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Pharmacotherapy of disorders in mental retardation

Abstract This is a review of pharmacotherapy in children and adolescents with mental retardation from the perspective of DSM and ICD disorders. The existing research is reviewed in young people with mental retardation but, when data are lacking, we examined the literature from adults with mental retardation and from typically-developing children. The literature is discussed for each of the following disorders: ADHD, anxiety disorders, bipolar disorder, conduct disorder, depression, enuresis, schizophrenia, self injury, and tics and movement disorders. With the possible exception of ADHD, there is a woeful lack of empirical data on most of these disorders in young people with mental retardation. Clinicians will often be forced to extrapolate from data on adults having mental retardation and from typically-developing children. The best policy is probably to treat such patients cautiously, while gathering data on the effects of such therapy in the hopes of beginning a data base.

Key words Pharmacotherapy – drug research – mental retardation – psychiatric disorder

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Introduction

With the development of many new drugs, there has been a renewed interest in pharmacotherapy in mental retardation. Research in the past was often directed to the suppression of nonspecific behavior problems, such as aggression or self injury (1). In recent years, however, there has been a noticeable swing of interest to the management of specific DSM and ICD disorders. Consequently, we will structure this review around DSM disorders. One consequence is often very small sample sizes. About 1 % of the population has mental retardation and, of course, only a fraction of these have additional psychiatric disorders ("dual diagnoses"). Hence, apart from common disorders, it can be very difficult to assemble a sizable group of subjects. This is even more true when the sample is confined to children and adolescents. Because of this, we were often forced to extrapolate from drug research with adults having mental retardation when discussing effects in younger patients. There are far more case reports than group studies on drugs in mental retardation. In this review, we have emphasized studies over case reports because of the natural tendency of clinicians to report treatment successes rather than failures.

One issue confronting drug researchers in mental retardation is that diagnoses of DSM and ICD disorders may be more difficult to establish as severity of retardation increases (2, 25). This is likely due to developmental changes, communication problems, and cognitive handicap, making it more difficult for the patient to introspect and to report on internal symptoms. Beyond these obvious reporting problems, these factors may even modify the presentation of the disorder (65). The net effect is that diagnostic reliability is probably significantly lower in young people with mental retardation than in typically developing young people. Finally, we did not review the literature on autistic disorder and other pervasive developmental disorders, despite the large overlap between them and

mental retardation. Autism is covered elsewhere in this supplement.

Literature search

In reviewing the literature, we relied heavily on computer searches to identify relevant studies. Our literature review was generated by using the PsychInfo database. The search consisted of a review of the literature published in English over the last 25 years. The psychological disorders researched were as follows: attention deficit/hyperactivity disorder (ADHD), anxiety disorders (e.g., general anxiety, obsessive-compulsive disorder, and post traumatic stress disorder), bipolar disorder, conduct disorder/oppositional defiant disorder, depression, psychosis (schizophrenia, schizoaffective disorder, and schizophreniform), tic disorder, and enuresis/encopresis. These psychological disorders were cross referenced with two main areas of interest. The first area cross reference consisted of mental retardation, mental deficiency, or intellectual handicap. The next area consisted of the terms psychotropic medication, medication, medicine, and psychopharmacology.

Pharmacotherapy in specific disorders

Attention deficit hyperactivity disorder (ADHD)

In contrast to most other disorders, there is a significant amount of research on pharmacotherapy of ADHD in young people with mental retardation. For brevity, we will rely on reviews by Aman (4), Arnold et al. (8), and Handen (33) to summarize the work with psychostimulants (methylphenidate, dextroamphetamine, amphetamine salts, and magnesium pemoline). Since 1980, at least 10 group studies (Ns = 10 to 30) have assessed methylphenidate or dextroamphetamine in children, adolescents, and adults with ADHD. With one exception, all were positive and statistically significant, indicating substantial benefit in managing motor overflow, attention span, and impulsiveness. Improvements were also seen in cognitive performance, some measures of social behavior, and independent play. The sole negative study included adolescents and adults, without established ADHD, and usually with profound mental retardation (see 4).

Aman (4) calculated the response rate to psychostimulants in all of the group studies using young people with a diagnosis of ADHD and found it to be 54 %. This is substantially below the rate of 75 % commonly given for typically developing children, but it indicates that psychostimulants are still a major therapy in young people having mental retardation and ADHD. There is also a number of single subject studies that have shown beneficial changes with methylphenidate and dextroamphetamine. We were unable to locate any studies that examined the effects of amphetamine salts (Adderall) or magnesium pemoline (Cylert) in this population (see 8). Aman (4) has presented a theoretical model postulating that focus of attention, IQ, and mental age may be useful predictors of psychostimulant response. On average, children with narrow attentional focus are expected to respond more poorly than those with broader attentional focus.

Given the use of tricyclic antidepressants as a second-line treatment for ADHD in typically developing youngsters with ADHD, there is a remarkable paucity of study in mental retardation. There are two case series reported where ADHD symptoms improved, but seizures were a problem in one case series (64). Baumeister et al. (9) summarized 22 studies of antipsychotic effects on hyperactivity in subjects with mental retardation. Overactivity was usually decreased, although amount of reduction was typically modest. At one time, carbamazepine was thought to have utility in ADHD, but most of the controlled studies (in typically developing children) were negative (50). Studies of fenfluramine in ADHD and mental retardation were largely positive, but reports of valvular dysfunction with fenfluramine have probably put an end to its use (28).

Anxiety disorders

Anxiety is a universal and normal experience. It is usually harmless and considered to be important for an individual's survival and adaptation to the environment. However, anxiety may be maladaptive when it is persistent, long-lived, or disruptive.

Individuals with severe or profound mental retardation may be one of the single groups most at risk for the development of behavioral disorders associated with anxiety. Therefore, anxiolytic therapy is being used with increasing frequency for mentally handicapped persons. This increased use suggests a new awareness on the part of the mental health clinicians who treat people with mental disabilities. Anxiolytic agents have been used in a small but significant minority of people with mental retardation, including those residing in the community and in institutions (53). The most common use of anxiolytics in the population with mental retardation has been to control disruptive behavior and generalized anxiety disorder. Because of the recurrent nature of generalized anxiety disorder, medication use may become intermittent.

The most commonly prescribed anxiolytic agents are benzodiazepines, which have been assessed in mentally retarded children. For example, LaVeck and Buckley (38)

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examined a variety of drugs used for children attending a training school. In one study, chlordiazepoxide (30 to 75 mg/day) or placebo was given to children who had mental retardation and unspecified behavior problems. Chlordiazepoxide produced a nonsignificant increase in undesirable behavior, and resulted in less continuous play, more toy changes, and more hyperactivity in a standard playroom situation (38). Krakowski (37) preformed an uncontrolled trial of chlordiazepoxide in 51 children having a variety of emotional and behavioral problems, including 12 children with mental retardation. Some 67 % of the group (and 50 % of those with mental retardation) were thought to respond favorably to the treatment. One of the symptoms regarded to be most responsive was anxiety (76 %). In more recent cases, Bond et al. (13) found that midazolam, an ultrashort-acting benzodiazepine used primarily as an anesthesia, was useful as PRN treatment in controlling recurrent aggression in three persons with mental retardation who were 14, 17, and 26 years of age. According to another report, clorazepate and alprazolam were found to be helpful for managing akathesia (31).

Ratey et al. (48) studied buspirone for managing anxiety and other behavior problems. The researchers compared the placebo and buspirone for six adults with both anxiety disorders and at least one aggressive or self-injurious incident per week. Five of the six subjects showed drug-related decreases in aggression (between 26 % and 63 %), whereas anxiety was rated by staff as increased in four subjects and as decreased in two. The authors concluded that buspirone can be useful in decreasing aggression, but that it had no clear effect on reducing anxiety in these subjects. Hence, buspirone may prove to be beneficial for some individuals with developmental disabilities, although it is not clear at this time what subject characteristics are likely to elicit a favorable response.

More systematic data are needed in evaluating the effects of anxiolytics in children and adolescents. Extrapolating results from studies of adults is problematic, as responses to medication may depend on the subject's developmental characteristics. Clinical investigations have found that responses in typically developing children and adolescents are distinct from those in adults. The benzodiazepines may pose greater risks for children and adolescents by conditioning them to deal with their own anxiety by using chemicals rather than coping skills, or by developing a potential dependency on drugs (7).

Anxiolytics have not been well studied in children and adolescents, and there are few studies of the efficacy and safety of anxiolytics in people with mental retardation. Because of the absence of sound scientific research on efficacy and safety of anxiolytics in people with mental retardation, these drugs should be used with caution and careful monitoring for benefits and side effects.

Bipolar disorder

The mainstay of the pharmacologic treatment of acute mania or bipolar disorder has been lithium, alone or in combination with neuroleptic treatment. With the exception of one double-blind long-term trial of lithium reported by Naylor et al. (45), all reports on the benefit of lithium have been single or multiple case reports of clinical or limited uncontrolled treatment (56). Naylor studied 14 patients ages 19 to 58 with borderline to severe mental retardation and bipolar disorder. All patients were given lithium (with levels between 0.6 and 1.0 mEq/l) or placebo, in a blind fashion, for one year. The number of weeks of illness was significantly lower in the treatment group. Rivinus and Harmatz (54) studied five persons with bipolar mood disorder and mental retardation. They were given lithium in a single-blind placebo controlled manner. Treatment for one year resulted in remission of symptoms. Mania reemerged after discontinuation of lithium. When lithium was restarted, all five entered another lengthy remission.

There is evidence that several anticonvulsant medications have a role in the treatment and prophylaxis of bipolar mood disorder in patients with mental retardation. The two most commonly used agents are carbamazepine and valproic acid. Reid et al. (49) compared carbamazepine to placebo in a double-blind, crossover fashion in 12 overactive adults with severe mental retardation. Those described as having elevated moods and distractibility responded to treatment, while those without mood disturbance did not. Glue (29) reported on 10 retarded adults with rapid cycling bipolar mood disorder treated with lithium, lithium and carbamazepine, and carbamazepine alone. Half of the patients showed partial or complete improvement on lithium alone or in combination with carbamazepine. None of the patients treated with carbamazepine alone responded. Sovner (63) reported on five individuals with bipolar mood disorder who failed treatment with neuroleptics and/or carbamazepine. All responded to standard treatment with divalproex sodium. Four had a dramatic response, while the fifth had a moderate response.

Bipolar mood disorder in childhood prior to adolescence is rare, and its occurrence in a child with mental retardation is even rarer and more likely to be missed (35). Thus the research on treatment of children with bipolar mood disorder and mental retardation is limited to case reports. Kastner et al. (36) reported three children successfully treated with valproic acid. All three had previous trials of both lithium and carbamazepine, either without clinical efficacy or with intolerable side effects. Lithium was associated with many side effects in children with mood disorders and concurrent cerebral palsy, movement disorders, and incontinence, and Kastner et al. felt that valproic acid or carbamazepine should be preferred over lithium for these reasons. Whittier et al. (69) reported on a 13-year-old girl who responded to valproic acid for dysphoric mania.

There is relatively little research on lithium in the pediatric population with bipolar mood disorder and mental retardation. Dostal and Zvolsky (24) and Goetzl et al. (30) reported that lithium therapy was effective in 14 of 17 retarded adolescents and young adults (82 %) with mental retardation in inpatient settings. Linter (40) reported on an adolescent boy with short-cycle manic-depressive psychosis and mental retardation who responded to lithium.

Conduct disorder

Aggressive children or adolescents constitute one of the most distressed and urgent referral groups in child psychiatry. The consequences of aggressive behavior can be devastating to the child's family, friends, school, society, and especially to the child himself. A majority of controlled studies and case reports concerning the treatment of aggression have been performed in adults. Therefore, clinicians have often relied on the literature based on adults to fill the void on the child and adolescent literature. The prevalence of conduct disorder in children and adolescents is estimated to be 9 % for males and 2 % for females according to the DSM, although actual rates tend to vary widely according to the method of measurement and the type of population studied (47).

The pharmacotherapy of conduct disorder in mental retardation has been poorly studied. Of the few studies on conduct disorder, most were performed using typically developing children or adolescents. Among the first drugs studied to treat aggression in children and adolescents was phenytoin, which failed to show favorable results (68). Controlled studies in conduct disorder using carbamazepine are uncommon; older studies contain conflicting information on carbamazepine (68). Carbamazepine warrants further study.

Psychostimulants have also been studied for the treatment of conduct disorder. Early investigators have reported positive results with the use of amphetamine sulfate in treating youths with conduct disorder (9). There has been continued support for amphetamines, methylphenidate, and other psychostimulants, although such changes are usually modest (9).

Haloperidol and lithium are currently the best studied pharmacotherapeutic agents known for conduct disorder. Studies of haloperidol for the treatment of conduct disorder in children and adolescents have generally yielded positive results. Cunningham et al. (20) reported effective use of haloperidol for aggressive, destructive children. More recent double-blind studies have addressed the use of haloperidol, and have demonstrated its efficacy in individuals with conduct disorder. Aman et al. (5) compared placebo and risperidone in 118 children with low IQs and conduct disorder or oppositional defiant disorder. The results indicated that risperidone reduced parent and clinician ratings of conduct problems on a variety of standardized scales. Several open studies support the use of lithium to aid in the treatment of children and adolescents with conduct disorders. Delong and Aldershot (21) reported limited success (15 % response rate) in the use of lithium for children with conduct disorder.

In conclusion, the current body of literature suggests that both haloperidol and lithium are effective psychopharmacological agents in the treatment of conduct disorder. The new "atypical" antipsychotics may also prove to be effictive. A dearth of empirical data from children and adolescents with conduct disorder and mental retardation forces researchers to rely heavily on findings from pharmacological findings in typically developing children with conduct disorder.

Depression

Sovner et al. (64) have done an excellent job summarizing the existing data on antidepressant therapy in people with mental retardation. By 1998, clinical outcomes for some 46 adults with mental retardation were reported in the literature. With the exception of a series of five profoundly retarded patients, the clinical response was reportedly positive in the majority of these patients. Agents used included amoxapine, desipramine, fluoxetine, fluvoxamine, imipramine, nialamide, and nortriptyline.

In general, investigators have had difficulty demonstrating significant improvement with antidepressant drugs in children and adolescents, even in those who are typically developing (67). Recently, Emslie et al. (26) demonstrated a statistically significant advantage for fluoxetine over placebo in 96 typically developing children with major depression. The response rate approached 60 % effectiveness. Viesselman (67) speculated that there may be developmental reasons why children and adolescents might respond better to SSRIs than to tricyclic antidepressants. He reported that children's dopamine and norepinephrine systems may not fully develop until early adulthood, whereas their serotonin system may be more mature in late childhood and adolescence.

In their review, Sovner et al. (64) identified three reports of antidepressant medication trials in children with mental retardation. All three reports indicated at least some benefit with the agents used. Two of the reports were conducted by the same author. Dosen (22) reported that nine of 12 patients with atypical depression responded to imipramine or amitriptyline therapy. Dosen (23) found imipramine to be helpful in one of two children with major depression, and tryptophan plus nicotinamide were helpful in two other youngsters with major depression.

Of course, developmental handicap may hamper the recognition and diagnosis of major depression in young people with mental retardation. Bryan and Herjanic (14) discussed depression and suicide among young people with handicapping conditions, and they offered several suggestions for identifying

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depression. The symptoms and signs that they identified included the following: a) low mood over several days characterized by sadness, tearfulness, low self esteem, and so forth; b) abrupt changes in behavior (e.g., sudden hostility, increased irritability, shift from even temper to angry outbursts); c) disturbed sleep patterns (insomnia, early wakening with apprehension or sadness, increased time in bed); d) changes in eating pattern or alteration in weight; e) physical complaints (headaches, stomach aches, continual fatigue); f) changes in school behavior (e.g., incomplete assignments, loss of concentration or memory); g) changes in energy level (increased listlessness, boredom, dejection); h) altered appearance (disheveled appearance, slowed gait, dejected posture); i) regression to earlier behaviors (e.g., thumb sucking, whining, bed-wetting); and j) expressions of grim thoughts (e.g., wanting to die, repeated references to death).

There is a serious need for systematic research both in young people and in adults with mental retardation. Almost all of the available reports are uncontrolled case series. Clinically, the SSRIs and the cyclic antidepressants are worthy of empirical trials. Further alternatives include bupropion, nefazodone, trazodone, and venlafaxine. As bupropion is contraindicated in patients with seizure disorder, its role may be more limited than the others, given the prevalence of epilepsy in mental retardation.

Enuresis

The pharmacologic treatment of enuresis in children and adults with mental retardation is a subject that has been more extensively studied than most other diagnoses. Enuresis causes significant anxiety for those experiencing it as well as for those who care for them. Approximately 20 % of five-year-old children wet the bed at least monthly, while by age six only 10 % wet the bed. There is a 15 % remission rate each year after age six.

While there are many behavioral techniques used to aid in reducing enuresis in typically developing children, only two drugs have been studied extensively: desmopressin acetate (DDAVP) and imipramine hydrochloride. Oxybutynin chloride is now receiving interest as a treatment.

Desmopressin

Desmopressin (the synthetic analog of vasopressin) acts by increasing water retention and urine concentration in the distal tubules of the kidney. This drug is administered intranasally using a unit-dose, spray pump delivery system. The starting dosage is 20 mcg (one spray) at bedtime, which can be titrated to a maximum dosage of 40 mcg. The duration of action is 10 to 12 hours. The medication is expensive, costing $ 1.50 per spray in the United States (59).

A review of 18 controlled studies in children (44) demonstrated that only about 24 % of children were completely dry while on medication and that 94 % relapsed after medication was discontinued. There were no studies on the effectiveness of DDAVP in children with mental retardation.

Imipramine

Imipramine acts directly on the bladder, combining an anticholinergic effect that increases bladder capacity with a noradrenergic effect that decreases bladder detrusor excitability. Initial rates of suppression in typically developing children ranged from 10 % to 60 % in eight controlled, double-blind studies. Relapse rates following treatment were more than 90 % (59). The low toxic/therapeutic ratio of imipramine is a major concern. Symptoms of overdosage include ventricular tachycardia, coma, and seizures.

The available data suggest that children with mental retardation have a less favorable response to imipramine (11). Two double-blind studies reported unfavorable results with imipramine in children with mental retardation. Rett (51) reported benefit in a double-blind trial of imipramine in a heterogeneous group of brain-damaged children with an average IQ below 65, and they also noted that more beneficial results were obtained in children with higher IQs. Smith and Gonzalez (62) reported improvement in a group of 34 institutionalized boys, with an average IQ less than 75, treated with nortriptyline.

Schizophrenia

As with other disorders, there is general agreement that schizophrenia is more common in people with mental retardation than in the general population. Turner (66) reviewed several surveys of schizophrenia in adults with mental retardation and concluded that most studies have found point prevalences around 3 %, which is about triple the rate found in the general population. Turner noted problems in establishing a reliable diagnosis in patients with mental retardation. In particular, certain features that may be associated with retardation (e.g., underactivity, slowness of thought and action, poverty of speech, emotional blunting and social withdrawal) may be difficult to separate from negative symptoms of schizophrenia.

We could find only two studies of antipsychotic drugs in patients with mental retardation and schizophrenia. Craft and Schiff (19) used fluphenazine decanoate to treat psychotic (“mentally ill”) and nonpsychotic residents living in units in England, Wales, and Ireland. They found a highly significant improvement in this mixed group, although this study had a number of significant design limitations. Some 22 of the 102 patients (22 %) developed extrapyramidal symptoms (EPS), but EPS occurred equally often in patients with and without

brain damage. Menolascino et al. (43) randomly assigned 31 schizophrenic patients with mental retardation and 30 schizophrenic patients with normal IQ to thiothixene or thioridazine treatment. Both groups showed highly significant improvements on a number of rating instruments that were completed by blinded staff members. The doses of both drugs were significantly lower for the subjects with mental retardation than for those with average IQs. Some of the data suggested that thiothixene alleviated symptoms faster than thioridazine in those with mental retardation. EPS were more common with thiothixene, whereas drowsiness was the main side effect with thioridazine. Neither of these investigations was truly a controlled study, as there was no placebo condition, and patients were always followed from a no-drug to a medicated condition. Others reported on the use of clozapine in five treatment-resistant adults with mental retardation (57). Four responded favorably to doses comparable to those used for treating schizophrenia in the general population. No EPS and no seizures occurred.

All of the above reports were based on adult samples. Campbell and Gonzalez (17) reviewed the research on antipsychotic drugs in typically developing schizophrenic children and adolescents. Controlled studies are rare. In one comparison study, thiothixene was considered superior to thioridazine in adolescents with chronic schizophrenia. One report based on chart reviews indicated that clozapine was effective in adolescents. Two controlled studies indicated that haloperidol and loxapine succinate were effective in schizophrenic children and adolescents. To the best of our knowledge, there is no database on pharmacotherapy in children and adolescents having both mental retardation and schizophrenia. Faced with this, it seems that clinicians have no choice but to use the standard of care that is applied with nonretarded patients. In the very recent expert consensus survey (27), the novel antipsychotics (exclusive of clozapine) were endorsed most heavily, followed by high-potency classical antipsychotics.

Self injury

Self injury is unlike most disorders discussed here because a) it is uncommon in the general population and b) it has received considerable research attention in patients with mental retardation. We rely heavily on a review by Aman (3) in summarizing research on pharmacotherapy in mental retardation. Self injury is much more prevalent as the severity of mental retardation increases. It tends to occur more commonly among adolescents and young adults than younger children and older adults, and it may be slightly more common among males because of certain X-linked syndromes (55). Most of the pharmacological research to date has been done with adults. We have to assume (but have no certainty) that analogous findings would be obtained with young people.

Antipsychotics

Aman (3) exhaustively reviewed the literature up to 1993, and Buitelaar (15) discussed the literature with children. At that stage, there were no well controlled studies of antipsychotic efficacy in children and adolescents with self injury. The existing studies with adults and mixed-aged groups most strongly supported a role for thioridazine, but the findings were mixed, and individual responses were variable within studies. The data for chlorpromazine were largely negative, and data for haloperidol were somewhat positive but primarily from flawed studies. Breese and his associates have pursued a D_1 dopamine model in which it is hypothesized that supersensitive D_1 dopamine receptors may be the cause of self injury in some patients (60, see 3). If correct, this model suggests that D_1 dopamine blockers (like clozapine) or mixed D_1 and D_2 blockers (like fluphenazine) may be more effective than most antipsychotics, which tend to act largely or solely on D_2 receptors. A study by Gualtieri and Schroeder (32) did suggest that fluphenazine was useful for managing self injury, but again there were design limitations in the investigation.

In recent years, there has been a major swing to the use of atypical agents in this field, at least in the United States. Three recent reports, mostly of an uncontrolled open treatment design, have suggested that risperidone may be quite helpful for suppressing self injury (18, 34, 41). In a recent expert survey in the mental retardation field, risperidone and olanzapine were endorsed over most other treatments for managing self injury (27). However, this reflects clinical opinion, and the finding needs to be confirmed with rigorous empirical studies.

The antipsychotics undoubtedly benefit some patients with severe self injury. However, at present we are unable to predict who the responders are likely to be. The field would benefit greatly from a rigorous comparison of placebo, a classical antipsychotic, and an atypical antipsychotic (ideally thioridazine and risperidone, respectively). Until such a study is done, clinicians will have to feel their way along using a trial-and-error approach.

Lithium carbonate

Aman (3) noted that one of two group studies showed improvement in self injury and the findings of a retrospective chart review were largely negative. Predictably, all of the published case reports were positive. The data are too sparse to draw conclusions, although there are enough positive reports to warrant cautious empirical trials in clinical practice.

Antidepressants

We are not aware of any studies with the monoamine oxidase inhibitors (MAOIs) or the tricyclic antidepressants to manage

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self injury in children or adults with mental retardation (3). Recently there has been interest in the idea that self injury may reflect an underlying depression and/or obsessive-compulsive variant in some patients with self injury. There has been a recent rash of studies and case reports using serotonergic antidepressants (clomipramine and the SSRIs) in children and adults with developmental disabilities.

Aman, Arnold, and Armstrong (6) reviewed this literature which encompassed some 49 reports. In general, the reports suggested beneficial effects on a variety of perseverative behaviors, including self injury, but most were case reports and uncontrolled studies. No differences were noted as a function of age (child *vs* adolescent *vs* adult) in these reports (6), although age characteristics were not always available to enable such an analysis. Aman et al. concluded that there were enough positive data reported to justify cautious clinical trials of serotonergic antidepressants in patients showing repetitive forms of self injury as well as other forms of perseverative behavior. Clomipramine and the SSRIs may well have different effects within the same patients.

Naltrexone

The notion that a dysfunction in the opiate system may underlie self injury has resulted in significant research with naltrexone and naloxone (58). Because of naloxone's brief half-life and the fact that it is administered intravenously, only naltrexone is a viable treatment in the clinical setting. There have been a number of studies and case reports with both drugs, with perhaps a majority indicating some suppression of self injury (58). However, some of the largest and most rigorous investigations have been negative (12, 70), including one study with children with autistic disorder (16). We believe that naltrexone is no more effective (perhaps less so) than antipsychotic drugs. Furthermore, even if the drug is helpful in managing self injury, this does not necessarily implicate the opiate system, as naltrexone has a mild anxiolytic action, a property that it shares with antipsychotics, lithium, and the antidepressants (3). In the expert survey (27), clinicians and researchers generally classified naltrexone as a second-line (or lower) intervention.

Other drugs

There are a number of case reports and loosely-controlled studies of beta blockers, such as propranolol and nadolol. Most have suggested that the beta blockers may be helpful for managing self injury, but more rigorous trials are needed to substantiate a role (3). Careful empirical trials may be tried in the clinical situation. Other drugs that have been tried include antianxiety drugs, psychostimulants, and carbamazepine. Currently the data are inconclusive on all of these (3).

Conclusion

Only tentative conclusions can be drawn. There is no established pharmacotherapy for self injury. In this situation it may be wisest to be guided by other features of the patient. For example if OCD symptoms (*beyond* the self injury itself) or depression are prominent, clomipramine or SSRIs may be indicated. If there is suspicion of psychosis or family history of such, thioridazine, risperidone, or olanzapine may prove optimal. If an anxiety component (especially with a somatic element) is present, the beta blockers may be tried first. If the self injury appears to drive itself or if the patient appears not to have the usual response to pain, naltrexone may warrant a trial. In the absence of clear guidelines, each treatment should be viewed as an empirical trial with the need for suitable clinical data.

Tics and movement disorders

Tourette's disorder is a well-studied condition impacting children with psychiatric disorders. While many neurotransmitters were implicated in the etiology of this disorder, it is now believed that the dopaminergic system and noradrenergic systems are involved. Two major clinical trials (39, 61) indicated that haloperidol and pimozide reduced the severity of tics by 65 %, but haloperidol appeared to be the more effective of the two medications. However, these medications are associated with side effects (including cognitive impairment, excessive sedation dysphoria, school phobia, and tardive dyskinesia) that may limit their effectiveness in children with mental retardation. Clonidine is less frequently associated with these side effects (39) but is only 25 % to 35 % effective in controlling tics.

The study of drug-induced movement disorders (including akathisia) in children in general has been relatively neglected. Polizos and Engelhart (46) reported that akathesia does occur in children treated with neuroleptics, but it was infrequent. In a study of 284 children treated for "childhood schizophrenia with autistic features" with a variety of neuroleptics, 23 % of patients developed extrapyramidal side effects, but only two cases of akathisia were reported. In one of the few prevalence studies of extrapyramidal side effects in children, Richardson et al. (52) examined 104 children and adolescents admitted to a state-operated psychiatric center. 61 children were receiving neuroleptics and 11 were receiving anti-parkinsonian medications. Mild akathesia was present in two adolescent patients.

Conclusions

It is clear that there is a dearth of empirical evidence relating to the usefulness of pharmacotherapy in most disorders affecting children and adolescents with mental retardation. One exception is ADHD, where psychostimulants have received a moderate degree of research attention. However, even in ADHD, we are not aware of any studies of tricyclic antidepressants, which comprise the second line of treatment in typically developing children with ADHD. The database for most other conditions is either sparse or nonexistent. Faced with this situation, practitioners have no choice but to extrapolate findings from typically developing children, and adults with mental retardation to children with mental retardation. In doing so, clinicians should proceed with appropriate caution and in a very data-based manner. In this way, we can at least begin to develop a somewhat anecdotal data base. However, extrapolation is not without its risks, as young patients with mental retardation may present important developmental differences from adults with mental retardation and typically developing children. For example, it has been suggested that lower functioning children with ADHD may have a lower probability of responding to psychostimulants than higher-functioning children with mental retardation (4). Clearly, this whole area requires much more research.

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