID.⁹ In people with ID and mood dysregulation, mood may be reported as angry, irritable, or depressed.

Manifestations of anxiety may also be present, including fear, restlessness, hyperarousal, and autonomic instability. Episodic behavioral outbursts may often occur, which can include verbal aggression, physical aggression toward people and property, and self-injurious behavior. The emotional states and behavior outbursts will develop with an intensity and duration that are out of proportion with the environmental provocation.

Mood dysregulation in adults with ID is not established as a discrete psychiatric diagnosis. However, it is very instructive to recognize this as a potentially important domain of psychopathology in people with ID presenting with problem behaviors. In a statistical model developed by Melville and colleagues,¹⁰ the psychopathology dimension of *affect dysregulation–problem behavior* was shown to have strong descriptive validity as a distinct domain of psychopathology in adults with ID.¹⁰ The affect dysregulation–problem behavior dimension had strong predictive validity for severity ratings and 5-year outcomes in measures such as the Global Assessment of Function, the Clinical Global Impression, and the Health of the Nation Outcome Scale for People with Learning Disabilities. The symptom profile within the affect dysregulation–problem behavior domain included physical aggression, verbal aggression, mood lability, irritable mood, and self-harm. This symptom profile is a frequent presentation in people with ID who present for mental health treatment, including the individuals described in the case studies below.

People with ID, particularly those with mild-moderate ID, can reliably self-report their emotions^{11,12} and can recognize facial expressions in others.¹³ However, numerous clinical factors in ID greatly increase vulnerability toward mood dysregulation and associated problem behaviors. Lower cognitive abilities often confer poorly developed social skills within peer groups starting at a young age. Individuals with ID may struggle with the interpretation of social cues and making appropriate responses to social situations.¹⁴ People with ID often experience significant difficulties coping with the challenges of daily life. When autism spectrum disorder is also present with ID, mood dysregulation may be exacerbated by communication difficulties, hypersensitivity to sensory stimulation, and cognitive inflexibility.¹⁵

Individuals with ID present numerous diagnostic and clinical assessment challenges with respect to mood dysregulation. Sovner¹⁶ outlined 4 main issues—baseline exaggeration, intellectual distortion, psychosocial masking, and cognitive disintegration—that contribute to difficulties with assessing affective disorders in people with ID (Table 1).

Take Home Points:

1. People with intellectual disability may be prone to difficulties with mood regulation due to poorly developed socialization and coping skills.
2. Clinicians should carefully identify environmental, medical, and/or pharmacologic causes for mood outbursts. Interpersonal conflicts, unwanted task demands, physical pain and discomfort, and use of medications, such as antidepressants and levetiracetam, may all contribute to labile and poorly regulated moods.
3. Although no pharmacologic treatments are well established for mood dysregulation in intellectual disability, anticonvulsants, antipsychotics, and electroconvulsive therapy may be useful in selected cases.

The diagnosis of *disruptive mood dysregulation disorder* is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a condition characterized by recurrent temper outbursts in the setting of persistently irritable or angry mood with an onset prior to age 10 years. It is a new diagnosis intended to address the observation of potential mischaracterization of children with persistent irritable mood as having bipolar disorder. The presence of ID is not addressed in the diagnostic criteria or description of disruptive mood dysregulation disorder in DSM-5.

The *Diagnostic Manual–Intellectual Disability*, 2nd edition (DM-ID 2) was developed as a resource for clinicians to aid in the proper diagnosis of mental disorders in this population.¹⁷ Specifically, the DM-ID 2 provides diagnostic criteria for all DSM-5 disorders adapted for use in mild-moderate ID and severe-profound ID. Additionally, it provides guidance on obtaining psychiatric history, assessing symptoms, and recognizing common behaviors in people with ID. DM-ID 2 diagnostic criteria for disruptive mood dysregulation disorder are similar to those in DSM-5.

The following cases will serve to illustrate the unique diagnostic and treatment challenges of mood dysregulation in adults with ID.

Aggressive and Self-Injurious Behavior in Mild ID

A 24-year-old woman was placed in a forensic residential facility after being charged with simple assault. She experienced a traumatic brain injury as a 4-year-old, which is thought to have contributed to her subsequent ID. Prior

TABLE 1: Difficulties in assessing challenging behavior in intellectual disability²⁷

Presentation	Explanation
Baseline exaggeration	Increase in challenging behavior frequency and/or intensity during the course of a mental illness. During times of stress, escalating behavior will prompt a mental health evaluation.
Intellectual distortion	The individual cannot accurately understand the questions posed by the evaluator, nor can he or she assemble the correct information to respond.
Psychosocial masking	Because of developmental delay, the individual might present symptomatology that occurs within a developmental framework that would be common in much younger individuals.
Cognitive disintegration	The individual may become grossly disorganized and psychotic because of the lack of “cognitive reserve” available to cope with the illness.

to her admission to the forensic facility, she had multiple out-of-home placements in the community because of her frequent problem behaviors. Her psychiatric diagnoses included disruptive mood dysregulation disorder, post-traumatic stress disorder, and mild ID. Medication history throughout the encounter is summarized in Table 2.

Generally, this individual is pleasant and charming. She usually maintains a neat and fashionable appearance. She enjoys shopping, eating out, and socializing with peers, family, and staff. She is talented at organizing social events for her peers.

While in the forensic facility, she often exhibited severe outbursts characterized by crying spells, kicking furniture, head-banging on windows, and aggression toward staff and peers. During less severe episodes, she engaged in verbal aggression toward peers or attempted to evade staff supervision. These episodes were often the result of perceived insults or other interpersonal conflicts with peers and staff. In most cases, the behavioral response was deemed to be significantly out of proportion to the identified antecedent. Frequently, oral or intramuscular medications were needed to manage acute behaviors. These emergency treatments were generally effective, but

TABLE 2: Pharmacotherapy trials in case 1

Time	Regimen/Changes	Comments
Baseline	Fluphenazine 5 mg twice a day Quetiapine 350 mg AM, 350 mg midday, 100 mg at bedtime Lithium 600 mg AM, 450 mg PM Sertraline 50 mg daily	
Month 5	Sertraline discontinued	Antidepressant deemed ineffective because of recurrent behavioral outbursts
Month 8	Medroxyprogesterone acetate depot 150 mg intramuscularly every 3 mo	Initiated after gynecology consult
Month 11	Clonazepam initiated and titrated to 1 mg twice a day	Complaints of anxiety and observed evidence of anxious behaviors
Month 12	Olanzapine 10 mg daily initiated Quetiapine tapered to discontinuation	For continued behavioral outbursts
Month 15	Aripiprazole 10 mg daily initiated Olanzapine tapered to discontinuation	Rapid weight gain noted with olanzapine
Month 16	Escitalopram 5 mg daily initiated, then discontinued within 3 wk	Initiated for observed perseveration. Abrupt increase in agitated behaviors noted.
Month 17	Lamotrigine initiated and titrated gradually to 200 mg daily Lithium tapered to discontinuation	For continued dysphoria and anxiety
Months 18-20	Aripiprazole titrated to 30 mg daily Fluphenazine tapered to discontinuation Lamotrigine discontinued	Attempts to simplify pharmacologic regimen
Month 27	Carbamazepine initiated and titrated to 800 mg daily	Some gradual improvements noted over time

the goal was to keep the use of unscheduled medications to a minimum.

In the aftermath of these episodes, she generally expressed contrition and processed the consequences of her actions with regard to her legal status and her community placement. The facility's direct care staff and therapist engaged with her to help develop coping skills that can be used to deal with her everyday stressors.

Notably, the psychology clinician assigned to her case found a recurring pattern of increased behavioral frequency around the time of her menses. During the course of several months, the most severe outbursts of property destruction and aggression recurred most frequently on a 4-week cycle. This issue was brought to the attention of the primary care physician, who referred the individual for a gynecology consult.

Case Discussion

Aggressive behavior like that displayed by the individual in this case has been frequently observed among people with mild and borderline ID in clinical settings.¹⁸ During her time in the forensic residential center, the treatment team was afforded the opportunity to quantify and characterize the nature of the behaviors associated with mood dysregulation. This individual's psychiatric disorder and undesirable environmental interactions were key factors contributing to her problem behaviors.

The systematic clinical approach of identifying variables that maintain challenging behaviors is known as *functional behavior assessment*.¹⁹ Upon the proper identification of these variables, or *reinforcers*, the treatment team can match the function that maintains the challenging behavior with an appropriate environmental or medical intervention for treatment. The 3 main categories of functions that lead to challenging behavior are social positive reinforcement, social negative reinforcement, and sensory/automatic reinforcement.²⁰ These paradigms are summarized in Table 3. In this case, the challenging behaviors were maintained by a combination of these functions and were amplified by the underlying mood disorder. This formulation requires a multipronged treatment plan that calls for the appropriate use of reinforcers for positive behaviors, interventions to improve coping with undesired situations, and medication management for labile and irritable mood.

In developing programming for this individual, the team provided her with opportunities to engage in the planning and execution of social events with her peers. She took the lead in creating invitations and decorating for holiday gatherings organized at the facility. A dramatic reduction

of problem behaviors was observed around these times. This is an example of using preferred activities as a positive reinforcer for reducing disruptive behaviors. The team also took great care to avoid placing her around peers who were known to irritate her and cause her to escalate her problem behaviors.

Because the antecedents of behaviors maintained through automatic reinforcement are internal to the individual, they present the greatest challenge in assessment.²¹ A medical workup is often necessary to detect physical health conditions that contribute to problem behaviors. The medical and psychiatric issues internal to this individual that were identified over time included anxiety, irritability, menstrual cramps, and gastrointestinal distress.

This patient was tried on many psychotropic drugs during this encounter, including selective serotonin reuptake inhibitor antidepressants, second-generation antipsychotics, mood stabilizers, and anxiolytics. These agents are among the most widely used drugs for the symptoms of mood dysregulation.²²

On 2 occasions, antidepressant trials were used to treat dysphoric mood. In both cases, the antidepressant was tapered and discontinued after a short duration of treatment. Antidepressants are often poorly tolerated by people with ID.²³ They may be especially problematic in cyclical mood disorders, where they can worsen cycling, irritability, and psychosis in vulnerable individuals.²⁴

There is limited evidence for the use of antipsychotics and mood-stabilizing agents for tantrums and aggression in ID. The notable exceptions are the second-generation antipsychotics risperidone and aripiprazole, which have been established as effective therapies for irritability in autism spectrum disorder (discussed in more detail below).²³ The very limited published evidence available for mood-stabilizing agents and anticonvulsants in adults with ID consists of small, uncontrolled trials with fairly heterogeneous patient populations.²⁵ These reports suggest that some improvements can be seen with the use of agents such as valproate, carbamazepine, lithium, and topiramate. However, these results are confounded by the potential therapeutic effects these agents have on underlying epilepsy and the impact of epilepsy treatment on behavioral symptoms.

This case also highlights the potential impact of menstrual behavior symptoms in ID. Socially unacceptable behavior symptoms and mood symptoms (eg, anger, social withdrawal) were noted to occur at a rate of 15% to 25% in cohorts of young women with developmental disabilities seen at a gynecologic clinic.²⁶ The North American Society for Pediatric and Adolescent Gynecol-

TABLE 3: Functions of challenging behavior in intellectual disability^{19,20}

Behavior Function	Examples of Reinforcers	Potential Therapeutic Approach
Social positive reinforcement—challenging behavior is maintained by contingent delivery of a socially mediated stimulus	<ul style="list-style-type: none"> • Adult attention • Tangible items (eg, food, toys) • Preferred activities 	Noncontingent provision of reinforcer in the absence of problem behavior and withholding of reinforcer in the presence of problem behavior. (Example: access to preferred item or activity is given to an individual after a period of not exhibiting problem behaviors.)
Social negative reinforcement—challenging behavior is maintained by contingent removal of a socially mediated stimulus	<ul style="list-style-type: none"> • Removal of task demands • Escape from undesired social situations 	Adjustment of task types to reduce aversiveness of demands Provision of choice of tasks to the individual. (Example: modify environment to avoid contact with people who may provoke agitated behavior in an individual.)
Automatic reinforcement—the act of engaging in the behavior itself (not the environment) reinforces the behavior	Behaviors that may provide relief from: <ul style="list-style-type: none"> • Pain/discomfort • Anxiety, distress • Auditory hallucinations 	Medical or psychiatric treatment of underlying biologic condition. (Example: treatment of auditory hallucinations with antipsychotic.)

ogy’s Committee On Adolescence²⁷ recommends that menstrual management can begin if physical and behavioral symptoms associated with menstrual cycles are creating difficulties with the patient’s activities. If medroxyprogesterone acetate depot is used for menstrual management, as it was in this case, careful consideration should be given to mitigate treatment risks, including weight gain and reduced bone mineral density. Dietary counseling may provide benefit for managing weight gain.²⁸ Except in rare cases, such as in genetic bone diseases (eg, osteogenesis imperfecta) or in those using long-term drug therapies affecting bone health (eg, glucocorticoids), routine bone mineral density testing is not recommended for patients using medroxyprogesterone acetate depot. However, calcium and vitamin D supplementation may provide some benefit for skeletal health.²⁹

Severe Problem Behaviors in Autism Spectrum Disorder and ID

A 22-year-old nonverbal man with profound ID and autism spectrum disorder was transferred to a state residential facility. The transfer occurred after numerous failed placements in community residential settings due to a long history of problem behaviors. The individual received a diagnosis of mood disorder, not otherwise specified and obsessive-compulsive disorder. Medical history was significant for Lennox-Gastaut syndrome, gastroesophageal reflux disorder, acne, and allergic rhinitis. The medications taken at the time of admission are summarized in Table 4.

Problem behaviors included self-injury (head slapping, head banging, and wrist biting), aggression, disrobing with no regard to privacy or ambient temperature conditions, elopement, pica (consumption of nonedible items), and urinary incontinence. Analyses of these behaviors determined that escape from undesired tasks or situations was the primary factor reinforcing assaults and elopement.

As this patient acclimated to the new setting, a more complete picture of problem behaviors became apparent. At baseline, the individual’s general mood appeared agitated and behavior consisted of stereotypic movements. However, behavior outbursts were quite frequent, consisting of destruction of furniture and other property, head banging on walls and windows, and attempts to grab and bite staff. These behaviors necessitated the use of as-needed emergency oral or injectable medications to reduce agitation up to 6 times a week during the first several months of admission.

Notably, a disrupted sleep pattern became evident. He spent most of the daytime hours asleep in his room and was awake during the night. The agitated and assaultive behaviors often occurred during these nighttime hours. Elopements from the residence were fairly common, which was often problematic because the individual would go outdoors without any clothing. Over time, the behaviors led to serious injuries to the head and shoulder.

Multiple medication trials and behavioral interventions were used, with very gradual improvements observed over time. Several months into the treatment course, levetiracetam was added to the regimen to address ongoing seizures. A daily dose of pyridoxine (vitamin B₆) was later

TABLE 4: Pharmacotherapy trials in case 2

Time	Regimen/Changes	Comments
Baseline	Clonidine 0.1 mg AM, 0.2 mg PM Risperidone 2 mg BID Bupropion XL 300 mg daily Sertraline 50 mg daily Fluvoxamine 100 mg BID Trazodone 50 mg at bedtime Melatonin 3 mg at bedtime Rufinamide 800 mg AM, 400 mg noon, 1200 mg PM	
First month after admission	Reduce risperidone to 3 mg/d, titrate sertraline to 150 mg/d Discontinue fluvoxamine, bupropion, trazodone, clonidine	Immediate attempts at simplification of medication regimen. Sleep-wake difficulty noted.
Month 2	Add doxepin 50 mg at bedtime	For insomnia
Month 3	Discontinue melatonin Start ramelteon 8 mg at bedtime	For persistent sleep-wake cycle disturbance
Month 6	Start clonidine 0.1 mg BID Start lithium 300 mg BID, titrated to 600 mg AM, 450 mg PM	Clonidine restarted for recurrent problem behaviors based on prior history of treatment. Lithium started for irritable mood.
Month 7	Start clonazepam 0.5 mg BID, gradual titration to 1.5 mg BID	Targeting hyperactivity
Month 11	ECT initiated: 3 times weekly for 2 wk, 2 times weekly for 3 wk, once weekly for 3 wk Taper clonazepam to 2 mg daily	Initiated for resistant mood dysregulation. Concurrent medication changes to optimize seizure quality.
Month 15	Risperidone discontinued Aripiprazole 10 mg daily started ECT reduced to every 14 d	Attempts to optimize treatment despite gradual improvements in behavior and seizure frequency
Month 18	Levetiracetam 250 mg BID initiated and titrated to 1000 mg BID	For improved seizure control as adjunct to rufinamide
Month 24	Clonazepam 2 mg daily changed to lorazepam 1.0 mg AM, 1.5 mg noon, 1.5 mg PM. Evening lorazepam held the night prior to ECT.	Use of shorter acting benzodiazepine to improve seizure quality with ECT
Month 25	Pyridoxine 100 mg daily initiated	For treatment of irritability secondary to levetiracetam
Month 30	Lithium discontinued	Mood symptoms continue to improve. Polyuria and acne noted with lithium.

BID = twice a day; ECT = electroconvulsive therapy.

added to the regimen because this is postulated to correct biochemical imbalances that underlie levetiracetam-associated mood instability.^{30,31} Trials of melatonin and doxepin were used for sleep-wake disturbance, with little success. Later, a trial of nightly ramelteon was used. After the timing of the ramelteon dosing was changed from 10 PM to 5 PM, the sleep pattern improved significantly. For the treatment of irritable behaviors associated with autism spectrum disorder, antipsychotic trials with risperidone, quetiapine, and aripiprazole were used before improvements were seen with the use of olanzapine. The medication trials are summarized in Table 4.

Because these problem behaviors continued despite the use of multiple medication trials, a consultation for the use of electroconvulsive therapy (ECT) was requested. The ECT psychiatrist agreed with the use of ECT with some adjustments to the medication regimen. Lorazepam was substituted for clonazepam, because its shorter half-life may allow it to cause less inhibitory effect on seizures during ECT. After several weeks of ECT, starting with a 3-times weekly regimen and tapering to 1 session every 2 weeks, dramatic improvements in the frequency and severity of all problem behaviors were noted. The individual's affect was noticeably less distressed and more

pleasant. Staff worked to more appropriately limit disrobing to times when the individual was in his own bedroom. The individual engaged in a more regular daytime recreational and vocational programming schedule and a consistent nightly sleeping pattern. The treatment plan going forward is to maintain long-term twice-monthly ECT treatments, attempt to taper antipsychotics to the lowest effective dosages, and facilitate placement in a community-based residential setting.

Case Discussion

Although high rates of psychiatric comorbidity, particularly with mood disorders, have been observed in people with autism spectrum disorder,^{32,33} it is useful to conceptualize this patient's presentation as a syndrome of persistent severe mood dysregulation.^{34,35} Outbursts of aggression, property destruction, and self-injury were manifestations of this individual's mood instability. Additionally, sleep disturbance is a complication that likely exacerbated these mood issues.

The use of second-generation antipsychotics for irritability in autism spectrum disorder, particularly the US Food and Drug Administration–approved agents risperidone and aripiprazole, has increased dramatically in recent years.³⁶ These agents have been shown to lead to significant improvements in the frequency of tantrums, aggression, self-injury, and stereotypic behavior patterns in children with autism spectrum disorder.^{37–39} Despite the limited published evidence in older adolescents and adults with ID and autism spectrum disorder, the use of second-generation antipsychotics is a widely accepted practice that is an important intervention for the management of irritable behaviors.⁴⁰

Electroconvulsive therapy is a well-established intervention for treatment-resistant mood disorders in the general population.⁴⁰ For people with ID, there is reluctance among practitioners to consider ECT because of a perceived risk of causing further brain damage, and difficulties in obtaining informed consent.⁴¹ Although there is a lack of rigorous clinical trials specifically in the ID population, ECT has been demonstrated as a potentially useful intervention for severe and treatment-resistant mood and psychotic disorders.⁴²

Whenever possible, it is recommended that the risks, benefits, and treatment alternatives be explained to the person for whom ECT is being considered. In cases where an adult has been assessed to lack the capacity to consent to ECT, consent must be sought from the individual's legal guardian. As such, the guardian must be fully engaged with the treatment team prior to and during the treatment process.

As in the general population, there may be risks of prolonged seizure activity and memory impairment with the use of ECT. These issues were not observed in this case. In fact, control of this individual's epilepsy improved during the course of ECT treatment. In people with epilepsy, an optimized anticonvulsant regimen can ensure seizure control during maintenance ECT.⁴³ It has been suggested that effects of maintenance ECT on enhancing GABA neurotransmission may impart therapeutic effects on intractable epilepsy.⁴⁴

It is important to consider the presence of medical conditions or drug side effects as possible contributors to problem behaviors. Typical medical issues encountered in people with ID presenting in psychiatric treatment settings include menstrual or dental pain, constipation, and gastroesophageal reflux disorder.⁴⁵ In the present case, gastroesophageal reflux disorder was well controlled and was not thought to be contributing to his problem behaviors.

Pharmacologic issues contributing to problem behaviors include irritability from anticonvulsants, such as levetiracetam, and disinhibition from benzodiazepine drugs.⁴⁶ Levetiracetam can be a valuable adjunctive treatment for resistant seizures in people with Lennox-Gastaut Syndrome,⁴⁶ but it has been associated with treatment-emergent pyridoxine (vitamin B₆) deficiency.⁴⁷ Pyridoxine deficiency can contribute to irritable mood because of its role as a cofactor for neurotransmitter synthesis. Pyridoxine was added as a supplement in this case based on published reports of its effectiveness for levetiracetam-associated irritability.^{30,31} This is a commonly employed practice based on the minimal cost and risk of supplementation. It often allows for maintenance of levetiracetam therapy in patients who would otherwise develop adverse effects on mood.

Normalization of sleep patterns is seen as an important target for the treatment of mood disorders. The individual in this case exhibited a delayed sleep-wake phase disorder, one of several circadian rhythm disturbances observed in many people with autism spectrum disorder.⁴⁸ Mutations in genes involved in circadian rhythm regulation have been implicated in the pathology of autism spectrum disorder.⁴⁹ Endogenous melatonin plays a key role in circadian rhythm regulation. As such, the melatonin receptor agonist ramelteon has been used successfully for sleep and behavioral disturbances in people with autism spectrum disorder.^{50,51} In this case, ramelteon treatment contributed to an improved regulation of the individual's sleep-wake cycle. The results in adjusting the sleep cycle may not be seen for several weeks, likely due to both behavioral and biochemical changes that occur over time. It is also notable, in this case, that ramelteon was eventually dosed in the early

evening, so that peak blood concentrations could occur to help support sleep onset at bedtime.

Risk/Benefit Considerations in Drug Treatment Selection

The cases illustrate the use of psychotropic drugs from multiple therapeutic classes for the treatment of complex cases of mood dysregulation in ID. Despite being underrepresented in controlled clinical trials of psychotropic drug use for behavioral problems,⁵² substantial percentages of adults with ID are reported to receive treatment with psychotropic drugs, particularly combination therapy regimens. In a study of 4069 community-dwelling adults with ID in New York State, 58% were receiving treatment with at least 1 psychotropic medication.⁵³ Among an Australian sample of 853 people with ID and behavior health concerns receiving psychotropic treatment, drugs from 2 or more classes were used concurrently in 53.8%.⁵⁴

Mood Stabilizers

Mood stabilizers, such as lithium, and anticonvulsants, including valproate, carbamazepine, and lamotrigine, are mainstays in the management of manifestations of mood dysregulation. Although published studies have methodologic flaws, including limited sample size, unvalidated outcome measures, and retrospective designs, they provide some support for the use of lithium, valproate, carbamazepine, and topiramate.

Lithium should be titrated to a target serum concentration of approximately 0.4 to 1.0 mEq/L. Lithium toxicity, including severe gastrointestinal upset and central nervous system depression, can occur when serum concentrations exceed 1.2 mEq/L. Other adverse effects of lithium include polyuria/polydipsia syndrome and elevated thyroid stimulated hormone concentrations.⁵⁵ There are certain neurodevelopmental syndromes associated with ID that are characterized by congenital hypothyroidism⁵⁶; therefore, lithium-induced hypothyroidism can be a special concern in this population.

Anticonvulsant mood stabilizers can offer benefits for treatment of mood disorder and co-occurring seizure disorders. Use of valproate, carbamazepine, and lamotrigine has also been associated with lower rates of concurrently prescribed antipsychotics or anxiolytics,⁵⁷ which reduces overall treatment burdens related to polypharmacy. Adverse effects, including blood dyscrasias, sedation, tremor, and cognitive disturbances, vary among individual treatments. As described in the case study above, certain anticonvulsants, such as levetiracetam, may worsen mood disturbances. The most frequently endorsed anticonvulsant adverse effects

noted in a sample of individuals with ID included affective disturbances, gait disturbances, and weight changes.⁵⁸

Antipsychotics

In people with ID, as with the general population, antipsychotic drugs are used for the treatment of schizophrenia and psychotic disorders, and as adjuncts for mood disorders.⁵⁹ Additionally, limited evidence suggests that they may be used at higher rates in ID than in the general population for autism spectrum disorder, dementia, and for management of problem behaviors without a clear psychiatric diagnosis.^{60,61}

Antipsychotic treatment risks may vary based on pharmacologic characteristics of the drug(s) used (ie, first- vs second-generation antipsychotic), medication dose, and individual patient factors (genetics, age, presence of brain injury). The long-term adverse effects of antipsychotics, including prolactin elevation, metabolic syndrome, and tardive dyskinesia, are a great cause of concern with these agents.⁶² Monitoring of antipsychotic therapy should include baseline and semiannual assessments of metabolic parameters (fasting glucose and lipids, hemoglobin A_{1c}).^{63,64} Body weight should be monitored monthly. The presence of treatment-emergent movement disorders should be assessed at least annually using a validated rating scale, such as the DISCUS.⁶⁵ Prolactin concentrations should be assessed at baseline and annually.⁶³

With the exception of their use in chronic psychotic disorders and in some cases of affective disorders, antipsychotic use in ID should not be maintained indefinitely. When used in the management of problem behaviors or irritable mood without a clear psychotic or mood disorder diagnosis, antipsychotic therapy should be reevaluated periodically, with ongoing consideration for dose tapering or medication withdrawal.⁶⁶ Tardive dyskinesia,⁶⁷ metabolic syndrome,⁶⁴ and prolactin elevation⁶⁸ are all exacerbated by prolonged duration of antipsychotic exposure. Although tardive dyskinesia can be irreversible, there can be substantial reversal of hyperprolactinemia and metabolic syndrome with the discontinuation of antipsychotic treatment.⁶⁹

Antidepressants

The body of published evidence supporting the use of antidepressant drugs in ID is especially limited. Some potential benefits of antidepressants in this population include delayed dementia onset in Down syndrome,⁷⁰ and management of anxiety and irritability in some cases of autism spectrum disorder.⁷¹

An open-label, retrospective, naturalistic study attempted to determine whether antidepressants were effective in

reducing the frequency and severity of a variety of problem behaviors (including aggression, self-injury, and other agitated behaviors) in people with ID.⁷² The sample of 38 individuals were heterogeneous as far as psychiatric diagnosis and concurrent psychotropic drug therapy. The investigators determined that overall behavior ratings were improved with the use of antidepressants. Acne, constipation, and weight changes were noted in some patients. Notably, 6 patients had a worsening of problem behaviors with the initial antidepressant trial, leading to antidepressant discontinuation in 2 patients and a switch to a better-tolerated agent in the other 2.

The presence of persistent depressed mood or anxiety may be a compelling indication for an antidepressant trial. However, many cases of mood dysregulation in ID can be treated with a lower risk of worsening behavior with the use of a mood stabilizer or short-term antipsychotic. With antidepressants, clinicians should be aware of additional treatment risks of seizures (tricyclic antidepressants and bupropion) and weight changes.

Conclusion

The manifestations of mood dysregulation can be very prominent in people with ID because of the underlying propensity toward mood disorders and the diminished cognitive ability to regulate behavioral responses. The assessment of problem behaviors should begin with a medical workup and should include formal behavioral assessments, such as a functional assessment. For treatment, behavioral approaches are often combined with pharmacotherapy to reduce the severity and frequency of behavioral outbursts. A comprehensive behavior plan can often include strategies for staff to control the individual's environment and improve self-regulation of behaviors.

There are significant limitations in the published literature on psychotropic drug therapies for people with intellectual disability. In the absence of published evidence, the clinician must employ principles of pharmacotherapy used in the general adult psychiatric population and adapt them for the unique characteristics seen in people with ID. Issues such as co-occurring seizure disorder or the potential behavioral adverse effects of antidepressants and anticonvulsants should be accounted for when initiating and monitoring medications. If successful, the impact on the individual's overall functioning, while usually occurring gradually, can be quite profound.

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