REVIEW

Psychopharmacological treatments in persons with dual diagnosis of psychiatric disorders and developmental disabilities

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People with developmental disabilities are at considerable risk for the development of comorbid psychiatric conditions. Psychopharmacological treatments may have a crucial role in a multidisciplinary and multimodal approach to the management of psychopathology in this population. Psychiatric illnesses that are particularly amenable include mood disorders, anxiety disorders, schizophrenia, and attention deficit hyperactivity disorders (ADHDs) and antidepressants, mood stabilisers, anxiolytics, antipsychotics, and stimulants should be considered, respectively. ADHD may also respond to α_2-agonists. Psychotropic agents such as β-antagonists can target aggressive, self injurious, and stereotypical behaviours and opioid antagonists may be helpful in treating self injurious behaviour and stereotypy. Selective serotonin reuptake inhibitors, newer anticonvulsants, and atypical neuroleptics are preferred when treating psychiatric disorders among people with developmental disabilities. This paper will review the major studies of pharmacological treatment of mental illness in individuals with developmental disabilities.

Prevalence estimates of psychopathology in individuals with developmental disabilities are larger than those observed within the general population.[1] For example, Reber reported on the comorbidity of several psychiatric illnesses with mental retardation, including schizophrenia, bipolar illness, major depression, attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder, and other anxiety disorders.[2] In the following review, and to remain consistent with the literature, the term "developmental disability" will be used interchangeably with "mental retardation" to refer to individuals who suffer from significant intellectual impairment and deficits in adaptive behaviours with onset before age 18 years.

A multidisciplinary and multimodal treatment approach is advisable in this population. Given that individuals with developmental disabilities are susceptible to the full range of psychopathology, a variety of treatment strategies should be considered, including environmental modifications, behavioural interventions, counselling, and psychopharmacology.

A significant number of people with developmental disabilities and concurrent psychiatric illnesses are treated with psychotropic agents. For instance, Spreat *et al* reported that among adults with mental retardation, 22% were prescribed neuroleptics, 5.9% antidepressants, and 9.3% anxiolytics.[3]

It should be noted that the literature on individuals with developmental disabilities and comorbid psychopathology is fraught with methodological limitations. For instance, it is often difficult to obtain informed consent for the initiation and prolonged continuation of psychotropic treatments.[4] And although there has been a recent increase in the number of studies devoted to this topic, there several limiting factors nevertheless remain. Borthwick-Duffy examined the epidemiology and prevalence of mental disorders in persons with intellectual disabilities.[5] In her review, she reported on 12 US and nine international studies, including the works of Corbett[6] and Lund.[7] In this review, several factors that influence the appropriate use of psychotropic medications in this population were examined. These factors are:

(1) Terms such as mental retardation, developmental disability, developmental handicap, and intellectual or learning disabilities are used interchangeably in the literature. Strict definitional criteria are not always adhered to. This can result in over-inclusion or under-inclusion of participants in the pharmacological studies dedicated to this group.

(2) The coexistence of two major pathologies (that is, intellectual disabilities and mental disorders) makes it difficult to disentangle the relative contributions of each to the individual's clinical presentation. For instance, it has been well documented that medical and physical problems observed among dually diagnosed individuals may be viewed as challenging behaviours or mental illness in this population. The presentation of behaviours and/or symptoms in these persons can be intertwined in the confines of the two phenomena; this is known as "diagnostic overshadowing".

(3) The use of the term "mental disorder", and the lack of agreement on operational definitions of mental disorder, impose yet another limitation in these studies by the under-inclusion or over-inclusion of subjects.

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Abbreviations: ADHD, attention deficit hyperactivity disorder; SSRI, selective serotonin reuptake inhibitors

(4) The pharmacological studies of the dually diagnosed are characterised by a lack of standardised clinical tools for these individuals, thus resulting in an inherent bias in this literature.

(5) The various studies on this topic do not include the full range of mental disorders. As such, they can be viewed as limited in their use, applicability, and generalisability.

In the present article, we will review the various psychotropic medications used in persons with dual diagnosis of developmental disabilities and psychiatric illnesses.

METHODOLOGY

Databases used include:

(A) Medline (1975 to December 2001) was searched using Ovid Online and the following terms: randomised clinical controlled trial (explode all subheadings or double-blind/all subheadings); (explode clinical trial in patients/ all subheadings); (crossover controlled clinical trial/crossover). These searches were combined with: (explode—learning disorders/ all subheadings) or (explode—mental retardation or handicap or disab?).

(B) PsycInfo (1975 to December 2001) was searched using Ovid Online using the following terms: randomised clinical controlled trial developmental disabilities/or mental retardation and psychotropic drugs/or psychopharmacology (explode all subheadings or double-blind/all subheadings); (crossover controlled clinical trial/crossover); (explode clinical trial in patients/all subheadings). These searches were also combined with (explode—learning disorders/all subheadings) or (explode mental retardation, handicap, or disab?).

(C) Databases were searched for reviews, reports on series of cases, individual case reports, and other pertinent clinical information in the English language.

RESULTS

A. Antidepressants

Antidepressants are used for several major psychiatric illnesses, including major depression and other depressive disorders.[8] Selective serotonin reuptake inhibitors (SSRIs) are the treatment of choice, given the more favourable side effect profile when compared with older antidepressants. However, lack of response after four to six weeks of treatment at therapeutic doses warrants reconsideration of the diagnosis and, if necessary, trials of other antidepressants such as other SSRIs, venlafaxine, trazodone, tricyclic antidepressants, or moclobemide.[8] Although the majority of studies include fluoxetine,[9] paroxetine was also found efficacious in treating depressed adolescents with developmental disabilities.[10]

An increasing number of psychiatric symptoms and illnesses have been linked to serotonin and thus may respond to serotonergic agents. For example, serotonergic antidepressants such as fluoxetine, sertraline, and clomipramine were found useful in treating obsessive compulsive disorder[11–13] and therefore could be used in conjunction with behavioural strategies. Furthermore, the serotonergic system may be implicated in the pathogenesis of behavioural disturbances such as stereotypy, self injury, and aggression. Clomipramine was found to be effective in the treatment of self injurious behaviour and stereotypy in people with concurrent developmental disabilities in two double blind, placebo controlled studies.[14 15] However, some authors have reported serious, adverse effects with the use of clomipramine in this population.[16] Among SSRIs, both paroxetine[17] and sertraline[18 19] were reported useful in treating behavioural disturbances in individuals with developmental disabilities. However, fluoxetine has been found to aggravate aggressive behaviours in persons with developmental disabilities.[20] An open label study of mirtazapine has demonstrated its modest level of effectiveness in the treatment of several symptoms associated with pervasive developmental disabilities, such as aggression, self injurious behaviour, irritability, hyperactivity, anxiety, depression, and insomnia.[21]

In brief, there is adequate evidence to suggest that antidepressants may be used in the treatment of persons with intellectual disability and comorbid major depression, other depressive and anxiety disorders, body dysmorphic syndrome, obsessive-compulsive disorder, eating disorders, smoking cessation, and functional eneurisis. In addition, antidepressants have been found to be efficacious in the treatment of challenging behaviours, such as aggression, self injurious behaviour, stereotypies, and distraction.[22]

Nevertheless, antidepressants should be used cautiously in this population, especially among those suffering from bipolar illness in the depressive phase. These medications can trigger a manic or hypomanic switch, especially in rapid cycling or mixed states, to which people with developmental disabilities are more prone.

Antidepressants studied in those with intellectual disabilities are shown in table 1.

B. Antianxiety medications (anxiolytics)

Benzodiazepines could be used as possible alternative treatment of anxiety disorders.[23 24] However, hostility, disinhibition, self injurious behaviour, and aggression were reported as paradoxical reactions to benzodiazepines, especially in people who exhibit evidence of stereotypical, self injurious behaviours before starting treatment with benzodiazepines.[25] In addition, benzodiazepines have an increased risk for abuse, tolerance, and dependence.[24] Therefore, the clinical consensus advises that benzodiazepines alone should only be used for a maximum of three weeks.[26]

Some clinicians use benzodiazepines for the treatment of sleep disorders. However, effective long term treatments for insomnia include behaviour modification, relaxation techniques, and the practice of good sleep hygiene. In addition, it may be advisable to consider trazodone as a non-addictive alternative to benzodiazepines for the treatment of insomnia.

Buspirone, a partial 5-hydroxytryptamine-1α (5HT-1) agonist, was found beneficial in the treatment of anxiety disorders, particularly generalised anxiety disorder. In addition, several studies have reported that buspirone improved agitation and behavioural problems, including aggression and self injury, in people with developmental disabilities.[27 28]

In summary, anxiolytics, particularly buspirone, may be used in the treatment of anxiety disorders, as well as agitation and challenging behaviours. Caution should be taken when anxiolytics are used in this group, as they can exacerbate agitation, aggressivity, and cause paradoxical excitement.

Anxiolytics studied in those with intellectual disabilities are shown in table 2.

C. Mood stabilisers

Lithium may be useful in the treatment of acute mania, cyclothymic disorder, and the prophylaxis of bipolar illness type I. In cases of cycloid psychosis, which occurs particularly in Prader-Willi syndrome, the treatment of choice is lithium.[29]

Craft *et al* reported that lithium is useful in the treatment of aggression in people with developmental disabilities.[30] Furthermore, several investigators assessed lithium as a therapeutic agent in the management of disruptive behaviours.[31] A number of studies reported that lithium might be beneficial in patients with developmental disabilities and concurrent aggression and mood lability.[32] In addition, several double blind placebo controlled trials found that lithium has beneficial effects on self injurious behaviour.[30 33] However, this population is more prone to developing toxic side effects to lithium and thus requires close monitoring.

Valproic acid is the treatment of choice of rapid cycling and mixed states,[34] illnesses that have a higher incidence among

Table 1 Various psychopharmacological treatments studied in persons with intellectual disabilities: antidepressants

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Masi *et al* 1997[10]	PRX 20–40 mg	9 weeks	7 adolescents MID	MDD	4/7 significant improvement
Sovner *et al* 1993[9]	FLX 20–40 mg/day	11 and 15 months	Woman in late 50s and man in late 30s	MDD/SIBs	SIBs and depressive symptoms reduced: maintained for 1 year
Brasic *et al* 1997[16]	CMP 25 mg initially 200 mg finally/day CPZ	Open study	5 female preadolescents SID	Autism + dyskinesias and motor tics	Reduction of dyskinesias and tics
Bodfish and Madison 1993[11]	FLX 40–80 mg/day	4 months baseline and treatment phases	16 adult MR	10 subjects OCD 6 controls	7/10 with OCD responded favourably: to FLX none of the controls
Wiener and Lamberti 1993[12]	SRT 50 mg/day	8 weeks	33 year old woman with MDD	OCD with fears about health, face rubbing, etc	Reported less anxiety with decrease in fears and OCD symptoms
Posey *et al* 2001[21]	MRTP	Open study	26 subjects with PDDs/ID	Aggression: SIBs, irritability, hyperactivity, anxiety, depression, insomnia	9/26 showed improvement varying from much improved to very much (modest effectiveness)
Davanzo *et al* 1998[17]	PRX	4 months open study	15 I/P adults with SID and PID	Aggression and SIBs	Aggression significantly reduced for 1 month: no effect thereafter. No change in SIBs
Hellings and Warnock 1994[71]	FLX 20–60 mg/day	24 months	3 adults with MID	Prader-Willi with stereotypy with intermittent explosive disorder	2/3 showed decrease in skin picking; the 3rd patient showed significant reduction in hoarding and explosive behaviour
Lewis *et al* 1995[14]	CMP	6–7 weeks	10 institutionalised adults SID	Repetitive behaviour	Body and object stereotypy were decreased; irritability and hyperactivity improved
Lewis *et al* 1996[15]	CMP	7–8 weeks	8 institutionalised adults with ID	Self injury and self restraint	6/8 subjects >50% reduction in SIB
Troisi *et al* 1995[20]	FLX 20 mg CBZP and neuroleptics	Open study	19 I/Ps with ID	Aggressive behaviour	Varied response; 9/19 showed increased aggression over time

CBZP, carbamazepine; CMP, chlomipramine; CPZ, chlorpromazine; FLX, fluoxetine; ID, intellectual disability; I/P, inpatient; MDD, major depressive disorder; MID, mild intellectual disability; MR, mental retardation; MRTP, mirtrazepine; OCD, obsessive-compulsive disorder; PDD, pervasive developmental disorder; PRX, paroxetine; SIB, self injurious behaviour; SID, severe intellectual disability; SRT, sertraline.

Table 2 Various psychopharmacological treatments studied in persons with intellectual disabilities: anxiolitics

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Ghaziuddin and Ghaziuddin 1990[24]	DZP	Withdrawal	1 female MID	Acute behavioural disorders: aggressivity, SIBs	Attention to withdrawal symptoms of antianxiety medication
Barron and Sandman 1985[25]	Sedative/ hypnotics	Paradoxical excitement	Various degrees of ID, perinatal trauma	SIBs, aggressive behaviours	Paradoxical responses had a lower M/A, positive history of perinatal trauma, increased SIBs and aggression before treatment
Ricketts *et al* 1994[28]	BSR 30 mg/day	Open study 6–33 weeks	5 adults with ID	SIBs, anxiety symptoms	Some response to BSR with decrease in SIBs (13%–72%)
Ratey *et al* 1991[27]	BSR	Multiple baseline placebo lead–in studies	6 ID adults	SIBs with aggression/anxiety symptoms	BSR very effective in reducing SIBs and aggression with anxiety. No cognitive side effects

BSR, buspirone; DZP, diazepam; ID, intellectual disability; M/A, mental age; MID, mild intellectual disability; SIB, self injurious behaviour.

people with developmental disabilities compared with those with normal IQ. There are only very limited data to support the use of anticonvulsant medications for behavioural disturbances. Valproic acid was found beneficial in patients with developmental disabilities and comorbid aggression, self injurious behaviour, and mood lability.[35] In addition, divalproex sodium was found well tolerated and beneficial in the treatment of aggression and self injurious behaviour in adults with developmental disabilities.[36] Furthermore, Kalachnik *et al* reported that antiepileptic drugs might have side effects underlying behavioural problems in people with developmental disabilities.[37]

Thus, mood stabilisers may be used in the treatment of acute mania, the prophylaxis of bipolar illness, type I, cyclothymic disorder, cycloid psychosis, and challenging behaviours. Certain guidelines must be followed with regard to before and after treatment laboratory testing when prescribing mood stabilisers.[38]

Mood stabilisers studied in those with intellectual disabilities are shown in table 3.

D. Antipsychotics (neuroleptics)

Antipsychotic medications are frequently prescribed for psychotic symptoms or behavioural disturbances in people with developmental disabilities. The rationale of employing neuroleptics for the treatment of self injurious behaviour stems from the model of Lesch-Nyan syndrome. According to this model, the dopaminergic system is implicated in self injury.[39] A number of studies have reported that neuroleptics are helpful in treating aggressive and self injurious behaviours.[40] In addition, neuroleptics were found effective in reducing stereotypical behaviours[41] at lower doses compared to those needed for managing self injurious behaviours.[42] Among the typical neuroleptics, fluphenazine and thioridazine have been shown to be effective.[43] In addition, zuclopenthixol is well tolerated and effective in treating behavioural disturbances in children and adolescents,[44 45] including disturbances of longstanding nature[43] in people with developmental disabilities.

Moreover, atypical neuroleptics such as risperidone show a better side effect profile than typical antipsychotics and are promising for the treatment of behavioural disturbances in people with concurrent developmental disabilities.[4 46] Several

Table 3 Various psychopharmacological treatments studied in persons with intellectual disabilities: mood stabilisers

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Verhoeven *et al* 1998[29]	Lithium	Open study	6 adult males with PWS	Mood disorder/anxiety symptoms; cycloid psychosis	Specific vulnerability to cycloid psychosis improved with lithium; possibly specific "psychopathological phenotype"
Pary 1991[32]	Lithium (serum concentration of at least 0.5 mEq/l to 1 mEq/l)	6–8 weeks	Review of case study. Description of clinical trial components	Aggressive behaviours	Good response, although types of aggression not specified
Craft *et al* 1987[30]	Lithium	Double blind 4 months	42 ID patients	Aggressive behaviours	Significant differences in mean weekly aggression and in frequency of aggressive episodes
Tyrer *et al* 1984[33]	Lithium + neuroleptics	Double blind/crossover trial 5 months	25 adults I/P with ID	Aggressive behaviours	17/25 showed greater improvement during the lithium phase. Pretreatment behaviours associated with good response were: less than 1 episode/week overactivity, stereotypies, female sex, and epilepsy
Ruedrich *et al* 1999[36]	Divalproex sodium 500–4000 mg/day	Open study 2–73 months	28 adults (20–63 years) with ID	Aggressive behaviour, SIBs	71% moderate to marked improvement 21% mild benefits
Sovner 1989[34]	Divolpraex sodium (levels between 50 µg to 100 µg)	Open study	5 adults with ID (1 fragile X, 2 with rapid cycling)	Bipolar disorder	4/5 marked improvement 1/5 moderate

ID, intellectual disability; I/P, inpatient; PWS, Prader-Willi syndrome; SIB, self injurious behaviour.

investigators have reported that risperidone is an effective therapeutic agent for the treatment of self injurious behaviour, aggression, and stereotypical behaviour.[47 48] Furthermore, Vanden Borre *et al* reported in a double blind, placebo controlled study that risperidone is a beneficial adjunctive therapeutic agent for treating behavioural problems in patients with developmental disabilities.[49] In addition, a double blind study and a randomised controlled trial showed that risperidone is well tolerated and effective for the treatment of behavioural disturbances in individuals with developmental disabilities.[50 51] A pilot study found that olanzapine is well tolerated and effective in reducing stereotypic self injurious behaviours in adults with developmental disabilities.[52] Finally, clozapine has been shown to be useful for the treatment of severe behavioural disturbances in people with developmental disabilities.[53] In addition, clozapine was found to be a safe, efficacious, and well tolerated agent for the management of treatment resistant mood and psychotic illnesses in people with developmental disabilities.[54–56]

Atypical neuroleptics have a more tolerable side effect profile than typical neuroleptics. There is an increased frequency of extrapyramidal side effects in people with developmental disabilities who are treated with typical neuroleptics, especially phenothiazines, butyrophenones, and depot preparations. Akathisia is the most common of the acute extrapyramidal side effects. Prevalence estimates of 13% of individuals affected by this is probably an underestimate given the fact that this condition is the most challenging extrapyramidal side effect to diagnose.[57] In addition, tardive dyskinesia is reported in 20%–30% of people with developmental disabilities being treated with antipsychotic medications.[58]

Another adverse effect of antipsychotics is the neuroleptic malignant syndrome. Risk factors for this include male gender, lower grade of developmental delay, and exposure to higher potency neuroleptics. Neuroleptic malignant syndrome can be lethal; fatality rates of 21% to 30% have been reported (approximately double the rate than that of the general population).[57] In 90% of cases, the causative neuroleptic had been introduced for the first time or reintroduced after a drug-free period.[57] Haloperidol and fluphenazine were the most frequently implicated drugs, and antipsychotic polypharmacy was found in 55% of cases.[57] The average time for the onset of neuroleptic malignant syndrome was eight days.[57] A recurrence rate of 44% was reported with rechallenging of patients with developmental disabilities with antipsychotic medication after recovering from neuroleptic malignant syndrome.[57] It is important to monitor patients receiving antipsychotics for the onset of symptoms suggesting neuroleptic malignant syndrome. Caregivers should be educated regarding the significance of symptoms such as high fever, muscle rigidity, and change in mental status, in order to seek immediate medical attention.

In sum, typical and atypical antipsychotics may be used in the treatment of psychotic symptoms of various aetiologies and challenging behaviours in individuals with intellectual disabilities.[58] Caution should be exercised in the use of typical antipsychotics in this group, as devastating side effects such as neuroleptic malignant syndrome can be associated with their use. Other, less catastrophic, but nevertheless important, side effects can include extrapyramidal symptoms, particularly akathisia and other dyskinesias. Atypical antipsychotics, although very efficacious in the treatment of challenging behaviours in this group, can potentially create side effects such as epilepsy, weight gain, and secondary diabetes.[38] Again, caution should be exercised when these medications are administered to persons with intellectual disabilities.

Antipsychotics studied in those with intellectual disabilities are shown in table 4.

E. Stimulants

Although several studies have found that individuals with developmental disabilities have lower response rates to stimulants in comparison with people without developmental disabilities,[59 60] stimulants have been shown to be helpful in treating ADHD among individuals with concurrent mild to moderate developmental disabilities.[61] However, the use of stimulants in people with severe to profound degrees of developmental disabilities is limited.[62] Furthermore, although preschool children with developmental disabilities and ADHD respond to methylphenidate at rates similar to those of school age children with dual diagnosis,[63] they are more prone to developing adverse effects.[63] In brief, stimulants may be used in people with intellectual disabilities and ADHD. However, stimulants may exacerbate tics, obsessions, compulsions, epilepsy, anxiety, or psychotic features.[61 62]

Stimulants studied in those with intellectual disabilities are shown in table 5.

F. Alpha$_2$-agonists

Clonidine could be used as third line of treatment after stimulants and antidepressants for ADHD. Clonidine was reported

Table 4 Various psychopharmacological treatments studied in persons with intellectual disabilities: antipsychotics

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Aman *et al* 1989[41]	HLPD 0.025–0.05 mg/kg/day	Crossover HLPD study 3 weeks	20 I/P adults with ID	Sterotypic behaviours	Slight reduction in stereotypic behaviours. Gross increase in motor activity under high doses
Zarcone *et al* 2001[50]	RSD	Double blind/crossover design 22 weeks with 6 months follow up	20 adults with ID	SIBs and aggressive behaviours	50% reduction in ABC. A subset of 5 subjects showed 4/5 improved
Malt *et al* 1995[45]	ZCPX *v* HLPD	Double blind/crossover 2–8 weeks	34 adults with ID	SIBs + aggressive behaviours	SHBS (schedule for handicapped behaviour and skills) showed significant improvement with ZCPX. CGI did not differentiate between the two
Buitelaar *et al* 2001[51]	RSD mean: 2.9 mg/day	6 weeks double blind	38 adolescents with ID hospitalised	Psychiatric disorders with severe aggression	Significant improvement on the CGI
Cohen *et al* 1998[48]	RSD	Open study	8 adults with MID	SIBs, aggressive behaviours	Significant reduction of aggression and SIBs
Horrigan and Barnhill 1997[47]	RSD 0.5 mg/BID	Open study	11 male young adults with ID	Aggression, SIBs, explosivity, sleep disorders	Substantial clinical improvement immediately
Vanden Borre *et al* 1993[49]	RSD 4–12 mg/day	Double blind/placebo crossover trial	37 adults with ID	Persistent abberant behaviours SIBs and aggressivity	ABC + CGI significantly superior to placebo
McDonough *et al* 2000[52]	OLZ 5–15 mg/day	15 weeks open study	7 adults with ID	Stereotypic form of chronic SIBs	3/7 clear improvement; 1/7 marginal progress; 1/7 deteriorated; 2/7 no major change
Cohen and Underwood 1994[53]	CLZ	Open study	6 adults with MID and PID	SIBs + aggression	Significant reduction in SIBs and aggression
Antonacci and de Groot 2000[56]	CLZ	Retrospective review I/P. 26/33 prospective 5–48 months	33 adults with ID	Schizophrenia, schizoaffective, bipolar, delusional, or psychotic disorder NOS	Statistically significant improvement on CGI
Buzan *et al* 1998[55]	CLZ	Review study/open study	Review article. 10 adults with ID. Total number of published cases 84	Psychoses/bipolar illness unresponsive to other agents	Great efficacy and well tolerated
Pary 1994[54]	CLZ	Review article on the use of CLZ in general population	Adults with ID	SIBs, aggressive, psychotic disorders	Potential diffuculies and side effects were reviewed for the ID group
Brylewski and Duggan 2001[4]	Antipsychotic medication	Review article. Randomised controlled trials	Persons with LD I/P institutionalised	Challenging behaviours	Very many adults with LD and challenging behaviour with no discernible mental illness are treated with these powerful drugs which pose ethical issues

ABC, Aberrant Behaviour Checklist, CGI, clinical global impression; CLZ, clozapine; HLPD, haloperidol; ID, intellectual disability; LD, learning disability; MID, mild intellectual disability; NOS, not otherwise specified; OLZ, olanzepine; PID, profound intellectual disability; RSD, risperidone; SIB, self injurious behaviour; ZCPX, zuclopenthixol.

Table 5 Various psychopharmacological treatments studied in persons with intellectual disabilities: stimulants

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Handen *et al* 1991[62]	MPH	Open study	27 children with ID	ADHD	Adverse effects were studied. Significant increase in motor tics and severe social withdrawal
Handen *et al* 1997[59]	MPH	12–65 months following double blind study	52 children (7–14 years) M-ID and borderline ID	ADHD	69% continued on medication. 72% improved although 2/3 of sample rated 98th percentile on hyperactive index and 22% had had I/P treatment during follow up
Handen *et al* 1999[63]	MPH 0.3 mg/kg/day	Double blind study	11 preschool (4–5.11 years) with ID	ADHD	Significant improvement on teachers rating. 8/11 medication responders
Aman *et al* 1997[60]	MPH 0.4 mg/kg/day FFRM 1–2 mg/kg/day	Double blind/placebo controlled	Children with ID	ADHD	Better results with FFRM, but more side effects such as drowsiness, dizziness, and anorexia

ADHD, attention deficit hyperactivity disorder; FFRM, fenfluramine; ID, intellectual disability; I/P, inpatient; MPH, methylphenidate.

to have limited effects on hyperactivity in people with developmental disabilities.[61]

Currently there is no compelling evidence supporting the use of clonidine in the treatment of Tourette's syndrome, other tic disorders, and impulsivity.[43]

G. Opioid antagonists

There have been controversial reports with respect to the efficacy of naltrexone for the treatment of self injury in people with developmental disabilities. Some investigators found it helpful,[64] while others indicated that naltrexone might worsen stereotypical and self injurious behaviours.[65] Casner *et al* conducted a retrospective study, and found that out of 56 (n = 8000 patients with developmental disabilities) patients, 32 were considered to have responded to treatment by their prescribing physicians but only 13 were judged to be improved according to the investigator's standards.[66] Casner *et al* reported a low frequency of serious side effects and a gradual

Table 6 Various psychopharmacological treatments studied in persons with intellectual disabilities: opiates and β-blockers

Author	Drugs	Duration	Subjects	Symptoms diagnosis	Results
Opiates					
Buzan *et al* 1995[64]	NLTX	Open study	3 adults with ID	SIBs	Good responses 3/3
Casner *et al* 1996[66]	NLXT	Restrospective long term study	56 adults	SIBs	50% were maintained on NLTX because of professional belief. 25% good responders
Willemsen-Swinkels *et al* 1995[65]	NLTX 100 mg initial dose then 50 mg/day	Double blind controlled 4 weeks	33 adults with ID	Autism + SIBs	ABC and CGI no therapeutic effects. On the contrary NLTX increased stereotypic behaviour
β-Blockers					
Ruedrich *et al* 1990[69]	PNL + NDL	Review study	1 case report with ID. Review of literature	Aggressive, SIBs	Literature review raised concern in the use of β-blockers in this group

ABC, Aberrant Behaviour Checklist; CGI, clinical global impression; ID, intellectual disability; NDL, nadolol; NLTX, naltrexone; PNL, propanolol; SIB, self injurious behaviour.

onset of improvement in behavioural disturbances.[66] Furthermore, a controlled study found that opioid antagonists improve self injurious behaviours only minimally.[67]

H. β-Blockers

Propranolol was found to be beneficial in managing aggressive and self injurious behaviours in some people with concurrent developmental disabilities.[68] A limited number of non-controlled trials showed some benefit to propranolol and nadolol on behavioural disturbances such as impulsiveness, aggressivity, self injurious behaviour, and stereotypies.[69]

Opiates and β-blockers studied in those with intellectual disabilities are shown in table 6.

DISCUSSION

This article provides the reader with a review of psychopharmacological agents used in persons with dual diagnosis of developmental disability and mental disorders. The various categories of these pharmacological treatments are outlined in groups that are addressing different mental health/behaviour problems. The purpose of this review is to facilitate clinicians to adopt an evidence based practice in the administering and monitoring of psychotropic medications.

This review found that SSRIs, newer anticonvulsants, and atypical neuroleptics are preferred medication choices for the treatment of psychiatric disorders among people with developmental disabilities. These findings are consistent with those reported by Santosh and Baird[43] and Madrid *et al*[70] in extensive reviews of the literature regarding the pharmacological management of behavioural and psychiatric disturbances in people with developmental disabilities.

Although the number of studies devoted to the use of psychotropic medication in persons with dual diagnosis remains rather small, there is adequate evidence to suggest that these medications are appropriate for use in this group. Although not exhaustive, the present review highlighted several key studies that indicate the efficacious use of these medications in persons with dual diagnoses. Additionally, the present review has also demonstrated that persons with intellectual disabilities are more vulnerable to side effects, with potentially catastrophic results, including fatalities.

It is essential to adopt an evidence based practice in the administration and monitoring of psychotropic medications within this population. Unfortunately, there are scant data regarding the use of psychotropic drugs in people with developmental disabilities. In addition, most studies are fraught with several limitations, including small sample sizes, non-controlled design, and poorly validated outcome measures. Consequently, most psychotropic medications are prescribed to people with developmental disabilities based on information gleaned from studies on individuals without developmental disabilities. Therefore, at the present time the approach to utilising psychopharmacological agents in persons with developmental disabilities is based primarily on consensus practices. The present review has sought to identify the key issues to keep in mind in the pharmacological treatment of individuals with developmental disabilities and comorbid psychopathology, in order to aid clinicians in making sound, evidence based treatment decisions.

CLINICAL GUIDELINES

The most important steps to be followed in a situation where a patient with intellectual disability is thought to be suffering from psychiatric disorder(s) are the following:

- Consider psychiatric disorder as a possible explanation of certain behaviour changes.
- Assess the problem behaviour.
- Diagnose the problem as a psychiatric disorder.
- Treat the problem with medication whenever appropriate.
- Follow up goals include:

(a) Monitoring effectiveness of medication used.

(b) Exploring the side effects, if any.

(c) Treating the side effects.

(d) Maintaining a minimal level of medication necessary to address the problems.

(e) Physical checkup regarding other physiological functions that can become affected by the prolonged use of medication.

It is to be remembered that the patient is in the centre of our caring, and that various pieces of the puzzle of wellness/disease are necessary to be in place in order to maximise the beneficial effects of all of the parts, and enhance the quality of life of persons with a dual diagnosis.

FUTURE RESEARCH

Future research directions should identify appropriate diagnostic criteria in persons with developmental disabilities to enable professionals to better identify psychiatric disorders and thus apply the appropriate diagnosis. Unfortunately, there is a paucity of studies of specific psychopharmacological interventions as they apply to persons with developmental disabilities. Multicentred studies that address specific biological treatments in people with developmental disabilities would further expand our current body of knowledge. It is hoped that these issues will be addressed in future research, so that our knowledge of evidence based treatments for this population is ameliorated.

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Psychopharmacological treatments in persons with dual diagnosis of psychiatric disorders and developmental disabilities

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