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ORIGINAL PAPER

A Systematic Review of Interventions Used to Treat Catatonic Symptoms in People with Autistic Spectrum Disorders

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Abstract A systematic review was conducted to examine the efficacy of a range of treatments for autistic catatonia. The review identified 22 relevant papers, reporting a total of 28 cases including both adult and paediatric patients. Treatment methods included electroconvulsive therapy (ECT), medication, behavioural and sensory interventions. Quality assessment found the standard of the existing literature to be generally poor, with particular limitations in treatment description and outcome measurement. There is some limited evidence to support the use of ECT, high dose lorazepam and behavioural interventions for people with autistic catatonia. However, there is a need for controlled, high-quality trials. Reporting of side effects and adverse events should also be improved, in order to better evaluate the safety of these treatments.

Keywords Autistic spectrum disorders · Catatonia · Electroconvulsive therapy · Behavioural therapy

Introduction

Autistic spectrum disorders (ASD) are a group of neurodevelopmental syndromes characterised by deficits in communication, social interaction and imagination (American Psychiatric Association 2000; World Health Organisation 1992). It is increasingly recognised that these syndromes are additionally associated with abnormalities in sensory processing (Kern et al. 2006) and motor function (Gowen and Hamilton 2013).

The term catatonia describes a cluster of abnormalities in speech, movement and behaviour. Historically, catatonia has been associated with psychosis, but is now recognised in a range of conditions, and most commonly occurs in patients with mood disorders (Fink and Taylor 2003). Given its unique presentation, it has been suggested that catatonia should be considered as a syndrome in its own right (Taylor and Fink 2003), but until recently it has been listed in diagnostic manuals only as a specifier that can be applied to other diagnoses. DSM-V (APA 2013) lists catatonia as a specifier for various psychotic and mood disorders, and also introduces Catatonia Not-Otherwise-Specified as a new diagnostic category. This allows a diagnosis of catatonia to be made where the underlying diagnosis is not known, or where it occurs outside of the diagnoses for which catatonia is a recognised specifier. DSM-V defines catatonia as being characterised by the presence of at least three of the following: catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, mannerisms, stereotypies, grimacing, echolalia and echopraxia.

There is increasing recognition that catatonia can present as a comorbid syndrome in ASD. Existing studies suggest that around 12–18 % of young people with ASD also present with catatonic symptoms (Wing and Shah 2000a; Billstedt et al. 2005; Ghaziuddin et al. 2012). Onset is typically between 10 and 19 years and often gradual; younger patients tend to present with isolated symptoms that may then progress over time into a full catatonic syndrome (Wing and Shah 2000a).

Diagnosis of catatonia in autism is complicated by the overlap in symptoms between these two conditions (e.g.

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mutism, echolalia, stereotyped/repetitive behaviours). There is also some disagreement as to whether catatonic symptoms in ASD are akin to catatonic states associated with other conditions. One view is that, rather than being seen as a comorbid condition, catatonic symptoms should be considered as expressions of autism occurring in a subgroup of this population (Hare and Malone 2004). Specific criteria have therefore been suggested, to define what has been termed 'autistic catatonia' or 'catatonia-like deterioration' (Hare and Malone 2004; Wing and Shah 2000a). Suggested features include: increased slowness affecting movement and verbal responses, difficulty in initiating and completing actions, increased reliance on physical or verbal prompting from others, increased passivity and apparent lack of motivation (Wing and Shah 2000a; Hare and Malone 2004). Due to the degree of overlap in symptoms, it has been proposed that key indicators of autistic catatonia are the emergence of new symptoms, or a change in the pattern of pre-existing symptoms (Ghaziuddin et al. 2005).

Several explanations for the apparently high co-occurrence of autism and catatonia have been proposed. Some authors have suggested a possible genetic link, with potential susceptibility regions on chromosome 15 implicated in both conditions (Chagnon 2006). Common structural abnormalities or changes in neural circuitry have also been hypothesized to link these conditions (Fink et al. 2006; Stoppelbein et al. 2006; Dhossche et al. 2006a). Abnormalities in GABA function have similarly been implicated in both autism and catatonia. GABA dysfunction has been hypothesised to play a role in the aetiology and pathophysiology of autism due to its impact on neural organization during early development, although empirical evidence is limited; GABA dysfunction is also implicated in catatonia, primarily due to the observation that effective treatments for catatonia enhance GABA function (Dhossche 2004; Dhossche and Rout 2006). Reports of traumatic or anxiety-provoking life events preceding the onset of catatonia additionally suggest a role for psychogenic factors (Dhossche et al. 2012; Wing and Shah 2000b). Catatonia is closely associated with mood disorders (Fink and Taylor 2003) and has been proposed to be an expression of severe anxiety—a motor response to fear which is akin to tonic immobility (i.e. the 'freeze' response) as observed in animals (Moskowitz 2004). Vulnerability to mood disorders and anxiety in people with ASDs may therefore contribute to the apparently high rates of catatonia in this population (Dhossche 2011; DeLong 2004).

The severity of catatonic symptoms in people with ASDs appears to vary considerably. Wing and Shah (2000a) describe a range of presentations from patients who develop slowed movements but remain mobile, to those who become totally immobile and dependent on others for all aspects of daily living. In many cases, severity also appears to fluctuate over time. Dhossche et al. (2006b) therefore propose that cases of autistic catatonia can be classified as mild, moderate or severe, based on the degree of associated impairment. They suggest that acute stupor (immobility lasting most of the day), and need for parenteral feeding are indicators of severe catatonia. In the most serious cases, where ability to maintain adequate nutrition is affected, catatonia may be life-threatening.

It is acknowledged that autistic catatonia is challenging to treat (Dhossche et al. 2006b) and symptoms may persist over many years. Published treatment guidelines propose that psychological approaches, high doses of lorazepam and bilateral ECT are the current treatments of choice (Dhossche et al. 2006b; Fink et al. 2006). It is suggested that these are used in a graded way, according to catatonic severity and response to previous treatments. ECT is reserved for the most severe cases or cases in which other approaches have proved ineffective. The psychological approach proposed involves reducing stress, encouraging participation in enjoyed activities, use of prompting and maintaining daily routine (Shah and Wing 2006). This approach can also be used in combination with other treatments.

To date, there has been no systematic review of treatment studies in this population. The current paper therefore aims to systematically review the available evidence, to determine what treatment approaches are used in patients with autistic catatonia and how effective these are in reducing catatonic symptoms.

Method

A systematic review was conducted, following recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Moher et al. 2009). Relevant studies were identified using online databases PsychInfo, MEDLINE and Scopus. Key search terms were autis* and catatoni*.[1] The search strategy was designed to identify papers where both these terms appeared in the title, abstract or keywords.

The papers identified in each database were combined and duplicates removed. Titles and abstracts were screened for relevance, then full texts checked for eligibility. Reference sections were manually searched for additional relevant papers. An overview of the search and screening process is displayed in Fig. 1.

[1] Where * indicates a truncated term.

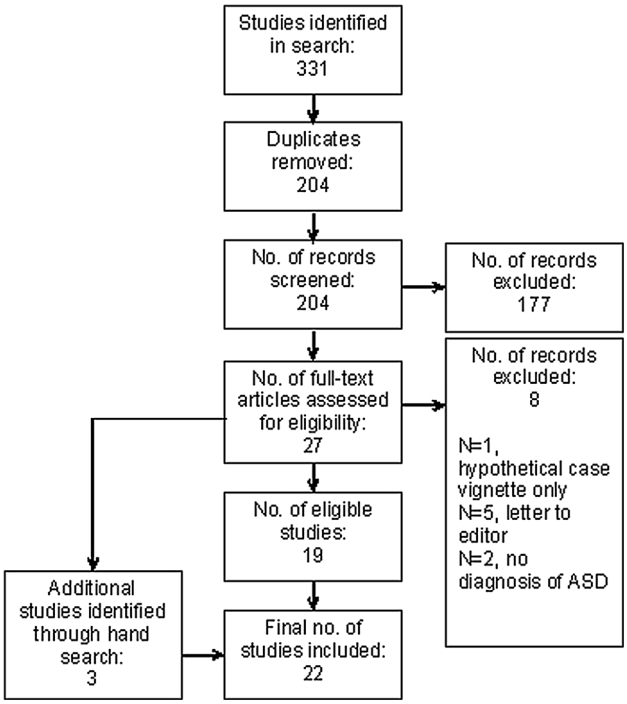

Fig. 1 Overview of search and screening process

Inclusion/Exclusion Criteria

Results were limited to papers published from 1980 onwards, due to changes in the definition of ASD at this time (APA American Psychiatric Association 1980). Only English-language papers were included. The review was limited to peer reviewed articles, and 'grey literature' (e.g. letters to the editor, conference presentations) was excluded.

For inclusion in the review, papers were required to describe an intervention aimed at treating catatonic symptoms, which was tested in at least one participant described as having both a diagnosis of ASD and catatonic symptoms. Single cases were permitted, as case studies constitute the majority of extant research in this population. Catatonic symptoms were broadly defined, and studies were included providing that the author labeled the symptoms as catatonic in nature. Pharmacological, psychological and other medical treatments were all included.

Data Quality

Data quality was rated using a checklist developed for the purpose of this review (*see Online Resource 2*), due to the lack of existing quality scales for evaluating single case designs. The checklist was based on existing quality rating checklists (Scottish Intercollegiate Guidelines Network 2011) and guidance on reporting of medical case studies (H. Cohen 2006; Green and Johnson 2006; McCarthy and Reilly 2000). Each paper was reviewed and given a score based on the number of criteria met, up to a maximum score of 19 (*see Online Resource 3*). For descriptive purposes, papers are referred to as low (scores 0–10), medium (11–15) or high (>16) quality based on the number of criteria met. Due to the limited number of relevant reports, no studies were excluded on the basis of the quality ratings. However, the quality ratings were used to guide interpretation of the results.

Results

The search and screening process identified 22 eligible articles. All studies identified were either single case studies, or small case series. A total of 28 individual cases were described across the articles identified. Several of these cases were described in more than one paper. The majority had been treated in the USA. Due to the breadth and variety of treatments considered and the lack of consistency of outcome measures utilized, a meta-synthesis of the findings was not appropriate. A narrative synthesis of the results is therefore presented below.

Electroconvulsive Therapy (ECT) Interventions (Table 1—see Online Resource 1)

Description of Cases

The review identified 11 relevant papers primarily describing ECT interventions, with a total of 12 cases reported. All papers were rated as low quality reports. All but one patient (Wachtel et al. 2008) were male, with ages ranging from 14 to 19 years. ASD diagnoses included Pervasive Developmental Disorder, Asperger's, high functioning autism and autism. Duration of catatonic symptoms ranged from a few months to around 6 years. Most cases were severe and in many cases, patients were physically unwell due to food refusal and subsequent malnutrition. The majority of cases presented with comorbid difficulties, including depression, anxiety disorder, OCD, delusions, psychosis, tics and Tourette syndrome. Several patients were also reported to present with suicidal ideation, self-injury and aggression. In the majority of cases, medical and neurological causes were excluded, typically through use of MRI, EEG and blood tests.

Intervention and Outcomes

Each patient received at least one course of ECT. The length of an initial course ranged from 7 to 29 sessions, typically at a frequency of 2–3 sessions per week. The majority of cases used bilateral electrode placement. Where reported, voltage,

pulse width and charge used varied widely between cases. The initial course of ECT was usually delivered during a period of inpatient treatment, with maintenance ECT then offered on an outpatient basis. Several patients were also receiving ongoing medication during ECT treatment, most commonly lorazepam. As this raises the seizure threshold, patients still receiving lorazepam were given flumazenil prior to each session of ECT.

Almost all cases reported a marked or dramatic improvement with ECT. In several cases, this was described as 'life-saving'. Improvement was usually defined using behavioural descriptions, with papers noting changes such as increased speech, reduced posturing, improved social interaction and increased activity. These gains were usually reported to occur after relatively few sessions, in some cases after a single session of ECT. Wachtel et al. (2008) reported specific changes in behavior frequency, including posturing (73 % reduction), initiating conversation (296.6 % increase) and responding to conversation (334.5 % increase). Similarly, Wachtel et al. (2010a) recorded a reduction in the combined frequency of self-injury, aggression and disruption from 135.22 incidents per hour to 1.55 per hour following ECT. One paper reported an 80 % reduction in catatonia, though it is unclear how this was quantified (Wachtel et al. 2010c).

A few papers report a more mixed response to ECT. In one case, unilateral ECT was followed by new posturing and the emergence of psychological pillow[2]. Bilateral ECT was more successful but the patient still presented with waxing and waning symptoms, and continuing mobility difficulties (Wachtel et al. 2010b). In another case, activities and social interaction were reported to have improved, but problems with walking and initiation remained (Dhossche et al. 2010).

Several cases reported rapid recurrence of symptoms when ECT was discontinued or suspended. In one case, catatonic symptoms re-emerged when ECT was suspended due to a detached retina resulting from self-injury, requiring a second acute course of ECT (Wachtel et al. 2008, 2010c). In another, ECT was suspended during treatment for malnutrition due to food refusal. The patient then lapsed into a 'catatonic stupor' with hypothermia and bradycardia (Wachtel et al. 2010b). In a third case, when ECT was stopped after an acute course of 11 sessions the patient relapsed within days, necessitating a second course of ECT (Wachtel et al. 2010c).

Maintenance and Follow-Up

Maintenance regimes described included various medications (aripiprazole, risperidone, sertraline, clonidine, antidepressants, lorazepam, olanzapine, lithium, duloxetine, lithium carbonate, rizuole, sulpiride), continued ECT or a combination of these treatments. Frequency of maintenance ECT ranged from 3 times per week to once every 2–3 weeks. Maintenance treatment appeared to be continued indefinitely in many cases, with one patient receiving at least 286 sessions of ECT (Wachtel et al. 2008). One patient was flying to another USA state to receive weekly maintenance ECT. In two further cases, maintenance ECT was recommended but not administered due to problems with accessing this in the patients' home states, due to legal inconsistencies across states in the USA regarding paediatric use of ECT.

Follow-up periods were not always clearly reported but appeared to range from 4 weeks to at least 14 months. Four cases indicated complete remission of catatonic symptoms, maintained with either medication or medication in combination with ECT. However, symptoms were noted to have increased when attempts to reduce the frequency of ECT were made. Seven cases described mixed outcomes, with residual or recurring symptoms following treatment and failure to return to full premorbid function. Attempts to taper ECT were often unsuccessful, with symptoms re-emerging as early as the second day after ECT (Wachtel et al. 2010c). One case (Fink et al. 2006) reported a complete return of catatonic symptoms 4 weeks after completing a course of ECT. The authors attributed this to the failure to discontinue ziprasidone during the course of treatment.

Side Effects

The majority of studies made no reference to any adverse effects of treatment. This is surprising, given the extensive literature that exists regarding reported side effects of ECT, e.g. reviewed in (Lima et al. 2013; Consoli et al. 2010; Read and Bentall 2010). Two studies reported no change in skills, cognition or functioning following ECT, based on clinician impressions and carer report. No study reported any formal measure of cognition or functioning. One case described no cognitive or functional decline 'since the acute course of ECT' but remained unclear from the paper whether the patient experienced decline *during* the acute course (Wachtel et al. 2010b, c). In one patient, ECT was described as causing 'mild delirium' (Wachtel et al. 2010a) and in another there was an increase in symptoms following an initial course of unilateral ECT (Wachtel et al. 2010b). There was one report of a prolonged seizure during the first ECT session, which was terminated with intravenous diazepam at 192 s (Zaw et al. 1999). No other adverse events or side effects were reported.

[2] A sign of catatonia; the patient holds his/her head a few centimetres above the bed whilst reclined, and is able to maintain this position for prolonged periods of time (Rajagopal 2007).

Summary of Findings

Despite assertions by several authors regarding the safety and efficacy of ECT in this population (Dhossche et al. 2010; Ghaziuddin et al. 2010; Wachtel et al. 2008; Fink et al. 2006), the evidence underlying these assertions is weak. The number of cases reported is small, and the quality of data is low, largely due to poor outcome measurement, incomplete description of treatments and failure to address confounding factors. What evidence is available suggests that there may be an initial response to ECT, usually resulting in partial resolution of catatonic symptoms. However, in almost all of the reported cases to date, this effect appears to be temporary. Maintenance ECT, often in combination with various medications, seems to be needed to sustain any benefit. Adverse effects of treatment are not adequately addressed, despite concerns about the possible side effects of ECT that are widely documented elsewhere, particularly in paediatric populations (Lima et al. 2013; Consoli et al. 2010a). As the literature consists entirely of case reports, there is a high likelihood that a significant publication bias exists. The cases that are reported are generally those where a dramatic initial response to treatment is noted. Reporting of outcomes is also poor, with most reports providing only clinician impressions of change, with few formal outcome measures.

Pharmacological Interventions (Table 2—see Online Resource 1)

Description of Cases

Seven relevant papers described primarily pharmacological interventions, with a total of 10 cases reported. All reports were rated as being of low quality, primarily due to poor outcome measurement and failure to address confounding factors. Patients ranged in age from 11 to 35 years and all but one case (Takaoka and Takata 2007) were male. ASD diagnoses included infantile autism, atypical autism and high functioning autism. Duration of catatonic symptoms ranged from a few weeks to at least 6 years. Reported comorbid diagnoses included: possible depression, possible bipolar disorder, psychotic disorders, Tourette syndrome, epilepsy and seizure disorder. In the majority of cases, medical and neurological causes had been excluded, typically using MRI, EEG and laboratory tests.

Intervention and Outcomes

Use of several classes of medications was reported, including benzodiazapines, typical and atypical antipsychotics, tricyclic antidepressants and SSRIs. Lorazepam was used in four cases (range 1–8 mg daily), either alone or in combination with clozapine (400 mg daily). Haloperidol was administered in 2 cases (range 2–14 mg daily), in one case alone and the other in combination with nortriptyline (75 mg daily). Nortriptyline (100 mg daily) was also used alone in one case. Other medications given were bromazepam (4 mg daily), fluvoxamine (500 mg) and unspecified 'antipsychotic medication'.

Clinician impressions suggested improvement in all cases, though in many cases with residual symptoms. Behavioural descriptions of improvement were also reported, for example increased speech, return to work/school. One study (Bozkurt and Mukaddes 2010) reported a reduction in Bush Francis Catatonia Rating Scale (BFCRS) score from 37 to 3. Another reported a change in score from 40 to 24 on the same measure, suggesting a large improvement but also significant residual symptoms (Schieveld 2006).

Maintenance and Follow-Up

In the majority of cases, medication was continued indefinitely or gradually tapered as symptoms improved. Doses were often adjusted flexibly in response to changes in symptom severity. In one case, further medications were added to the maintenance regime, specifically thioridazine and imipramine were added to haloperidol (Realmuto and August 1991). Length of follow up ranged from 2 weeks to 6 years. Where outcome beyond the acute treatment period was reported, four studies noted no reoccurrence of symptoms and three reported either fluctuating symptoms or further catatonic episodes. Increases in symptoms prompted changes in medication, with doses in some cases reaching very high levels (e.g. lorazepam 14 mg/day).

Side Effects

A small number of adverse events were reported across the studies, though these were not considered to be related to treatment. One patient (Realmuto and August 1991) was reported to have had a single seizure after 3 years of treatment with thioridazine. In another case (Ohta et al. 2006), epilepsy re-emerged following treatment with bromazepam after an absence of over 5 years. One patient presented with excessive laughter, bruxism[3] and binge eating 13 months after start of treatment, requiring further intervention (Realmuto and August 1991). No paper reported any side effects of treatment.

The interventions described raise concerns about the use of usually high doses, particularly lorazepam doses well above current recommended levels (British Medical Association and Royal Pharmaceutical Society of Great

[3] Excessive grinding of the teeth and/or clenching of the jaw.

Britain 2013). The use of polypharmacy is also implicated in several cases. Recent reviews suggest significant risks associated with this approach, including increased likelihood of adverse reactions, harmful drug-to-drug interactions and over- or under-dosing (Kukreja et al. 2013). The interventions described are sometimes in conflict with previously stated recommendations, particularly the advice that antipsychotic medications should be avoided due to the risks of exacerbating catatonic symptoms or precipitating neuroleptic malignant syndrome (Fink et al. 2006).

Summary of Findings

Overall the review identified few studies of pharmacological interventions, with a wide variety of medications and doses employed. This makes any synthesis of the evidence extremely difficult. The quality of all the studies reviewed was low and therefore outcomes should be interpreted cautiously. Several papers listed previous pharmacological interventions that were ineffective, suggesting a significant reporting bias for efficacious interventions. The description of failed medication trials in many of the ECT papers described above further supports this suggestion. Where medication was reported to be effective, continued use appeared to be needed to sustain any improvement. The exception was one case in which medication appeared to have been used only acutely (Bozkurt and Mukaddes 2010). This case was unusual in that the patient was significantly younger than other reported cases (11 years), with very recent onset of catatonic symptoms. In all other cases, continued medication appeared to be needed. Full resolution of symptoms appeared to be rare. In most cases, treatment was only partially effective, with continuing fluctuations in symptoms or periodic episodes of catatonia.

Behavioural and Sensory Inventions (Table 3—see Online Resource 1)

Description of Cases

The search identified five papers that described primarily behavioural, or sensory interventions, involving a total of six cases. All cases reported were of either medium (Hare and Malone 2004; Consoli et al. 2010b) or low quality (Cohen et al. 2009; Dhossche and Wing 2006; Shah and Wing 2006). Quality scores were generally low due to incomplete description of treatments offered, poor outcome measurement and failure to address confounding factors. All patients were male and aged 13–23 years, with diagnoses of ASD including Asperger's, disintegrative developmental disorder and autistic disorder. Duration of catatonic symptoms ranged from 12 months to 3 years. Two cases had comorbid diagnoses of psychotic disorder (Cohen et al. 2009) and one was described as having depressed mood (Consoli et al. 2010b). In some cases, medical explanations for the catatonic symptoms had been excluded through neuroimaging and laboratory tests. However, in other cases no medical workup had been conducted.

Behavioural Treatments

Three studies described behavioural interventions, delivered in community settings (Dhossche and Wing 2006; Hare and Malone 2004; Shah and Wing 2006). Shah and Wing (2006) described an intervention involving psychoeducation for carers, reducing stress, encouraging engagement in activities, use of prompting and maintaining structure/routine. They reported a case in which this approach was used, resulting in clinician-rated impressions of increased movement, faster responses and greater independence. The symptoms continued to improve over time, with provision of an appropriate specialist day service. Dhossche and Wing (2006) reported a case treated using this same treatment algorithm. The patient had progressive catatonic symptoms and had previously refused medication. After 9 months, the symptoms were judged to be improved, but with continuing mobility problems including slowness, freezing and poor coordination. The patient's parents were noted to be pursuing alternative treatments.

Hare and Malone (2004) described a more targeted behavioural intervention, designed to increase speed of stair use. 15 sessions of intervention, involving environmental changes and behavioural coaching were offered. The intervention resulted in significantly reduced time to ascend (modal time reduced from 12 to 1 s; $U = 31.0$, $p = 0.019$) and descend stairs (modal time reduced from 75 to 1 s $U = 0.5$, $p < 0.001$). Improvements generalised to other settings and were maintained at 18 months.

Packing Therapy

The remaining three cases were accounts of packing therapy, delivered in inpatient settings (Cohen et al. 2009; Consoli et al. 2010b). Packing therapy is described as a treatment designed to promote sensory integration, which involves wrapping patients in damp sheets while inviting them to express their feelings, sensations and fantasies (Cohen et al. 2009). Cohen et al. (2009) reported a case series in which two patients had diagnoses of ASDs. 18 sessions of packing therapy were given during an inpatient admission and in conjunction with various medications. A clinician judgment of efficacy was made in both cases. BFCRS scores also reduced from 30 to 15, and 29 to 9 respectively. The third account of packing therapy was

reported in Consoli et al. (2010b). The patient was given an unspecified number of sessions of packing during an inpatient admission, in conjunction with medication. This resulted in a decrease in BFCRS scores from 32 to 11, with catatonic symptoms described as reduced but still present. The authors reported that the improvement was not sustained despite continued lorazepam, with BFCRS scores rising to 29–32. At 6 months after treatment, a course of bilateral ECT (9 sessions) was given resulting in BFCRS score 15. Maintenance ECT was then prescribed.

Summary of Findings

Given the limited data available in this area, and the lack of high quality evidence, no clear conclusions can be drawn about the efficacy of behavioural and sensory interventions. Patients receiving packing therapy appeared to derive some short-term benefit, but the presence of various confounding interventions (medication, ward milieu etc.) precludes any clear conclusion as to the efficacy of this approach. Behavioural interventions seemed to provide some benefit, although symptoms resolved only partially in all cases. The number of cases described is also extremely small. The literature includes both specific, targeted interventions (Hare and Malone 2004) and more general supportive interventions (Shah and Wing 2006). These interventions include various components, and it remains unclear which are necessary to produce change. Further evaluation studies, including clear treatment protocols and objective measures of outcome, would be a valuable addition to the evidence base in this area.

Discussion

Summary of Findings

The findings of this review suggest that catatonic symptoms in people with ASD are treated using a range of interventions, including ECT, various medications and a range of behavioural and sensory approaches. However, the evidence as to the efficacy, or effectiveness, of these interventions is extremely limited. The majority of reviewed studies were single case designs, with fewer than 30 cases included in the final review. The quality of most reports was low. Interventions were frequently only partially described and outcome reporting relied heavily on clinician impressions, rather than objective measures of change. It also seems likely that there is a significant publication bias, with most published papers describing positive outcomes. The accounts of previous unsuccessful treatments described in many of the papers strongly support this possibility. In particular, several reports list unsuccessful medication trials before administration of either ECT, or an effective pharmacological intervention.

The evidence that is available suggests ECT and high dose lorazepam may have some acute effect on catatonic symptoms in ASD. However, in many cases response was only partial, with some residual symptoms, or fluctuations in symptoms over time. Long-term maintenance of any improvement seemed reliant on either maintenance ECT, or continued medication. Attempts to taper frequency of ECT or dosage of medication often appeared to result in increased symptoms.

Behavioural treatments seemed to have had some positive outcomes in relation to symptom reduction, although no case had complete resolution of symptoms. These treatments are comprised of several components and so it is unclear which elements are needed for change. It also seems likely that the utility of these treatments is limited to patients who are not severely medically compromised.

The effect of packing therapy in this population remains unclear, due to problems with the design of the reported cases; in all cases patients were receiving other treatments and were cared for in a ward setting. It is therefore unclear whether any improvement can be attributed to the packing therapy itself.

There is some indication in the papers reviewed that early intervention may be beneficial. Catatonia in general is believed to become harder to treat with chronicity; the current literature emphasizes the need for early, effective treatment (Dhossche et al. 2006b; Fink and Taylor 2003). It has also been speculated that catatonia-like features in people with ASD may render them more vulnerable to later catatonic deterioration, although the precise nature of this relationship is unclear (Wing and Shah 2006). It is notable that in the papers reviewed here, the cases with more positive outcomes often concerned younger patients with recent onset of catatonic symptoms, e.g. (Realmuto and August 1991; Bozkurt and Mukaddes 2010). Treatment of chronic cases appears more likely to be only partially successful.

This is the first systematic review of existing treatments for autistic catatonia, although previous papers have reported selective reviews of the literature. The review highlights the lack of strong evidence in this field. The evidence base consists entirely of case studies, small case series and clinical opinion. These methods of research are appropriate in a field where no treatment is well established, and case reports therefore contribute valuable new information (Green and Johnson 2006; McCarthy and Reilly 2000). However, the quality of study design and reporting in the papers reviewed was often low. The extent to which the evidence can be said to support the use of any intervention is therefore very limited. It does however provide directions for future research, particularly the need for controlled treatment trials.

Challenges for Future Research

There are various methodological challenges in conducting research with this population. The relative rarity of autistic catatonia, combined with low awareness among the public and professionals is one such challenge. Given this rarity, multi-centre study designs are likely needed in order to recruit sufficient numbers to conduct controlled trials. Patients may be very unwell and may deteriorate further if not successfully treated. The use of control treatments or waiting list conditions is therefore unlikely to be feasible or ethical. The use of clear research and treatment protocols will be important to ensure consistency and allow comparison across cases. Establishing a reliable and valid measure of autistic catatonia would improve characterization of this patient group, and provide a more objective measure of outcome.

A further consideration for future research is the presence of psychiatric comorbidities in many of the cases reported to date, and the wide range of symptom severity. This suggests that the intersection of ASD and catatonia may still represent a widely heterogeneous population of patients. It may be that the efficacy of treatment strategies varies significantly between subgroups within this population. Designing trials large enough to explore these possible differences in treatment response is a significant challenge.

There are also ethical and legal issues in relation to the current recommended treatments, particularly use of ECT and high doses of psychiatric medication. These concerns are heightened where these treatments are used in paediatric populations and for patients who may not be able to make decisions about their own treatment. Several of the ECT papers from the USA highlight the discrepancies in access to this treatment across states, and also the reluctance of many parents to consent to this intervention.

Side Effects

The lack of consideration of adverse effects and treatment side effects in the existing literature is surprising and should be addressed in future studies. ECT in particular has been linked to various adverse effects, although this evidence remains controversial. Recorded side effects in young people include headache, confusion, subjective memory loss and prolonged seizures (Rey and Walter 1997). It is suggested that most negative effects on memory and cognition resolve within 3–6 months (Abrams 2002; Wachtel et al. 2010c), but even short-term effects may be highly significant when regular maintenance ECT is given. Repeated administration of ECT over a lengthy period may also have cumulative effects, which are not well documented particularly in paediatric populations.

Conclusions

This review highlights the lack of high quality evidence available to guide treatment decisions in this population, and the need for further research. Dhossche et al. (2006b) emphasised that their treatment recommendations should be "viewed as best estimates pending future controlled studies". Since these guidelines were published, there have been few further studies and no controlled trials. The available evidence suggests that a wide variety of approaches are currently used to treat autistic catatonia. These include ECT, various pharmacological agents, behavioural and sensory interventions. There is some evidence that ECT and pharmacological interventions may have short-term benefits, with ongoing treatment needed to maintain this improvement. There is similarly some evidence that behavioural treatments may provide benefit, with fewer associated risks. Following all types of treatment, patients may continue to display catatonic symptoms and are unlikely to return to baseline levels of function. This may be particularly true where there has been a long duration of catatonic symptoms before effective treatment. There is some indication that early intervention may be more successful. It could be hypothesised that screening for catatonic features and providing early support might reduce later incidence of catatonic deterioration in people with ASDs. Prospective, long-term studies in paediatric populations could be used to examine this possibility.

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Conflict of interest The authors declare that they have no conflict of interest.

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