An investigation of circadian rest-activity levels in adolescents with autistic spectrum disorders, and a systematic review of treatments for autistic catatonia.

A thesis submitted to the University of Manchester for the Degree of Doctor of Clinical Psychology in the Faculty of Medical and Human Sciences

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Hannah DeJong

School of Psychological Sciences
Section for Clinical and Health Psychology
Contents list

List of tables 3
List of figures 3
List of appendices 3
Abstract 4
Declaration 5
Copyright statement 6
Acknowledgements 7

Paper 1: A systematic review of interventions used to treat catatonic symptoms in people with autistic spectrum disorders.
Abstract 8
Introduction 9
Method 10
Results 13
Discussion 23
References 27

Paper 2: Using actigraphy to examine activity and circadian rest-activity levels in young people with autistic spectrum disorders
Abstract 32
Introduction 33
Method 34
Results 39
Discussion 43
References 50

Paper 3: Critical appraisal
Overview 59
Literature review 60
Empirical paper 61
Dissemination 64
Conclusions 70
References 73
List of tables

Table 1. Demographic and clinical characteristics 45
Table 2. Circadian rhythm variables 45
Table 3. Activity counts by quartile and total daily activity 46
Table 4. Activity counts by quartile and total daily activity for weekdays and weekends 46

List of figures

Figure 1. Overview of search and screening process 14
Figure 2. Total daily activity for weekdays and weekends 47
Figure 3. Activity counts by quartile for weekdays and weekends 48

List of appendices

Appendix 1: Author guidelines for Journal of Autism and Developmental Disorders 77
Appendix 2: Literature review data tables 91
Appendix 3: Quality assessment tool 107
Appendix 4: Quality assessment ratings 110
Appendix 5: Participant information sheets 116
Appendix 6: Consent form 121
Appendix 7: Evidence of project approval 123
Appendix 8: Example participant feedback 125
Appendix 9: Report for schools 129
Appendix 10: Initial information for parents 132

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An investigation of circadian rest-activity levels in adolescents with autistic spectrum disorders, and a systematic review of treatments for autistic catatonia.

Hannah DeJong
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Abstract
The thesis presents a series of papers exploring catatonic symptoms and circadian rest-activity levels in autistic spectrum disorders (ASD). The thesis is presented in paper-based format and encompasses a literature review, an empirical paper and a critical appraisal.

Paper 1 is a systematic review of available treatments for autistic catatonia. Catatonic symptoms are thought to occur in around 8% of young people with ASD, and it has been suggested that biological timing abnormalities may play a key role in the development of these difficulties. Twenty two papers were included in the final review, detailing treatment of a total of 28 cases of autistic catatonia. Both adult and paediatric cases were included. The range of treatments described encompassed electroconvulsive therapy, various psychotropic medications, behavioural and sensory therapies. The review highlights limitations in the available literature and suggests avenues for future research.

Paper 2 explores circadian patterns in activity using actigraphy. A case series of 8 young people with an ASD diagnosis were recruited from specialist schools and asked to wear an actigraph for one week. Parents completed questionnaire measures of ASD traits and symptoms of autistic catatonia. Findings indicated a high degree of variability in circadian rest-activity cycles, both between participants and across the week. The study findings have implications for future research into circadian rest-activity levels in this population, as well as possible therapeutic applications.

The final paper in the thesis presents a critical appraisal of the research, including discussion of strengths and limitations of the work, theoretical and clinical implications and directions for future research. Some personal reflections on the process of conducting the research are also included.
Declaration

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Paper One

A systematic review of interventions used to treat catatonic symptoms in people with autistic spectrum disorders.

Prepared in accordance with author guidelines for submission to Journal of Autism and Developmental Disorders (Appendix 1).


Word count: 5,760
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
A systematic review of interventions used to treat catatonic symptoms in people with autistic spectrum disorders.

Autistic spectrum disorders (ASD) are a group of neurodevelopmental syndromes characterised by deficits in communication, social interaction and imagination (APA 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 3 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, Dhossche & Marcotte, 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. 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 Figure 1.

Inclusion/exclusion criteria

Results were limited to papers published from 1980 onwards, due to changes in the definition of ASD at this time (APA, 1980). Only English-language papers were included. The review was limited to peer reviewed articles; ‘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 (Appendix 3), 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

1 Where * indicates a truncated term
2011) and guidance on reporting of medical case studies (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 (Appendix 4). 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.

Figure 1. Overview of search and screening process
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 A – Appendix 2)*

**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 14-19 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 ‘lifesaving’. 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; Wachtel et al. 2010c). In another, ECT was suspended to allow 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

\(^2\) 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).
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. 2010a; 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 it remained unclear from the paper whether the patient experienced decline during the acute course (Wachtel et al. 2010b; Wachtel et al. 2010c). 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 seconds (Zaw et al. 1999). No other adverse events or side effects were reported.
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 B – Appendix 2)

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 11-35 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 1-8mg daily), either alone or in combination with clozapine (400mg daily). Haloperidol was administered in 2 cases (range 2-14mg daily), in one case alone and the other in combination with nortriptyline (75mg daily). Nortriptyline (100mg daily) was also used alone in one case. Other medications given were bromazepam (4mg daily), fluvoxamine (500mg) 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, 4 studies noted no reoccurrence of symptoms and 3 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 14mg/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.

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\(^3\) Excessive grinding of the teeth and/or clenching of the jaw.
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 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 (11yrs), 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 C– Appendix 2)*

**Description of cases**

The search identified 5 papers that described primarily behavioural, or sensory interventions, involving a total of 6 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 psycho-education 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 seconds; $U=31.0, p=0.019$) and descend stairs (modal time reduced from 75 to 1 seconds $U=0.5, p<0.001$). Improvements generalised to other settings and were maintained at 18 months.

**Packing therapy**

The remaining 3 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 ASD. 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 predominance of single case designs and expert opinion means that the overall level of evidence is low – these studies are considered to be level 4 or 5\(^4\) according to the Sackett criteria (Sackett et al. 2000). 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 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.

\(^4\) Where level 1a represents the highest level of evidence (randomized controlled trials) and level 5 represents the lowest level of evidence (expert opinion).
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), although limitations in follow up mean that the extent to which these outcomes are sustained is unclear. Treatment of chronic cases appears more likely to be only partially successful, and as many of the cases report gradual deterioration in symptoms over time, there appears to be a need to treat quickly and effectively. Chronicity of symptoms seems to be the key factor, but age may provide a useful proxy for chronicity, given the predictable onset of symptoms during adolescence. There may therefore be opportunities for targeted screening and early intervention within this age group.

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 highlighting the need for controlled treatment trials.

A limitation of the review is that data extraction and quality ratings were performed by a single reviewer, and may therefore be more prone to error or bias than if double rating had
been employed. The quality rating scale and ratings are however available as supplementary material (Appendices 3 and 4) to ensure transparency of this process.

**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.
References


Paper Two

Using actigraphy to examine activity and circadian rest-activity levels in young people with autistic spectrum disorders

Prepared in accordance with author guidelines for submission to Journal of Autism and Developmental Disorders (Appendix 1).

Word count: 5,759
Abstract

Circadian dysfunction may be implicated in the aetiology of autistic spectrum disorders (ASD), and may account for difficulties across a range of domains. One means of assessing circadian rest-activity levels is by using actigraphy. This method was utilised in a case series of 11-17 year olds with ASD, to characterise circadian rest-activity cycles. Findings indicated a high degree of individual variation in circadian patterns of activity and significant differences between weekends and weekdays. These results extend the understanding of circadian rest-activity cycles in ASD, and suggest a possible increased dependence on externally imposed routines. The study also demonstrates the feasibility of using actigraphy in this population. Theoretical and clinical implications of these findings are discussed.

Keywords: autistic spectrum disorders, circadian rhythm, actigraphy, autistic catatonia, physical activity
Using actigraphy to examine activity and circadian rest-activity levels in young people with autistic spectrum disorders

Autistic spectrum disorders (ASD) are a class of neurodevelopmental conditions defined by impairments in communication and social interaction, along with patterns of restricted, repetitive behaviour (American Psychiatric Association 2013). It is increasingly recognised that ASD is also associated with a range of other difficulties, including abnormalities in sensory processing (Kern et al. 2006), cognitive processing styles (Charman et al. 2011) and impaired motor skills (Gowen and Hamilton 2013). There is therefore considerable interest in developing accounts of ASD that link and integrate these apparently disparate domains. Several such accounts emphasise the possible role of abnormalities in biological rhythms and timing mechanisms.

Biological rhythms

Biological rhythms occur at varying levels, ranging from milliseconds to seasonal effects across the course of a year. However, the most commonly studied biological rhythms are circadian rhythms, that is cycles occurring across approximately 24-hour periods. Expressions of these rhythms include cyclical changes in hormone production, body temperature and the sleep-wake cycle.

Circadian functions are centralised in the suprachiasmatic nucleus (SCN) but also encoded by ‘circadian oscillators’ in other areas of the brain and throughout the body. The SCN appears to play a role in the co-ordination and synchronization of these peripheral oscillators (Lamont et al. 2007). Melatonin is a key hormonal regulator of this system, and is understood to be involved in the signalling of temporal cues from the SCN. It therefore helps to drive daily rhythms and to synchronize peripheral oscillators with the central circadian clock (Pevet and Challet 2011).

Although encoded by internal biological mechanisms, circadian functions are also subject to influence by external environmental cues. These environmental cues are known as ‘zeitgeibers’ or ‘time givers’. Light is probably the most powerful external circadian synchronizer, and can be used to generate phase shifts in circadian rhythms. However, other
variables such as mealtimes, exercise and social interactions are also thought to be important regulators of the circadian cycle (Vitaterna et al. 2001).

**Biological rhythms and ASD**

Several theorists have proposed a role for abnormalities in biological timing mechanisms in ASD, often citing the very poor intuitive sense of time reported by many people with ASD. Boucher (2001) proposed that timing deficits may underlie many symptoms of autism, particularly deficits in language and memory. Within a hierarchical system of biological clocks with varying periodicities, she suggests that people with ASD may either have impairments at different levels or deficits in how these levels are integrated. This would have various effects on the ability to link and integrate information across time, with subsequent impact on language and memory performance.

Brock et al. (2002) suggest that difficulties with ‘temporal binding’ (i.e. reduced synchronization of neural activity) could contribute to the cognitive and social features of autism, by causing difficulties with integrating information across local neural networks. They hypothesise that a reduction in temporal binding could account for many features of autism, including visuo-perceptual abnormalities, poor use of context in language processing, executive dysfunction and some deficits in socialisation and communication. Similarly, Amos (2013) proposes that poor temporal synchrony in ASD would lead to an uncoupling of related stimuli, which could account for difficulties in motor control, multi-modal sensory processing and social interaction.

Developmental researchers are increasingly emphasising the role of synchrony and timing in the parent-infant relationship, and its role in supporting development of various skills, including social interaction, communication and emotional regulation (Feldman 2007a, 2007b). There is now evidence that physiological oscillators provide an important foundation for these social rhythms, with robust biological rhythms predicting later relational synchrony (Feldman 2006). If children with ASD have impaired biological rhythms, this work has implications for understanding the social and communicative features of ASD, and the developmental course of these difficulties.
Evidence from various sources suggests that timing mechanisms are indeed affected in ASD. Changes in circadian rhythms, including a high prevalence of circadian sleep disorders and more variable circadian sleep-activity cycles, have been reported in both children and adults with ASD (Glickman 2010; Hare et al. 2006a, 2006b; Wiggs and Stores 2004). Studies have begun to show deficits in both temporal perception (Allman 2011; Allman et al. 2011) and temporal memory (Poirier et al. 2011), suggesting problems with the encoding of temporal information.

Evidence from endocrine research also suggests possible circadian abnormalities in ASD. Several studies have found reductions in melatonin synthesis and availability in ASD populations (Melke et al. 2008; Nir et al. 1995; Rossignol and Frye 2011). There is evidence that circadian fluctuations in cortisol are also altered in ASD (Corbett et al. 2006; Corbett et al. 2008; Nir et al. 1995). Recent studies have identified associations between endocrine changes and specific symptoms of ASD. For example, reduced nocturnal melatonin secretion appears to be associated with repetitive behaviour and social communication impairments (Tordjman et al. 2013). A small number of studies have reported improvements in the behavioural symptoms of autism with melatonin treatment, including improvements in communication, social withdrawal and stereotyped behaviours (reviewed in Tordjman et al. 2013).

Genetic studies similarly suggest involvement of timing mechanisms in ASD. Although ASD is likely to be polygenic, several models have proposed a role for ‘clock genes’ in the aetiology of ASD. A small number of studies have now identified ‘clock gene’ abnormalities in both people with ASD and their families (Bourgeron 2007; Nicholas et al. 2007; Wimpory et al. 2002).

**Actigraphy**

One means of investigating circadian rhythms is using actigraphy, a method of measuring activity over time, using an accelerometer worn on the body. Actigraphy has most commonly been used to examine sleep, with sleep inferred from periods of inactivity. However, the data collected can also be used to examine rest-activity patterns across the day, in order to characterise circadian cycles.
The use of actigraphy as a research method has increased in recent years, following a series of influential position papers from the American Academy of Sleep Medicine (Littner et al. 2003; Morgenthaler et al. 2007; Thorpy et al. 1995). Actigraphy is unobtrusive and can be used in a participant’s natural setting. This is particularly important when studying young people with autism, who may find deviations from their usual environment and routine difficult to tolerate. Reviews indicate that actigraphy has good validity and reliability, particularly when aggregated over several days of recording (Tryon 2004; Wood et al. 2008; Sadeh 2011).

*Initial study design*

The study was initially designed to explore links between autistic catatonia and changes in circadian rest-activity levels. It has been proposed that autistic catatonia may be related to alterations in biological timing mechanisms, as these are thought to be involved in the ability to link together movements across time in order to produce complex actions (Hare and Malone 2004). It has also been noted that autistic catatonia is sometimes associated with day/night reversal (Wing and Shah 2000), which may indicate abnormalities in circadian function. The study was therefore designed to examine these hypothesised links, using actigraphy as a measure of circadian rest-activity levels.

However, recruiting sufficient numbers of participants with clinically significant symptoms of autistic catatonia proved to be extremely difficult. It became apparent that identifying a large enough experimental group would not be possible. A decision was therefore made to broaden the study criteria and include any young person with an ASD diagnosis, regardless of autistic catatonia symptoms. There is increasing recognition that autistic catatonia may more accurately be thought of as occurring along a spectrum of severity (Wing and Shah 2006; Breen 2014). It was therefore anticipated that an exploration of associations between circadian rhythms and autistic catatonia would be possible using correlational analyses.

When the final data was examined, it emerged that there was relatively little variation in catatonic symptoms within the participant group. No participants met the proposed clinical cut-off of 3 or more symptoms and core scores ranged only from 0-7, out of a maximum possible score of 24 (Breen 2014). Due to this lack of variation, meaningful analysis of relationships between catatonic symptoms and circadian rhythm variables
would not have been possible. A decision was therefore made to shift the aims of the analysis, and to focus on characterising circadian rest-activity levels in ASD more generally.

**Aims**

The aim of the study then was to use actigraphy to examine circadian patterns in the rest-activity cycles of young people with ASD. Actigraphy has previously been used in a small number of studies of ASD (e.g. Wiggs and Stores 2004; Hare et al. 2006a, 2006b; Baker et al. 2013; Bandini et al. 2013; Memari et al. 2013). However, most previous work has primarily focused on sleep or overall physical activity, rather than circadian rest-activity cycles. There are no previous actigraphic studies of circadian rest-activity levels in paediatric or adolescent samples. The current study therefore extends existing work on circadian function in ASD by applying actigraphy in a novel sample.

Due to the paucity of previous research in this area, the study was primarily exploratory. However, it was hypothesised that young people with ASD may present with less robust rest-activity cycles, resulting in reduced stability of these patterns. It was also predicted that there would be a high degree of heterogeneity, as previous findings have suggested unusually variable circadian function in this population (Glickman 2010). The results are therefore presented as a case series, with analysis emphasising individual patterns of circadian rest-activity levels and comparisons between participants.
Method

Participants

8 young people identified as having a diagnosis of ASD participated in the study. All participants were in full time education and aged 11-17 years. Participants were identified and recruited through specialist high schools in the North of England. The final sample included students from 4 different schools – two were schools specifically for pupils with ASD or social communication difficulties; two were schools for pupils with mild to moderate learning disabilities. The researcher initially approached each school and asked them to distribute a letter about the study to potential participants (see Appendix 10). Parents of approximately 120 pupils were sent this letter. Parents who agreed to be contacted were then given further details about the study, including the participant information sheets.

Procedure

The researcher provided each parent/carer with information about the study, including written participant information sheets (full version and easier-read version for young people; Appendix 5). Young people and parents/carers were given an opportunity to ask questions about the study, and time to consider their participation as needed. Parents/carers of young people who agreed to participate were asked to provide written consent. The young people participating were asked to give either verbal or written assent as appropriate. Ethical approval was granted by the local University Research Ethics Committee (Appendix 7).

Research appointments with parents took place in a quiet room at the participant’s school (N=2) or were conducted over the telephone (N=6), with questionnaires sent by post. As all data was collected using either written questionnaires or actigraphy, the mix of telephone and face-to-face appointments is not expected to have any significant impact. These conversations were simply used to provide information about the study. General demographic and clinical information was collected and parents completed the questionnaire measures described below (see Measures section).
Participants were asked to wear an actigraph (Phillips Respironics Actiwatch 2) continuously for 1 week, on their non-dominant wrist. This is consistent with recommendations that at least 3 consecutive 24-hour periods are examined when collecting actigraphic data (Littner et al. 2003), and allowed for comparison between weekdays and weekends. These actigraphs are waterproof and so can be worn during bathing, swimming etc. Activity data was sampled across 15 second epochs. In conjunction with wearing the actigraph, participants were asked to complete a diary, with support from parents as needed. The diary was used to record bed times, waking times, any unusual events (e.g. feeling unwell, disturbed sleep) and any times the actigraph was removed. This was to allow exclusion of any non-typical periods of data collection from the analysis. To ensure that the data was comparable across subjects, and represented a ‘typical week’, all data was collected during school term time.

After 1 week, the researcher collected the actigraph, diary and any questionnaires not completed during the initial session. Any queries about how to complete questionnaires were clarified, and these were checked for missing data. Each young person who participated was given a copy of their actigraph data (Appendix 8). Young people and parents were also given the opportunity to discuss their data with the researcher.

**Measures**

*Autism Quotient Questionnaire (AQ) Adolescent Version (Baron-Cohen et al. 2006)*

The AQ is a non-diagnostic screening measure that can be used to rapidly quantify autistic traits. The adolescent version contains 50 items and is rated by a parent/carer. This measure has good face validity and construct validity, as well as high test-retest reliability. A proposed clinical cut-off of 30 has been found to have good sensitivity and specificity (Baron-Cohen et al. 2006).

The measure was developed for young people aged 10-15 years. However, it retains the items and structure of the adult version (Baron-Cohen et al. 2001) and differs only in that it is parent/carer rated, rather than self-rated. The adolescent version was therefore used for all participants in the current study, in order to maximise consistency across the sample.

*Autistic Catatonia Questionnaire (ACQ) (Breen 2014)*
The ACQ is a third-party rated measure of catatonia-like symptoms developed for use in people with ASDs. Evidence suggests that catatonia-like symptoms in people with ASD are common and may be normally distributed (Breen 2014). The ACQ was therefore included to screen for catatonia-like symptoms as these are likely to affect activity levels and are hypothesised to be associated with abnormalities in biological timing mechanisms (Hare and Malone 2004).

The first 6 items of the ACQ were used to screen for catatonic symptoms. These items correspond to the proposed core features of autistic catatonia (Wing and Shah 2000; Hare and Malone 2004). Each item is rated in terms of presence, frequency and severity. The six ‘presence’ items can be summed to calculate a ‘Core Autistic Catatonia Score’, which has validity as a clinical screening tool (Breen 2014). Each item is scored from 0 to 4, giving a total possible ‘Core’ score of 24. Items can also be classified as present (item score ≥ 3) or absent (item score ≤ 2), with the presence of 3 or more symptoms considered to be indicative of possible autistic catatonia.

**Actigraphic analysis**

Actigraph data were downloaded and analysed using *Actiwatch Activity and Sleep Analysis 7* (Cambridge Neurotechnology, UK). An initial visual inspection of the data was conducted. Incomplete quartiles from the start and end of the collection period were excluded from analysis. Shorter periods of missing data (< 60mins) were imputed using average activity counts for the hour preceding and following the missing period. Periods of missing data were identified through visual inspection of the actigraph and use of participant diaries. These periods were typically accounted for by times participants had removed the actiwatch during showering or swimming. No participant had more than one missing segment in any 24 hour period.

Non-parametric circadian rhythm analysis was used, as this method does not require any assumptions about the waveform of the data (Van Someren et al. 1999). The following non-parametric indices were extracted:

i) **L5 and M10 onset**: The average time of onset of the least active 5-hour period [L5] and the most active 10-hour period [M10] across a circadian cycle. This
provides an indication of the extent to which an individual’s circadian cycle is coordinated with a typical 24-hour cycle.

ii) **Relative amplitude (RA):** Derived from the normalised difference in activity between the L5 and M10 periods. It indicates the degree of variation in activity between the most active and least active phases within a 24-hour cycle. Possible values range from 0-1, with higher values representing greater divergence between the most and least active phases.

iii) **Intradaily variability (IV):** A measure of fragmentation in an individual’s patterns of activity over a 24 hour period. It is based on the frequency and extent of transitions between periods of rest and activity. Scores range from 0-2 with higher values indicating a more fragmented pattern.

iv) **Interdaily stability (IS):** A measure of the invariability in rhythms of activity from day to day. It provides an indication of the strength of coupling between the circadian rhythm and supposedly stable zeitgebers (e.g. light). Possible values range from 0-1, with higher values indicating greater stability.

v) **Periodicity:** The length of time taken for completion of one ‘best fit’ circadian cycle.

In addition, overall levels of activity were extracted for each 24-hour period and for each quadrant of a 24-hour period (00:00-06:00, 06:00-12:00, 12:00-18:00, 18:00-00:00). Activity analyses, L5 and M10 variables were also calculated separately for weekdays and weekends.

**Statistical analysis**

SPSS version 20 was utilised for all additional statistical analyses. Means and standard deviations were calculated for age, ACQ and AQ scores. Actigraphy variables were examined in tabular and graphical form, with counts for weekdays and weekends explored separately as outlined above.
Results

Demographic and clinical characteristics (Table 1)

8 young people participated in the study. Participants were aged 11 to 17 years (M=13.6 years, SD=2.2 years). All participants were male. ASD diagnosis had typically been made by a psychiatrist or child psychologist, using a specialised measure such as the Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 2000) or Diagnostic Interview for Social and Communication Disorders (DISCO) (Wing et al. 2002). AQ scores were generally consistent with these diagnoses – all but one participant (G) scored above the proposed screening threshold of 30 (Baron-Cohen et al. 2006). Mean AQ score was 37 (SD=5.40).

Parents of two participants (C and F) reported additional diagnoses and concomitant medication use. Participants presented with between 0 and 2 of the six symptoms measured by the ACQ, with Core Scores ranging from 0 to 7 (M=2.75, SD=2.71). No participant scored above the proposed clinical cut-off of ≥3 symptoms present. Due to the narrow range of ACQ scores in this sample, it was not possible to conduct any further analysis of relationships between catatonic symptoms and rest-activity patterns. The remaining analysis therefore focuses more broadly on circadian rest-activity cycles in adolescents with ASD.

Actigraphy

Circadian rhythm variables (Table 2)

Periodicity appeared to be within normal limits for all participants, with values ranging from 23:51 to 24:03. Similarly, RA, IV and IS were broadly consistent with values from previous studies, although the lack of an appropriate control group makes further analysis of these variables difficult.

On weekdays, L5 and M10 onsets were fairly typical for most participants, with the exception of Participant E who had a rather delayed L5 onset. At weekends, L5 and M10 onsets were often slightly later. This effect was particularly strong for participants E and G, who had notably late L5 onset at weekends (04:00). Participant E also had a significantly

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5 Parents of a further 7 young people consented to their participation, but these young people refused to wear the actigraph and therefore no data were collected.
delayed M10 onset (14:00). These patterns suggest a possible phase delay, which is more pronounced at weekends.

In contrast, one participant (H) presented with earlier L5 and M10 onset at weekends. In combination with early waking times (median: 05:30), this suggests a possible phase advance for this participant.

Activity counts

There was a high degree of individual variation in total activity counts, with the most active participant (H) generating a daily activity count almost 3 times that of the least active participant (C) (Table 3).

For most participants, patterns of activity over 24 hour periods were broadly similar. That is, activity in the 00:00-06:00 quartile was minimal with activity levels then rising through the morning and afternoon (06:00-18:00), before falling in the evening (18:00-00:00) (Table 3). Two exceptions to this pattern were participants E and H who were unusually active during the 00:00-06:00 quartile. Inspection of the actogram and diaries suggested that this was for different reasons in each case – participant E due to late sleep times and participant H due to very early waking times. Participant F was also unusual in that activity peaked in the morning (06:00-12:00) and then fell across the remaining quartiles.

Overall activity levels were lower at weekends for most participants (A, B, C, E, G). Two participants (D and F) were similarly active across weekend and weekdays. One participant (H) was substantially more active at weekends (Table 4; Figure 2).

Patterns of activity across the day differed at weekends for all participants except Participant D (Figure 3). Participants A, B, C and G had reduced levels of daytime activity at weekends, an effect that was most pronounced during the morning quartile (6:00-12:00). In contrast, Participant H had increased activity during the daytime compared to weekdays, and this was most apparent in the morning (06:00-12:00). Participant F continued to display a morning peak in activity at weekends, which was even stronger than during the week. Participant E presented with the most unusual pattern of weekend activity, with an apparent shift in phase. The lowest activity count was in the 06:00-12:00 quartile, with activity then
rising across the day and remaining fairly high into the 00:00-06:00 quartile. This suggests a possible circadian phase delay, consistent with this participant’s late L5 and M10 onsets at the weekend.

Table 1. Demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Participant</th>
<th>Age (yrs:mths)</th>
<th>Other diagnoses</th>
<th>Medication</th>
<th>AQ score</th>
<th>ACQ core score</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>12:02</td>
<td></td>
<td></td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>12:00</td>
<td></td>
<td></td>
<td>38</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>15:00</td>
<td>Epilepsy</td>
<td>Carbamazepine Lamotrigine</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td>D</td>
<td>12:02</td>
<td></td>
<td></td>
<td>34</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>12:06</td>
<td></td>
<td></td>
<td>38</td>
<td>3</td>
</tr>
<tr>
<td>F</td>
<td>16:00</td>
<td>ADHD OCD Dyspraxia</td>
<td>Methylphenidate Atomoxetine Sertraline Risperidone</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>G</td>
<td>17:04</td>
<td></td>
<td></td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>H</td>
<td>11:06</td>
<td></td>
<td></td>
<td>41</td>
<td>6</td>
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</table>

Table 2. Circadian rhythm variables

<table>
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<tr>
<th>Participant</th>
<th>Start date for recording</th>
<th>L5 weekdays</th>
<th>L5 weekends</th>
<th>M10 weekdays</th>
<th>M10 weekends</th>
<th>RA</th>
<th>IV</th>
<th>IS</th>
<th>Periodicity</th>
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<td>22:00</td>
<td>09:00</td>
<td>11:00</td>
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<td>.646</td>
<td>.722</td>
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</tr>
<tr>
<td>B</td>
<td>17/01/14</td>
<td>23:00</td>
<td>02:00</td>
<td>07:00</td>
<td>11:00</td>
<td>.934</td>
<td>.732</td>
<td>.599</td>
<td>24:01</td>
</tr>
<tr>
<td>C</td>
<td>07/03/14</td>
<td>00:00</td>
<td>01:00</td>
<td>08:00</td>
<td>11:00</td>
<td>.949</td>
<td>.617</td>
<td>.707</td>
<td>24:03</td>
</tr>
<tr>
<td>D</td>
<td>25/04/14</td>
<td>00:00</td>
<td>01:00</td>
<td>09:00</td>
<td>08:00</td>
<td>.984</td>
<td>.685</td>
<td>.723</td>
<td>23:59</td>
</tr>
<tr>
<td>E</td>
<td>25/04/14</td>
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<td>04:00</td>
<td>10:00</td>
<td>14:00</td>
<td>.827</td>
<td>.693</td>
<td>.614</td>
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</tr>
<tr>
<td>F</td>
<td>16/05/14</td>
<td>00:00</td>
<td>01:00</td>
<td>07:00</td>
<td>08:00</td>
<td>.884</td>
<td>.793</td>
<td>.673</td>
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</tr>
<tr>
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<td>10:00</td>
<td>.905</td>
<td>.596</td>
<td>.702</td>
<td>24:01</td>
</tr>
<tr>
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<td>21:00</td>
<td>11:00</td>
<td>10:00</td>
<td>.978</td>
<td>.687</td>
<td>.749</td>
<td>23:59</td>
</tr>
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Table 3. Average activity counts by quartile and total daily activity

<table>
<thead>
<tr>
<th>Participant</th>
<th>00:00-06:00</th>
<th>06:00-12:00</th>
<th>12:00-18:00</th>
<th>18:00-00:00</th>
<th>Total daily activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5.39</td>
<td>82.09</td>
<td>118.74</td>
<td>49.71</td>
<td>255.92</td>
</tr>
<tr>
<td>B</td>
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<td>59.15</td>
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<td>45.59</td>
<td>185.65</td>
</tr>
<tr>
<td>C</td>
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<td>71.60</td>
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</tr>
<tr>
<td>D</td>
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<td>51.29</td>
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</tr>
<tr>
<td>E</td>
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<td>63.26</td>
<td>134.38</td>
<td>107.63</td>
<td>332.76</td>
</tr>
<tr>
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<td>77.49</td>
<td>58.25</td>
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</tr>
<tr>
<td>G</td>
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<td>76.34</td>
<td>63.84</td>
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</tr>
<tr>
<td>H</td>
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<td>152.73</td>
<td>186.15</td>
<td>100.20</td>
<td>458.05</td>
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</table>

Table 4. Activity counts by quartile and total daily activity for weekdays and weekends

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<th>06:00-12:00</th>
<th>12:00-18:00</th>
<th>18:00-00:00</th>
<th>Total daily activity</th>
</tr>
</thead>
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<td>W/E</td>
<td>W</td>
<td>W/E</td>
<td>W</td>
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</tr>
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</tr>
<tr>
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<td>11.40</td>
<td>59.57</td>
<td>36.26</td>
<td>78.79</td>
</tr>
<tr>
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<td>19.53</td>
<td>17.58</td>
<td>135.60</td>
<td>186.99</td>
<td>178.81</td>
</tr>
</tbody>
</table>
Figure 2. Total daily activity for weekdays and weekends
Figure 3. Activity counts by quartile for weekdays and weekends.
Figure 3 Activity counts by quartile for weekdays and weekends (continued)
Discussion

This study explores circadian patterns of activity in a group of young people with ASD, using actigraphy. Actigraphy has not previously been used to assess circadian rest-activity levels and temporal patterns of activity in adolescents with ASD. This work therefore extends the use of this method and provides further insight into circadian functioning in ASD. The use of a case series design allows for exploration of individual differences within this population, which may be masked when analyses focus primarily on averaged group values.

The findings indicate that summary circadian variables (IS, IV, RA and periodicity) are broadly within normal limits. However, due to the absence of a control group, it is not possible to exclude subtle changes in these variables. Given how robust circadian rhythms are in the normal population, it is possible that even small changes may be significant. For most participants, L5 and M10 onset were within a typical range during the week, with a slight delay at weekends. However, for two participants weekend L5 onsets were unusually late. One of these participants also had an unusually delayed M10 onset at weekends.

Overall activity varied widely between participants, with the most active recording a daily activity count nearly 3 times that of the least active. For the majority of participants, daily activity was lower at the weekend. However in one case, weekend activity was substantially higher. Weekend reductions in activity could reflect a reliance on structure and routine to prompt activity, resulting in reduced activity outside of the school setting. Alternatively, it may indicate a preference for sedentary activities, resulting in lower activity at times when young people are free to choose their own activities. Similarly, for the participant who was more active at weekends, this could reflect a preference for very active pursuits or could instead suggest that the school routine has a regulatory function for this participant.

For most participants, levels of activity across the day followed a consistent pattern, comprising low activity between 00:00-06:00 which rose throughout the day before falling again in the evening quartile (18:00-12:00). This pattern appears to be consistent with societal norms and suggests preserved entrainment to environmental zeitgebers. However, two participants had unusually high activity counts during the 00:00-06:00 period – one due to late sleep times and the other due to early waking times. Another participant had an unusual pattern of activity, with activity levels peaking in the morning quartile (06:00-12:00) before falling across the rest of the day.
Patterns were broadly similar at weekends for most participants, though often with somewhat reduced activity levels, particularly in the morning. One participant had increased daytime activity at weekends. For the participant with a morning peak in activity, this peak was further enhanced at weekends. Another participant displayed a highly unusual cycle of activity at weekends, characterised by a shifted pattern that indicates a possible phase delay. The exaggeration in this pattern at weekends suggests that the delay may be masked during the week by externally imposed routines (e.g. fixed bed times and waking times).

Overall, the findings suggest a high degree of variation in circadian patterns of activity, with variation occurring both between days of the week and across participants. This may reflect specific variability within the ASD population. Previous endocrine studies have suggested an absence or blunting of the circadian system in some people with ASD (reviewed in Tordjman et al. 2013), which might be predicted to create variability and increase dependence on external cues to maintain daily rhythms. The significant changes in weekend activity, compared to weekday activity, found for some participants could reflect a high degree of reliance on environmental cues (e.g. set waking times, school routines) to maintain a stable circadian rhythm. The results are also likely to underestimate this effect, as family routines will similarly provide a degree of temporal stability at weekends.

However, variability in this sample could be at least partially attributable to age effects. It is well established that significant alterations in circadian function occur during adolescence. In particular, changes to the homeostatic and circadian systems during adolescence appear to result in later sleep onset times and increased prevalence of delayed sleep-phase syndromes (Crowley et al. 2007; Hagenauer et al. 2009). Conflict between these biological changes in adolescence and social variables, such as early school start times, can result in a phenomena known as ‘social jetlag’. This term describes a mismatch between biological and social time that tends to result in a build up of ‘sleep debt’ during the working week, which is then compensated for by longer sleep times at weekends (e.g. Wittmann et al. 2006). This sleep-activity pattern appears to be common in adolescent samples. It is therefore possible that much of the variability found in the current study is attributable to age effects and the impact of social demands, particularly school start times. Indeed, one study has demonstrated similar delays in sleep and wake times at weekends for high-functioning adolescents with ASD and typically developing controls (Baker et al. 2013). Further work in this area utilising appropriate control groups would help to investigate whether ASD has effects on rest-activity patterns, independent of known developmental effects.
Limitations

Interpretation of the findings is limited by the small sample size and lack of a control sample of typically developing adolescents. The sample is rather heterogeneous, particularly with regard to additional diagnoses and medication use. IQ and pubertal status also varied across the participant group. However, as no data was collected on these factors, it was not possible to explore their potential impact on the rest-activity data.

Due to challenges encountered during recruitment, data was collected across a broad time period (December – May). This potentially introduces further variability into the data, due to seasonal changes in circadian cycles. No data was collected within the 3 weeks following start of British Summer Time, in order to minimise potential disruption to rest-activity cycles resulting from this change.

Participants were self-selecting and several participants who initially expressed an interest in participating in the study were unable to tolerate wearing the actigraph. It is therefore unclear how representative this group are. Discussions with school staff involved in recruitment suggested that sensory sensitivities were a key reason for young people electing not to take part. Intellectual disability and communication skills also seemed to be a factor, in that participants who were more able to understand the purpose of the actigraph appeared to be more likely to tolerate wearing it.

Challenges encountered and changes to the study design

Recruiting participants who presented with symptoms of autistic catatonia, as was originally proposed, proved to be a significant challenge. Lack of recognition of the symptoms by school staff and parents contributed significantly to these difficulties. In many cases, staff and parents were unfamiliar with the term catatonia, and struggled to differentiate between this and other movement difficulties occurring in ASD, e.g. dyspraxia, repetitive/stereotyped movements. Given the lack of recognition of catatonia, it was also difficult to engage parents and schools with research in this area. In a small number of cases, schools identified pupils who they felt would be suitable but parents refused to participate in the research, typically citing lack of time or other pressures. This may reflect presence of additional demands for families whose children experience catatonic symptoms.
Directions for future research

For participants who opted into the study, compliance with the actigraphy protocol was extremely high. All 8 participants continued wearing the actigraph for the full week, with few periods of missing data. This suggests that actigraphy may be a feasible research method within this population, and can be used in a way that is acceptable to many young people with ASD.

Replication of this work with a larger sample and inclusion of appropriate control groups would extend the current findings. Combining actigraphy with other measures (e.g. melatonin secretion, core body temperature) would provide useful information about the relationship between rest-activity cycles and endogenous circadian factors.

Further research could usefully explore the impact of external cues on maintaining stable circadian rhythms, either through direct manipulation of these cues or by examining naturally occurring changes in routine (e.g. school holidays). It would also be informative to explore whether circadian rhythms remain consistent over longer periods of time. If circadian functions are indeed less robust in young people with ASD, it might be predicted that this group would show a greater degree of fluctuation over time than matched controls.

The results of the current study also highlight the importance of considering variability, both between participants and across days of the week, in the design and analysis of future studies.

Clinical applications

If people with ASD are indeed more reliant on external cues to maintain stable rhythms, this has significant implications for the design of educational and residential services for people with ASD. Tordjman and colleagues (2013) suggest a role for chronotherapeutic strategies in ASD, including environmental variables such as light, set meal times and sleep times, as well as therapeutic use of melatonin. An improved understanding of circadian functions in ASD is likely to aid the ongoing development of such approaches.
Due to the heterogeneity found in the current study, as well as previous research, it seems likely that a highly individualised approach is needed. Actigraphy may therefore provide a useful clinical tool for assessing patterns of rest-activity and identifying therapeutic targets.

Given the proposed role of circadian function in the aetiology of various symptoms of ASD, therapeutic interventions that support stable daily rhythms have the potential to confer a wide range of benefits.

Conclusions

As outlined above, it is believed that circadian abnormalities may play an important role in the aetiology of ASD. Developing an understanding of circadian function in ASD may therefore be key to understanding these conditions and could have therapeutic applications. The present study extends knowledge of circadian rest-activity levels in young people with ASD, by using actigraphy to characterise the rest-activity cycles of this group. The findings indicate a high degree of variability in circadian rhythms, both between individuals and across different days of the week. The extent to which these effects are specific to ASD, rather than reflecting age and puberty-related changes, remains unclear. Further research utilising actigraphy, and with the inclusion of appropriate control groups, has the potential to elucidate and extend these findings.
References


Paper Three

Critical Appraisal

Word count: 4,876
Critical appraisal

Overview

The thesis presents a series of papers exploring catatonic symptoms and circadian rest-activity levels in autistic spectrum disorders (ASD).

Paper 1 addresses available treatments for catatonic symptoms in ASD, through a systematic review of the existing literature in this field. Catatonic symptoms are thought to occur in around 8% of young people with ASD, and it has been suggested that biological timing abnormalities may play a key role in the development of these difficulties (Hare and Malone 2004). Catatonic symptoms have significant implications for quality of life and independence. Understanding the mechanisms underlying these symptoms and developing effective interventions are therefore important clinical issues. All the reports identified were either single case descriptions or small case series. Although published treatment algorithms for autistic catatonia exist (Dhossche et al. 2006; Fink et al. 2006), the review indicates a lack of evidence to support any specific treatment for autistic catatonia, with very few published cases available. Existing treatments include electroconvulsive therapy, high dose benzodiazepines and behavioural interventions.

Paper 2 explores circadian patterns in activity using actigraphy. A case series of 8 young people with an ASD diagnosis were recruited from specialist schools and asked to wear an actigraph for one week. Parents completed questionnaire measures of ASD traits and symptoms of autistic catatonia. Findings indicated a high degree of variability in circadian rest-activity cycles, both between participants and across the week. The study findings have implications for future research into circadian function in this population, as well as possible therapeutic applications.

This final paper provides a critical evaluation and discussion of the research process. The development of the research and its strengths and limitations are considered, as well as implications for clinical practice and future research. Some personal reflections on the process of conducting the research are also shared.
Literature review

Topic selection

A number of potential topics for the systematic review were explored. A review of the literature pertaining to biological timing mechanisms and circadian function in ASD seemed appropriate but the researcher identified recent reviews in these areas (Botbol et al. 2013; Glickman 2010). Similarly, a review of movement difficulties in ASD was considered, but a recent review addressing this topic was identified during an initial search (Gowen and Hamilton 2013). The topic finally selected for the review was existing treatments for catatonic symptoms in ASD. Although treatment algorithms have been proposed for this population (Dhossche et al. 2006; Fink et al. 2006), it did not appear that any systematic review of available treatments had previously been conducted. The relative frequency of catatonic symptoms in ASD, and their implications for daily functioning, suggests that this is an area with some clinical significance (Wing and Shah 2000).

Study identification and inclusion

The set of search criteria selected appeared to be effective in identifying relevant papers. Few additional papers were found through hand searching of references. The inclusion criteria were broad, as it seemed likely that the literature in this field was fairly limited. The main reasons for excluding papers were that the paper was a letter to the editor, ASD criteria were not met, or no intervention was described. The majority of the cases identified were retrospective reports of single cases, rather than planned treatment evaluation. This may explain the prevalence of ‘letter to the editor’ reports.

In a number of cases the same patient had been described in several reports, often without clearly stating that the information had been previously presented elsewhere. This caused some difficulties with establishing which reports to include, and ensuring that cases were not replicated. One paper described a ‘composite case’, designed to be illustrative of autistic catatonia and was therefore excluded (Kakooza-Mwesige et al. 2008). A few of the reported cases were found within the text of broader papers, where they were cited as case examples. These cases were included in the review, but were typically of poor quality due to the lack of available detail.
Assessing quality

Single case designs form the vast majority of the available evidence in relation to treatments for autistic catatonia. Single case designs can contribute valuable new information where there is no established treatment and therefore are highly relevant to this field. A decision was made then to retain single case designs, although typically these would be excluded from a systematic review. As single case designs are usually excluded, there are few established measures of quality for these types of reports. An idiosyncratic measure of quality was therefore developed, which could be used to rate single case designs and that addressed considerations specific to this field (Appendix 3). The development of this measure was informed by existing quality measures (Scottish Intercollegiate Guidelines Network 2011) and available guidance on reporting of medical case studies (Cohen 2006; Green and Johnson 2006; McCarthy and Reilly 2000).

Single case designs are typically regarded as providing low quality evidence, compared to other methods such as controlled trials. However, there is considerable variation in quality within single case designs, ranging from clinical anecdote to semi-controlled single case designs. Ratings in the current review ranged from low to medium quality. Papers with low quality ratings were still included in the review, but discussed with careful consideration of the design limitations. The ratings and quality measure were made available as online supplementary material through the journal (Appendix 4), to ensure that the quality rating process was transparent.

Qualitative information

A small number of self-reported accounts of autistic catatonia appear in the reviewed literature. Although an analysis of these accounts was not within the scope of the systematic review, the researcher found it helpful to consider these very personal descriptions of catatonia. The experiences described by these patients powerfully highlight the emotional and practical impact of catatonic symptoms, and emphasise the need for effective treatments.

One patient described her experience of catatonia as: “oppressed feelings... as if some uncontrolled force is pulling me down to the ground” and noted that: “my frozen posture lasts for a couple of hours” (Takaoka and Takata 2007). Another patient described his experience as follows:

“I am so afraid that I am not going to be able to communicate anymore. I am currently in a frozen state. Can you imagine your brain not sending the message to
your feet to move? I hear everything that people say to me but I am unable to process the information. I need to get out of this state of catatonia. I am so afraid I will be frozen forever and I won’t be able to talk with you or my mom again. I am troubled by my loss of independence. I don’t even know I have to eat or go to the bathroom without being told. Sometimes my fear of losing my grip on reality is overwhelming. Catatonia is like being non-existent. My limbs don’t move without being told. My hands don’t move willing or non-willingly. I do not know how to get out of a chair anymore. Can you imagine how humiliating all of this is? I am currently taking medication to help me join the functional world again. The medicine does not seem to be making any significant difference. I have a very difficult time walking from one destination to another without constant touching on my back to remind me to move. Recently my hand stuck out and my arm was frozen for what seemed like over an hour. People must think that I am a statue when I do this. I feel hopeless when this happens but I have not given up on my dreams to be the very best of what I am.” (Wachtel et al. 2010b, p. 582)

These descriptions suggest that gathering subjective accounts of catatonic symptoms in people with ASD has the potential to generate valuable insights into this condition. This is an area of research that appears to be largely unexplored, with the vast majority of reports giving only third party accounts of autistic catatonia. This can be contrasted with the increasing recognition of the value of service-user perspectives in research both within mental health (Thornicroft and Tansella 2005) and intellectual disability settings (Ramcharan and Grant 2002). Greater consideration of service-user perspectives therefore has the potential to improve understanding of both the nature of autistic catatonia and the impact of available treatments. Service-user perspectives on treatment may be particularly relevant in evaluating ECT for autistic catatonia, as significant discrepancies between clinician and service-user views on ECT are well established (Rose et al. 2003).

Personal reflections

A challenge for the researcher in conducting the review was the predominance of medical approaches in the literature. Given that the researcher’s professional background is in psychology, many of the technical aspects of treatment were initially unfamiliar (e.g. medication types and dosage, ECT parameters). However, it was considered important to evaluate both medical and psychological approaches to treatments, in order to have a holistic picture of current knowledge in
this area. It also seemed valuable to bring a psychological perspective to this area of research, which to date has primarily been psychiatric in orientation.

Some of the research reviewed was distressing in content, both in terms of the symptoms presented and the level of restriction imposed by some interventions. For example, one report described the case of a young man engaging in very high levels of self-harm, at times “requiring up to 7 adult staff to contain him” (Wachtel et al. 2010a). In many cases, patients had been treated as inpatients for long periods with little reduction in symptoms. The literature also raises ethical concerns, particularly in regard to issues of capacity and consent. As a result of these factors, the process of reading and reviewing these papers was sometimes emotionally challenging. The researcher was aware of a tension between this response, and the need to review the papers objectively and impartially.

When the review was submitted to a journal for peer review, one of the reviewers was highly critical of the way in which the ECT literature had been presented. The reviewer emphasised the “remarkable track record of ECT in [the resolution of catatonia] since the inception of convulsive therapies” and asserted that the review “serves the author’s bias of promoting anti-ECT sentiment, which is not science, and not in the service of the autism community”. Whilst aware of ongoing controversy around use of ECT, the researcher was surprised by the strength of feeling elicited by this work. This response perhaps highlights some of the challenges encountered by researchers attempting a critical appraisal of a field that is characterised by polarised opinions.

**Strengths and limitations**

One of the strengths of the review is that it takes a rigorous, systematic approach to the literature in a field that is typically dominated by clinical opinion. It is perhaps surprising that this literature has never previously been subject to systematic review; published treatment guidance to date has been based on more selective, narrative review processes (Dhossche et al. 2006; Fink et al. 2006). Another strength of the review is the inclusion of a broad range of treatment strategies including ECT, pharmacological, behavioural and sensory approaches. This means that the review provides a comprehensive picture of treatment for autistic catatonia, rather than being restricted to a particular ‘family’ of interventions.
Limitations of the review include the lack of consistency across the papers reviewed, meaning that synthesis of the findings was difficult; it was not possible to perform any statistical meta-analysis. Another possible limitation of the review is the heterogeneity of cases, due to a wide range of comorbid conditions and varying degrees of severity. The lack of an established measure of autistic catatonia meant that it was impossible to account for these differences in severity in any meaningful way. Current treatment algorithms suggest that treatment selection should be dictated by the severity of catatonic symptoms. However, the lack of an established measure of catatonic severity within this patient group means that it is unclear to what extent this occurs in a systematic or consistent way.

The review was also limited to English-language papers and is therefore dominated by research from the USA and UK. It is possible that additional relevant papers would have been identified if papers published in other languages had been included. There is likely to be considerable geographical variation in the extent to which different interventions are utilised, particularly given the legal issues around use of ECT. Several of the American reports included in the review noted that patients had travelled ‘out of state’ in order to access ECT due to restrictions on its use within their home states.

Future research

The review indicates a need for further research in this field, particularly high quality controlled studies involving larger numbers of patients. However, the review also highlights significant challenges to conducting this type of research. The relative rarity of catatonic syndromes in ASD, combined with the wide range of severity and comorbid conditions observed, is a particular challenge. It is likely that multicentre trials will be necessary in order to recruit sufficient numbers of participants for this type of research. It is hoped that by disseminating the review through a major intellectual disability journal, this may stimulate interest in this field and encourage researchers to begin addressing the limitations of the current evidence base.

Considering the small number of clinicians represented in the treatment literature, it seems likely that other clinicians are treating cases of autistic catatonia but have not recorded or disseminated their findings. One approach to developing the published literature then would be to gather and synthesise this knowledge by surveying clinicians working in the field.
Given the proposed role of timing dysfunction in autistic catatonia, it is interesting that many of the existing treatments for this condition appear to have circadian effects. ECT has effects on melatonin production (Krahn et al. 2000) and has been demonstrated to restore disrupted circadian rhythms in patients with depression (Szuba et al. 1997). Benzodiazepines can cause phase shifts in circadian rhythms (Benedetti et al. 2004). Some behavioural treatment approaches may also promote regular circadian cycles, as they emphasise participation in activities and maintaining stable daily routines (Shah and Wing 2006). It seems plausible then that some of the existing treatments for autistic catatonia may have chronotherapeutic effects. Future studies examining circadian function in patients with autistic catatonia would help to test these hypotheses. If autistic catatonia is related to circadian dysfunction, this may provide a key target for treatments and preventative interventions.

Clinical implications

The lack of established treatments presents a dilemma for clinicians, as there is little evidence to guide practice. Given the relative rarity of autistic catatonia, it is also likely that many clinicians will have little practical experience of treating these difficulties. Interventions should therefore be used cautiously, with careful consideration of likely advantages and risks of each approach. Although lacking in strong evidence, the current literature does suggest a role for behavioural intervention, particularly for milder symptoms. Given the increased severity of symptoms over time in many cases, there seems to be a possible role for early intervention and perhaps targeted screening of ‘at risk’ populations. Better consensus around how to define and measure autistic catatonia is likely to support this process, as is increased professional awareness of these types of difficulties.

Empirical paper

Development of the study design

The original proposal for the empirical paper was to explore links between autistic catatonia and changes in circadian rest-activity levels. It has been proposed that autistic catatonia may be related to alterations in biological timing mechanisms, as these are thought to be involved in the ability to link together movements across time in order to produce complex actions (Hare and Malone 2004). It has also been noted that autistic catatonia is sometimes associated with day/night reversal (Wing and Shah 2000), which may indicate abnormalities in circadian function. However, the relationships
between catatonia-like symptoms and timing mechanisms in ASD have never been directly examined.

A study was therefore designed to explore these hypothesised links using actigraphy and a recently developed measure of autistic catatonia (Breen 2014). Actigraphy was chosen as the method of enquiry, as it is an established method for gathering objective and reliable data on circadian rest-activity levels. Actigraphy is also non-intrusive, can be worn without disruption to daily activities and has been previously tolerated well by participants with ASD (Hare et al. 2006a, 2006b; Wiggs and Stores 2004). The proposal was to recruit a group of young people who met criteria for autistic catatonia, and a control group of participants with ASD but no catatonic symptoms.

However, recruiting sufficient numbers of participants with clinically significant symptoms of autistic catatonia proved to be extremely difficult. It became apparent that identifying a large enough experimental group would not be possible within the available timeframe. A decision was therefore made to broaden the study criteria and include any young person with an ASD diagnosis, regardless of autistic catatonia symptoms. There is increasing recognition that autistic catatonia may more accurately be thought of as occurring along a spectrum of severity. Many people with ASD present with one or more symptoms, though they may not meet criteria for the full syndrome (Wing and Shah 2006). There is also some recent evidence that symptoms may be continuously distributed within the ASD population (Breen 2014). It was therefore anticipated that an exploration of associations between circadian rhythms and autistic catatonia would be possible using correlational analyses.

The challenges encountered in conducting a study of autistic catatonia, and particularly in recruiting sufficient number of participants, highlight the difficulties inherent in this area of research. This perhaps helps to account for the rather limited evidence for treatments, as highlighted in Paper 1, and further emphasises the need for co-ordinated multi-centre research trials.

Final research design

When the final data was examined, it was apparent that there was relatively little variation in catatonic symptoms within the participant group. No participants met the proposed clinical cut-off of 3 or more symptoms and scores ranged only from 0-7, out of a maximum possible score of 24 (Breen 2014). This lack of range may partly be accounted for by the small sample size, but could also
reflect the fact that recruitment was from schools rather than specialist clinical services. Due to this lack of variation, meaningful analysis of relationships between catatonic symptoms and circadian rhythm variables would not have been possible. A decision was therefore made to shift the aims of the analysis, and to focus on characterising circadian rest-activity levels in ASD more generally.

Several theories propose a role for biological timing, particularly circadian function, in the aetiology of ASD (e.g. Boucher 2001; Brock et al. 2002; Tordjman et al. 2013). A growing body of evidence, including behavioural, endocrine and genetic research, is now providing support for this hypothesis. However, very few studies have used actigraphy to examine circadian cycles in rest and activity. This method has never previously been applied in a paediatric sample. The data collected were therefore used to provide a detailed characterisation of the circadian rest-activity cycles in a small case series of adolescents with ASD.

Due to changes to the study design throughout the course of the project, no control group was recruited. This presented some difficulties in the interpretation of the data and needs to be addressed in future studies. If more time had been available, an appropriate control group could have been recruited, to enable comparisons of circadian rest-activity levels between participants with ASD and typically-developing controls.

**Challenges to recruitment**

Recruitment presented a significant challenge throughout the research process. This seemed to be partly due to the rarity of autistic catatonia but also lack of recognition of the symptoms. Staff at many of the specialist schools contacted had never heard of autistic catatonia and struggled to differentiate between this and other movement difficulties (e.g. dyspraxia, stereotyped movements). There were also challenges in communicating with other healthcare professionals, who seemed to use different terminology to refer to similar difficulties. For example, a colleague from Occupational Therapy recognised the description of catatonic symptoms as being present in some of her patients. However, she was not familiar with the term ‘catatonia’ and noted that she would describe these patients as having ‘low arousal levels’ or being ‘under-stimulated’.

In a small number of cases, school staff reported having worked with young people presenting with catatonic symptoms. However, these students had typically moved on to more specialist provision due to concerns about managing these symptoms safely within school. One teacher reported
working with a student who began ‘grinding to a halt’ when moving between lessons, resulting in
the student needing to be physically carried. This raised concerns about health and safety, and staff
training, eventually resulting in a decision that the student could not be safely accommodated at
that school.

Recruiting young people with ASD more generally also proved to be challenging. One barrier was the
requirement for parents and school staff to support participation. Many schools reported that they
were already participating in several research studies and were concerned about burdening students
and parents. In the context of secondary education, there are also many competing demands on
school staff. Current issues highlighted by teachers include long working hours, administrative
burden, OFSTED inspection, frequent assessment and changing government policy, including
significant ongoing changes to provision for children with Special Educational Needs (Department for
Education 2013; Easton and Brzyska 2012; Illingworth 2007). Involvement in research therefore
represents an additional demand on an already stretched group of professionals. Similarly for
parents, having a child with ASD presents additional demands, with effects on parental stress and
time pressure (Karst and Hecke 2012). Therefore, although efforts were made to minimise the time
burden presented by the research, this may still have presented a barrier to participation for many.

Challenges to use of actigraphy

A significant challenge for the research was the conflict between the sensory sensitivities that
frequently present in ASD (APA 2013; Kern et al. 2006) and the need to wear the actigraph for an
extended period. Many parents and teachers reported uncertainty as to whether young people
would be able to tolerate wearing the device. A flexible approach was adopted and the researcher
emphasised to parents/teachers that it was possible to adapt the way in which the actigraph was
worn. However, several young people either refused to wear the actigraph or removed it within a
few hours. Some young people and parents reported that this was due to sensory discomfort. Other
young people seemed to find the actigraph unsettling due to its novelty, or were upset that the
actigraph resembled a watch but did not in fact tell the time. Concerns about ability to tolerate the
actigraph may also have prevented other parents/young people volunteering for the research, and
may account for some of the recruitment difficulties encountered.

It is possible that a lack of familiarity with actigraphy also affected recruitment. However, efforts
were made to explain the research procedure in a clear and accessible way, including use of pictorial
and simplified written or verbal information as appropriate. Pictorial information used included photographs of the actiwatch and examples of rest-activity data, presented in graphical form. The use of similar technology in smart phones and tablet computers provided a means of explaining the study with reference to something already familiar to many participants. It did seem that the procedure was generally well understood by young people and for those who agreed to participate, compliance with actigraphy was good.

It is possible that with further training and education for the parents and young people involved, uptake may have been higher. For example, opportunities to acclimatise to the actigraph or to wearing something on the wrist, prior to starting data collection, may have facilitated participation. Fawkes et al. (2014) have recently reported on a program of education and training for parents, designed to improve compliance with an actigraphy protocol and demonstrated that this training resulted in an increase in the number of useable nights of data. However, despite improved night-time recording, compliance with 24-hour recording was still low (29%). It is also unclear whether training would be similarly helpful for an adolescent sample, where parents are perhaps only minimally involved in supporting data collection.

Despite the challenges, for many participants taking part in the study seemed to be a positive experience. Several young people expressed an interest in science and technology, and felt that the study was consistent with these interests. Many were curious about the actigraph and how it worked. Participants also reported enjoying the opportunity to see graphs of their own data (Appendix 8), and generally seemed to find this visual representation interesting and accessible.

*Theoretical implications*

The study findings indicate a high degree of variability in the rest-activity cycles of young people with ASD, both between participants and across a week. However, the extent to which these effects are specific to ASD, rather than reflecting the impact of age/puberty, requires further study. As circadian functions are thought to be involved in the aetiology of ASD, improved understanding of these functions has potential to increase our understanding of the broader development and symptomology of ASD.

As well as having implications for our understanding of the core symptoms of ASD, insight into circadian rhythm dysfunction has potential relevance for common comorbidities in ASD. For
example, comorbid mood disorders are common (Matson and Williams 2014) and there is evidence that these disorders are closely linked to circadian dysfunction (Wirz-Justice 2006). Similarly, people with ASD have an elevated number of gastrointestinal symptoms (McElhanon et al. 2014) and circadian rhythm disruption is implicated as a risk factor for gastrointestinal dysfunction (Caruso et al. 2004; Knutsson and Bøggild 2010).

**Suggestions for future research**

It would be interesting to extend this work with larger groups of people with ASD. This would allow an exploration of links between circadian dysfunction and specific symptoms of ASD, or comorbid conditions. Another extension of this work would be to measure the impact of chronotherapeutic interventions on ASD symptoms. Chronotherapeutic strategies could include both pharmacological and psychosocial interventions (e.g. melatonin, scheduling, sleep hygiene).

Future research could examine specific relationships between symptoms of autistic catatonia and circadian rest-activity levels, as planned in the original study. Use of several recruitment sites would facilitate recruitment of a large enough sample. It may also be helpful to recruit from specialist clinical services, as it seems likely that young people with more severe catatonic symptoms will be in contact with these services.

**Clinical applications**

Paper 2 found a high prevalence of unusual circadian patterns and sleep routines in a group of young people with ASD. The impact of this on other areas of functioning is currently unclear, but it might be predicted that being ‘out of sync’ with environmental demands (e.g. school start times, imposed bed times) could have significant implications across a range of domains including quality of life, social interaction, cognitive performance and educational achievement. It may therefore be appropriate to more routinely assess circadian function and sleep in ASD, in order to screen for potential difficulties in this area. As the circadian disruption observed across participants was highly variable, an individualised approach is likely to be needed. However, relatively simple interventions, such as providing a consistent school routine, may be effective in stabilising circadian patterns of rest and activity – there was evidence from the current study that weekday rhythms were better synced with clock time than weekend patterns. This raises questions about how routines that
provide circadian stability can be maintained during weekends and holidays, or at transition from school to adult services.

Actigraphy may have utility in future research and as a tool for planning individualised programs of intervention. However, it appears that some young people are likely to find this method difficult to tolerate. Adaptations may improve tolerability for some people, but alternative measures of circadian function may also be needed.

**Dissemination**

Individual feedback was given to each participant, consisting of graphs of their activity and sleep over the week in which data was collected. Parents and young people were also given the opportunity to discuss the results with the researcher if they wished to do so. A report summarising the study findings was sent to each school that participated (Appendix 9). Several schools indicated that this information would be shared with parents or school governors, for example through reports and newsletters.

Paper 1 has been published in Journal of Autism and Developmental Disorders. It is hoped that Paper 2 will also be published in an intellectual disability journal; this is currently being prepared for submission.

**Conclusions**

A systematic review of the literature on treatment for autistic catatonia (Paper 1) indicates that little is known about effective treatment for this condition. Currently, limited evidence supports the use of ECT, high dose benzodiazepines and behavioural interventions. However, significant further investigation is needed to establish long-term outcomes and side effects, and to maximise the efficacy of these treatments.

The findings of Paper 2 suggest a high degree of variability in circadian rest-activity levels in adolescents with ASD, including both individual difference and weekend effects. The degree to which these changes are specific to ASD, rather than reflecting age effects is unclear and requires further examination. It is possible that variability in rest-activity cycles reflects underlying abnormalities in circadian regulation, but further research is needed to examine this hypothesis.
References


Appendix 1

Author guidelines for Journal of Autism and Developmental Disorders
Instructions for Authors

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Double-Blind Peer Review

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All JADD manuscripts should be submitted to Editorial Manager in 12-point Times New Roman with standard 1-inch borders around the margins.

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- Line 6: Text begins, references and tables, figure caption sheet, and figures may follow (page break between each and see format rules)

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1. Order of manuscript pages

Title Page with all Author Contact information & Abstract with keywords and the corresponding author e-mail information.

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Appendix

Figure Caption Sheet

Figures

Tables

Author Note

MANUSCRIPT SUBMISSION

RELATED BOOKS - SERIES - JOURNALS

Journal

Child & Youth Care Forum

Editors: Editor-in-Chief: Carl F. Weems

BACK NEXT 1/10

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Citation

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- Negotiation research spans many disciplines (Thompson 1990).
- This result was later contradicted by Becker and Seligman (1999).
- This effect has been widely studied (Abbott 1991; Barakat et al. 1995; Kalso and Smith 1988; Medvec et al. 1996).

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Appendix 2

Literature review data tables
<table>
<thead>
<tr>
<th>Reference</th>
<th>Participant information</th>
<th>Catatonia</th>
<th>Acute intervention</th>
<th>Immediate outcome</th>
<th>Maintenance intervention</th>
<th>Follow up</th>
<th>Quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailine &amp; Petraviciute</td>
<td>Male, 19 years (twins)</td>
<td>PDD/Asperger’s Moderate learning disability Dyslexia Depression</td>
<td>Onset at 17yrs. Freezing during activities, posturing, rigidity, decreased speech (yes/no responses only). Mutism and food/sleep refusal following exams. EEG, MRI and laboratory tests negative.</td>
<td>Lorazepam 1mg gave improvement but discontinued due to memory problems/restlessness. 19 sessions bilateral ECT over 27 weeks. 15% energy for 7 treatments, 25% for session 8-9, 40% for session 10, 60% for remaining treatments.</td>
<td>Aripiprazole 5mg</td>
<td>Regressed verbally after ECT stopped. Attends technical school and has part time job.</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Male, 19 years (twins)</td>
<td>PDD/Asperger’s Moderate learning disability Tourette syndrome Anxiety</td>
<td>Onset at 18yrs. Freezing during activities, poor concentration, less sociable, reduced interests. No medical investigations reported.</td>
<td>Lorazepam discontinued because of over-sedation. 19 sessions bilateral ECT. 15% energy for all treatments.</td>
<td>Aripiprazole 5mg</td>
<td>Attends technical school and has part time job.</td>
<td>Low</td>
</tr>
<tr>
<td>Dhossche et al (2010)</td>
<td>Second case Male, 19 years</td>
<td>High functioning autism Tics Depressive disorder with self-injury and suicidal ideation Delusions of persecution</td>
<td>Onset at 17yrs. Loss of interest in activities, withdrawal, mutism, catatonic posturing, rigidity, difficulty initiating movement, gait abnormalities. Blood work, review of major systems, head computed tomography and EEG negative.</td>
<td>Little benefit from fluoxetine, risperidone, lorazepam, carbamazepine. 18 sessions bilateral ECT with MECTA Spectrum 5000 Q unit. Lorazepam reversed by flumazenil. Pimozide 0.5mg 2x per day for tics – discontinued due to side effects.</td>
<td>Gradual response to ECT – responding to conversation, eye contact, increased activities. Walking remained slow with initiation difficulties. Tics reduced but not eradicated.</td>
<td>After discharge: risperidone 0.5mg, sertraline 100mg, clonidine 0.15mg 3x per day. Maintenance ECT every 2-3 weeks.</td>
<td>Low</td>
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<tr>
<td>Fink et al (2006)</td>
<td>Patient P Male, 17 years Pervasive developemental disorder Normal IQ</td>
<td>Onset 6 mths before – long periods of kneeling with reports of pain, decline in self-care, bradykinesia, bradyphrenia. Laboratory workup including EEG and MRI negative.</td>
<td>Paroxetine, clomipramine, venlafaxine, fluoxetine, mirtazepine, duloxetine, valproate, ziprasidone, and quetiapine elicited no benefit. Course of 18 bilateral ECT.</td>
<td>Remarkable improvement during treatment (speaking and laughing) but not sustained – returned to pre-ECT presentation, rigid, psychomotor retardation.</td>
<td>None reported</td>
<td>None reported</td>
<td>Low</td>
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<td>Fink &amp; Bauer (2008)</td>
<td>Male, 17 years Autism Tics Obsessive compulsive disorder Depressive mood disorder</td>
<td>Onset at 14yrs. Mutism, reduced food intake, slowing of movement, needed more prompting to initiate activities – lack of spontaneous activity. Sparse speech. Movements like ‘watching a movie in slow motion’. Medical screening including ophthalmologic examination, electrocardiogram, MRI and blood tests.</td>
<td>Citalopram, risperidone and ziprasidone with little benefit. Hospitalized. 18 sessions of bilateral ECT.</td>
<td>Dramatic improvement in movements, speech, appetite and interpersonal interaction. More verbal, more spontaneous movement, able to complete ADLs.</td>
<td>Antidepressant medication</td>
<td>Improvements were maintained but did not regain premorbid functioning. Family considered response to ECT lifesaving.</td>
<td>Low</td>
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<tr>
<td>Ghaziuddin et al (2010)</td>
<td>Male, 18 years Autism Mild learning disability Deafness</td>
<td>Onset at 12yrs with decline in function and motor slowing – home videos corroborate. Hospitalized for dehydration and weight loss, diagnosed with catatonia. Psychomotor slowing, posturing, episodic excitement, history of stupor, stereotyped movements, unresponsive. Medical workup including MRI, EEG, karyotype and Fragile X testing, metabolic panels, all negative.</td>
<td>Previous treatment with benzodiazepines, including high doses of lorazepam. Hospitalized. 12 sessions bilateral ECT (mean motor seizure 28s, EEG seizure 59s, charge 349mC, pulse width 0.6ms). MECTA device.</td>
<td>Reduced stereotyped movements, ceased posturing, fewer aggressive episodes, improved continence and more independent in ADLs.</td>
<td>Maintenance ECT recommended but not received due to problems with access in home state.</td>
<td>4 weeks after discharge – reoccurrence of some symptoms including withdrawal and episodic excitement.</td>
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<td>Male, 16 years Autism Moderate learning disability Psychosis NOS with aggression</td>
<td>Freezing and posturing (e.g. crouching, standing on one leg), followed by aggressive episodes. Medical workup including neuroimaging (MRI and CAT), EEG, blood and urine tests, rheumatology all negative. Thyroid problem identified.</td>
<td>Previous trials of various psychotropic medication and behavior therapy. 29 sessions bilateral ECT (3 per week).</td>
<td>No posturing, minimal agitation and aggression by 6th session.</td>
<td>Maintenance ECT every 2 to 3 weeks – currently totals 55 sessions over 14mths. 15mg lorazepam. Trial of propanalol discontinued due to increased aggression. Behaviour plan for home and school.</td>
<td>Lives at home and attends school. Brief periods of agitation but without aggression. No adverse effects of ECT including loss of skills or intellectual functioning.</td>
<td>Low</td>
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<tr>
<td>Wachtel et al (2008)</td>
<td>Female, ~ 16 years Autism Early deprivation Learning disability Tourette's syndrome Self-injury requiring restraints</td>
<td>Onset at 16yrs with spastic movements, progressing to rigidity, staring and unresponsive to voice/touch. Deterioration over time with increased self injury, immobility, frenzied agitation, food refusal, posturing, mutism. Medical and neurological causes eliminated with laboratory testing, MRI and EEG.</td>
<td>Treatment with lorazepam (up to 8mg daily) temporarily successful – increased alertness, interaction, speech and appetite. Citalopram 35mg for possible underlying depression. 12 right unilateral ECT (3 per week) with MECTA Spectrum 5000Q. Starting dose 128mC, average dose 305mC, average seizure length 46s. Postponed due to detached retina. 13 right unilateral ECT (3 per week) – 160mC, 374mC, 49s. Began tapering to 2 per week at 576mC, then increased to bilateral ECT at 3 per week (pulse width 2, 60Hz, 3s, setting 800mA for charge 576mC) for 6 mths. Citalopram 30mg.</td>
<td>Eye contact and speech increased after 3 sessions. Reduced posturing and negativism after 7 sessions. After 9 sessions - no posturing, improved sleep, food intake and social interaction. Reoccurrence of catatonia during postponement.</td>
<td>Treatment with bilateral ECT twice weekly as outpatient. Tapered to 2 per week – reoccurrence of symptoms. Increased to 3 per week with olanzapine and 450mg lithium. Return to 2 ECT per week.</td>
<td>Now received total of 286 bilateral ECT. Caregivers do not report negative effects on cognition or daily functioning. Steady progress in school and has resumed daily routine.</td>
<td>Low</td>
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See also: Wachtel et al (2010)
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<tr>
<td>Wachtel et al (2010a)</td>
<td>Male, 19 years Autism Mild learning disability Tics Suicidal ideation, aggression, self-injury and depressive symptoms</td>
<td>Posturing, psychomotor agitation, staring, unresponsiveness and echolalia, with onset during hospital admission at 16 yrs. Laboratory and imaging studies, and subspecialty evaluations, all within normal limits.</td>
<td>Various unsuccessful medication trials, including development of akathisia and extrapyramidal symptoms. Use of restraints. Bilateral ECT with MECTA Spectrum 5000Q. Ongoing medication – lorazepam and duloxetine. Lorazepam reversed with flumazenil. Initial charge 288mC, mean charge 350mC and average seizure 97s. 3 per week for 7 sessions then tapered.</td>
<td>Calm, cooperative and more sociable after first treatment. Self reported improvement – ‘much better’ and having a ‘good day’. No posturing, mutism or staring. Combined self injury, aggression and disruption reduced from 135.22/hr to 1.55/hr. Restraints removed and staffing reduced.</td>
<td>ECT reduced to twice weekly due to mild delirium. Concomitant use of duloxetine, lithium carbonate, lorazepam and riluzole with ECT x2 per week.</td>
<td>Increase in depression, catatonia, self injury and aggression when ECT frequency reduced. ECT and medication regime combined used to sustain symptom remission.</td>
<td>Low</td>
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<tr>
<td>Wachtel et al (2010b)</td>
<td>Male, 14 years Autism Mild learning disability</td>
<td>Onset at 14yrs, with increased time to complete tasks and increased need for prompting. Occasional freezing and unresponsiveness, slowed movement, rigidity and waxy flexibility. Posturing, echolalia, reduced speech. Reduced intake of food and fluids. Medical and neurological testing all negative, including MRI, CT, EEG, EKG, echocardiogram, Holter monitoring and laboratory investigations.</td>
<td>Lorazepam up to 24mg provided some relief but only temporary. 10 right unilateral ECT (starting at 288mC, average of 434mC, average seizure 61s). Lorazepam tapered over ECT treatment. Bilateral ECT x3 per week, starting at 432mC and increasing to 576mC. After 12 sessions, lorazepam (1mg x3 per day) resumed with flumazenil to reverse prior to ECT. ECT suspended during treatment for malnutrition and dehydration. Bilateral ECT resumed with charge 576mC also olanzapine 1.25mg x2 per day, lithium carbonate 450mg x2 per day.</td>
<td>Poor response to unilateral ECT; developed new posturing and psychological pillow. Some response to bilateral but waxing and waning symptoms. Posturing, rigidity, staring, mutism and autonomic instability resolved. Sustained difficulty with walking retropulsion, reduced arm swing, highly dependent on prompts. Lapsed into catatonic stupor when ECT suspended, including hypothermia and bradycardia.</td>
<td>Medication and ECT continued but sessions reduced to once weekly.</td>
<td>Excellent overall sustained symptom remission in terms of systemic, motor, verbal and behavioural signs of catatonia. Parents state he did not return to previous academic and self care ability. Discharged home with weekly ECT. Resumed activities and independence in ADLs. Now received 156 bilateral ECT, with no reported cognitive or functional decline since acute course of ECT.</td>
<td>Low</td>
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<td>See also: Wachtel et al (2010c)</td>
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<tr>
<td>Wachtel et al (2010c)</td>
<td>Patient 1 Male, 14 years Autism Non verbal</td>
<td>Psychomotor slowness and episodes of immobility. Required assistance with ambulation, feeding and self-care. Catatonia diagnosed based on published criteria. EEG conducted; negative findings.</td>
<td>Alprazolam and diazepam – no effect. Loprazepam 24mg – remained severely impaired. Outpatient course of 7 bilateral ECT, 3 per week – pulse width 1, 60Hz, setting 800mA for maximal charge 576mC with MECTA 4000 Q. After break of 1 week, 4 further sessions with same parameters.</td>
<td>Improved dramatically with about 80% reduction of catatonia. Relapse within several days resulting in second course of 12 bilateral ECT. Relieved catatonia. No evident cognitive side effects but formal testing not performed.</td>
<td>Maintenance ECT recommended but not taken up due to travel demands.</td>
<td>Functioning at around 50% premorbid level.</td>
<td>Low</td>
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<tr>
<td>Zaw et al (1999)</td>
<td>Male, 14 years Autism Moderate learning disability Severe depressive episode</td>
<td>Progressive posturing, mutism and akinesia over previous 4mths. Increased muscle tone and rigidity, facial grimacing, waxy flexibility, occasional excitement/over-activity, need for physical prompting. Modified Roger’s scale for catatonia indicated moderately high scores. Physical investigations negative, including EEG, CAT, MRI, lumbar puncture, blood tests and eye examination. Neurologist also consulted.</td>
<td>Intravenous sodium amytal 0.2g – no resolution of motor symptoms. Imipramine 75mg for depression with no perceptible change after 6 weeks. Single dose of zolpidem 7.5mg caused marked improvement, as rated on Roger’s scale, lasting &gt;24hrs. Bilateral ECT using thymatron Dgx constant current (0.9A) brief pulse machine. 2x per week for 13 sessions. 40Hz, 1ms pulse, charge 50mC, mean seizure 58s, mean seizure energy index 1556, mean post-ictal suppression index 70%.</td>
<td>Significant response after 3rd ECT – improved mobility, resolution of rigidity, return of facial expression. Further progress as treatment continued – return of speech, self-care and activity levels. Full resolution of symptoms.</td>
<td>Sulpiride 100mg x2 per day, increased to 400mg x2 per day. Lithium carbonate, aiming to maintain blood level around 0.5mmol.L.</td>
<td>Progress maintained on medication for 12 mths since discharge.</td>
<td>Low</td>
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<tr>
<td>Bozkurt &amp; Mukkades (2010)</td>
<td>Male, 11 years</td>
<td>Slowness in movements, loss of self-care skills, food refusal, incontinence, reduced social interaction, mutism, posturing, waxy immobility. BF-CRS: 37</td>
<td>Lorazepam 1mg/day</td>
<td>After 2 weeks, BF-CRS: 3</td>
<td>None reported</td>
<td>None reported</td>
<td>Low</td>
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<td></td>
<td>Autistic disorder</td>
<td></td>
<td>Inpatient</td>
<td>Return to school</td>
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<td>IQ 71</td>
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<td></td>
<td>Possible depression</td>
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<td>Dhossche (1998)</td>
<td>Male, ~18 years</td>
<td>Alternating agitation and severe psychomotor slowing, immobility, staring, waxy flexibility, posturing, decreased verbal output. Medical workup including clinical neurological examination, CT, laboratory tests and chromosomal analysis. 46 XY karyotype without Fragile X identified.</td>
<td>Lorazepam 2.5mg x 3 per day</td>
<td>Frequency of stuporous episodes and posturing diminished markedly.</td>
<td>Clozapine 500mg. Lorazepam tapered to 2.5mg/day. Discharged.</td>
<td>No reoccurrence of full blown catatonia over 4 years. Restricted social and occupational functioning.</td>
<td>Low</td>
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<tr>
<td>See also: Schieveld (2006)</td>
<td>Infantile autism</td>
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<td>Clozapine 400mg/day</td>
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<td></td>
<td>IQ 103</td>
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<td>Schizophrenia</td>
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<td>Ohta et al (2006)</td>
<td>Case 4</td>
<td>Onset at 19yrs. Slow movements, repetition of bizarre behaviours, freezing, echolalia, immobility and posturing. MRI and ECG conducted. Slight paroxysmal abnormalities identified. Onset at 15yrs – motoric immobility lasting around 1 yr. Second episode at 21yrs – standing motionless with one leg raised, increased aggression. No medical workup reported.</td>
<td>Bromazepam 4mg</td>
<td>Symptoms tended to abate but were not ameliorated completely.</td>
<td>Medication continued.</td>
<td>Fuctuation in symptoms over following 5 yrs – initially worsened then resolved to point that medication was tapered off.</td>
<td>Low</td>
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<td>Male, 27 years Autism</td>
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<td>Increased doses of antipsychotic medication.</td>
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<td></td>
<td>IQ 40</td>
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<td>Abnormalities gradually faded.</td>
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<td></td>
<td>Tourette syndrome</td>
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<td>Case 7</td>
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<td></td>
<td>Male, 27 years ASD</td>
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<td></td>
<td>IQ 19</td>
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<td>Realmuto &amp; August (1991)</td>
<td>Male, 16 years</td>
<td>Autistic disorder IQ 79 Auditory and visual hallucinations</td>
<td>Onset at 16yrs. Met Joseph et al (1992) criteria - mutism, akinesia, catalepsy plus negativism, posturing. Refusal to eat. Routine laboratory tests normal. MRI showed borderline prominent lateral and third ventricles.</td>
<td>Hospitalised for 4 days. Haloperidol 2mg, 3x per day. Single dose of 5mg haloperidol.</td>
<td>Increased eye contact and eating. Decreased posturing and negativism.</td>
<td>Ongoing medication including thioridazine (up to 600mg/day), haloperidol (15mg/day), imipramine (100mg). Continued nortriptaline only after discharge</td>
<td>Low</td>
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<tr>
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<td>Male, 21 years</td>
<td>Autistic disorder IQ 52 Possible bipolar disorder</td>
<td>Onset at 21yrs with stiffness, upper extremity tremor, diaphoresis, mute unresponsive, food refusal. Met Joseph et al (1992) criteria – mutism, akinesia, catalepsy, mannerisms, negativism. Laboratory studies, neurological examination, EEG and MRI negative.</td>
<td>Hospitalised for 16 days. Haloperidol 1mg, 2x per day, with nortriptaline (75mg/day).</td>
<td>Gradual improvement</td>
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<td>Low</td>
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<tr>
<td></td>
<td>Male, 20 years</td>
<td>Autistic disorder IQ 32 Possible bipolar disorder</td>
<td>Onset at 20yrs. Insomnia, anorexia, rumination, mutism and decreased activity. Cataleptic in doorways, posturing while removing coat. Negativistic, non-compliant, waxy flexibility. Met Joseph et al criteria – mutism, akinesia, catalepsy, negativism, posturing. Laboratory tests and EEG conducted. Some non-specific diffuse cerebral dysfunction identified.</td>
<td>Nortripyline 100mg for 5 mths.</td>
<td>Increased activity, cessation of catalepsy and posturing.</td>
<td>Medication tapered.</td>
<td>After 13mths presented with shouting, excessive laughter, binge eating and bruxism. Treated with 900mg lithium. No further catatonic symptoms reported.</td>
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<tr>
<td>Schieveld (2006)</td>
<td>Case 1 Male, 13 years Autism Severe learning disability</td>
<td>Onset of catatonia at 13 years. Immobility/stupor and posturing/catalepsy. BF-CRS: 40</td>
<td>Lorazepam 8mg per day in 3 doses.</td>
<td>BF-CRS: 24 after approx. 9 mths. Started speaking for first time.</td>
<td>Ongoing medication.</td>
<td>Recurrence of catatonic behavior, especially posturing/catalepsy. Lorazepam increased to 14mg per day.</td>
<td>Low</td>
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<tr>
<td>Takaoka &amp; Takata (2007)</td>
<td>Female, 28 years High functioning ASD IQ 106 Reported depression</td>
<td>Onset around 22 years. Freezing, slowed actions, reduced speech. Consistent with Wing and Shah (2000) definition. Neurological examination normal.</td>
<td>Fluvoxamine 500mg/day</td>
<td>After two weeks, improved mood and restored ability to complete everyday actions.</td>
<td>Medication continued.</td>
<td>No further episodes over 25 months.</td>
<td>Low</td>
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<tr>
<td>Dhossche &amp; Wing (2006)</td>
<td>Case 2 Male, 35 years Atypical autism Moderate learning disability Seizure disorder Possible psychosis NOS</td>
<td>Psychomotor retardation, standing motionless for hours, odd postures, reduced speech, increased need for assistance with daily living. No medical workup reported. Pre-existing diagnosis of grand mal seizures.</td>
<td>Lorazepam 4mg x 2 per day.</td>
<td>Decreased psychomotor slowness, fewer freezing episodes, increased socialization. Resolved after 3mths. Return to baseline and resumed work.</td>
<td>Lorazepam continued, with antipsychotic and antiepileptic. Plan to taper lorazepam if gains are maintained.</td>
<td>None reported</td>
<td>Low</td>
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<tr>
<td>Cohen et al (2009)</td>
<td>Case 1 Male, 17 years Autistic disorder Psychosis NOS</td>
<td>Duration &gt;12 months BF-CRS: 30 Routine blood tests, EEG, neuroimaging, CSF exploration and metabolic screening.</td>
<td>18 sessions packing therapy over 2.5 months. Inpatient. Clomipramine, alanzapine, lorazepam.</td>
<td>Improved cold sensitivity. First word spoken during packing. No reported side effects. BF-CRS: 15</td>
<td>None reported</td>
<td>None reported</td>
<td>Low</td>
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<tr>
<td></td>
<td>Case 2 Male, 13 years Asperger's disorder Schizophrenia</td>
<td>Duration &gt; 12 months BF-CRS: 29 Routine blood tests, EEG, neuroimaging, CSF exploration and metabolic screening.</td>
<td>18 sessions packing therapy over 3.5 months. Inpatient. Amisulpride.</td>
<td>Improved cold sensitivity and clinical improvement. No reported side effects. BF-CRS: 9</td>
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<td>Dhossche &amp; Wing (2006)</td>
<td>Male, 17 years Asperger’s disorder</td>
<td>Onset at 15yrs. Reduced and slowed speech, poor posture, refusal to enter classrooms, slowed walking, poor motor skills, reduced engagement in activities. Needs support to stand and complete self-care. No medical workup reported.</td>
<td>Behavioural intervention, as defined by Shah and Wing (2006)</td>
<td>Increased speech and independent walking by 9mths. Continuing motility problems including slowness, clumsiness, poor coordination, freezing.</td>
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<td>Hare &amp; Malone (2004)</td>
<td>Male, 18 years Autistic spectrum disorder Mild learning disability (IQ in low 60s)</td>
<td>Onset at 15yrs. Difficulty initiating actions, needs physical assistance, getting ‘stuck’ and stopping during actions, poor coordination, difficulty crossing thresholds, unusual gait. Up to 3 hours to ascend flight of 18 stairs. No medical workup reported.</td>
<td>Baseline – 10 sessions no intervention. Intervention – 15 sessions, environmental changes and interpersonal factors (prompting and praise).</td>
<td>Ascent: modal time per step reduced from 12 seconds to 1 second. Descent: modal time per step reduced from 75 seconds to 1 second. Generalised to other staircases.</td>
<td>None reported</td>
<td>Outcomes maintained 18mths after intervention</td>
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<td>Shah &amp; Wing (2006)</td>
<td>Male, 23 years Autism Low average non-verbal IQ</td>
<td>Onset between 16 and 19 years. Slow movement, difficulty with initiation, reduced food intake, little speech, freezing, reduced independence. No medical workup reported.</td>
<td>Behavioural intervention, involving increasing activities, prompting, psychoeducation and reducing stress.</td>
<td>Less rigid in postures and movements, improved range of movements, less reliance on prompts, able to feed himself with minimal prompts, faster responses, reduction and then cessation of repetitive movements.</td>
<td>Placement at suitable day centre – one-to-one support, structured activities, calm atmosphere.</td>
<td>Continued to make progress, regaining speech, mobility and independence.</td>
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Abbreviations: NOS = Not Otherwise Specified; BF-CRS = Bush Francis Catatonia Rating Scale; ECT = electroconvulsive therapy
References


Appendix 3

Quality assessment tool
Quality assessment tool for single case studies of autistic catatonia

Participant information
0 = not reported
1 = age and gender reported

Diagnosis of ASD
0 = stated
1 = justified with reference to diagnostic criteria
2 = formal measure, e.g. DISCO, ADOS

Intellectual function
0 = not reported
1 = reported either as category (i.e. mild, moderate, severe LD) or IQ score

Diagnosis of catatonia
0 = stated
1 = justified with reference to diagnostic criteria
2 = formal measure/ rating scale used

Onset/duration of catatonia
0 = not reported
1 = reported

Treatment
0 = minimal description
1 = described with some detail but not fully specified
2 = described fully, with enough detail to allow replication

Potential confounding factors
0 = no attempt to control potential confounding factors
1 = some attempt to control potential confounding factors, e.g. use of baseline period, avoiding other changes to environment/ medication during target intervention
2 = attempt to control all potential confounding factors
Blinding

0 = no reported attempt at blinding
1 = outcome rated by clinician/researcher blind to treatment

Outcome

0 = clinician impressions only
1 = behavioural outcomes OR patient/family report
2 = objective measure or rating, e.g. frequency recording, rating scales

Statistical analysis

0 = no statistical analysis of outcomes
1 = some analysis, e.g. frequency recording, graphs
2 = formal statistical analysis

Adverse effects

0 = no reporting on adverse effects / side effects for treatments where these are known to occur
1 = adverse effects / side effects (or lack thereof) described

Follow up

0 = no follow up reported
1 = follow up of at least 6 mths, with clinical impression/self-report of outcome
2 = follow up of at least 6 mths, with formal measure of outcome

Total scores range from 0 – 19.

0-10 = low quality
11-15 = medium quality
≥16 = high quality
Appendix 4

Quality assessment ratings
Quality rating checklists: Electroconvulsive therapy interventions

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Appendix 5

Participant information sheets
Using actigraphy to investigate circadian rhythm in young people with autistic catatonia.

Participant Information Sheet (for parents/guardians)

You and your child are being invited to take part in a research study as part of a student project. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully and talk about it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you want to take part. Thank you for reading this information.

Who will conduct the research?

Hannah DeJong, Trainee Clinical Psychologist
Department of Clinical Psychology, School of Psychological Sciences, Zochonis Building, University of Manchester M13 9PL.
hannah.dejong@postgrad.manchester.ac.uk
07843 161 302

The researcher is supervised by:

Dr Dougal Hare, Senior Lecturer
Department of Clinical Psychology, School of Psychological Sciences, Zochonis Building, University of Manchester M13 9PL.
0161 306 0400
dougal.hare@manchester.ac.uk

Dr Penny Bunton, Clinical Lecturer
Department of Clinical Psychology, School of Psychological Sciences, Zochonis Building, University of Manchester M13 9PL.
0161 306 0400
penny.bunton@manchester.ac.uk

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Using actigraphy to investigate circadian rhythm in young people with autistic catatonia.

Autistic catatonia is a description for a set of symptoms that occur in a small number of young people with autism. It includes symptoms such as slowing or reduction in movements, difficulties with initiating or completing actions, and increased reliance on prompting from other people.

Actigraphy is a way of measuring movement and activity levels, using a small sensor that is worn like a watch. This data can be used to explore changes in circadian rhythm – the ‘body clock’ that helps control activity levels and sleep patterns.
What is the aim of the research?

The aim of the research is to find out whether young people who show symptoms of autistic catatonia have differences in their circadian rhythm, compared to other young people with autism. This may help us understand why some young people with autism develop these symptoms. It may also help us find possible treatments.

Why have I been chosen?

You have been chosen to take part in this study because your child has a diagnosis of autism. You have been contacted because you expressed an interest in this research.

Around 15 young people will take part in the study. Participants will be identified through special schools and support groups in the north of England.

What would I be asked to do if I took part?

You will be asked to answer some questions about your child’s diagnosis and symptoms. This will be collected using written questionnaires.

Your child will then be asked to wear an actigraph (a small sensor usually worn on the wrist like a watch). It needs to be worn both during the day and at night, for about a week. You will be asked to complete a simple sleep diary to indicate times of going to bed and waking, and any unusual events over the week. You will then be asked to return the actigraph and diary.

The actigraph is non-intrusive and should be comfortable to wear on the wrist. If your child does find it uncomfortable, the sensor can be attached to a piece of clothing at the hip or shoulder. Your child can also withdraw from the study at any time if he/she decides he/she does not wish to wear the actigraph.

What happens to the data collected?

The data collected will form part of a student project. The results may also be published in academic journals. Any articles produced from the data will be anonymous and it will not be possible to identify you or your child from the information given.

You can also choose to receive a written report about your child’s individual data. This will give information about his/her activity levels, sleep patterns and circadian rhythm. You may find this information helpful and may also wish to share it with your child’s school.

How is confidentiality maintained?

All data will be stored in a locked filing cabinet, in a secure office at the School of Psychological Sciences. The data will be stored anonymously, i.e. it will be labelled with an identifying number and not by name. Any data stored electronically will be password-protected and accessible only to the researcher and supervisors.

What happens if I do not want to take part or if I change my mind?

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to
take part but change your mind, you are free to withdraw at any time. You do not need to
give a reason and there will be no detriment to yourself or your child.

**Will I be paid for participating in the research?**

You will not be paid for participating in the research. You can choose to receive an individual
report about your child’s data if you would like this. The researcher can also discuss the
report with you and answer any questions you may have.

**What is the duration of the research?**

Completing the questionnaires will take about 20 minutes. Your child will then be asked to
use the actigraph for 7 days and you will be asked to help them complete a simple sleep
diary.

**Where will the research be conducted?**

The appointments with the researcher may be conducted at your child’s school.
Alternatively, you may prefer to speak to have the questionnaires posted to you.

**Will the outcomes of the research be published?**

The outcomes of the study will be submitted to an academic journal for publication. Please
ask the researcher if you would like to receive a copy of the submitted article once this is
available.

**Criminal Records Check (if applicable)**

The researcher has undergone a full enhanced criminal records check and has been
approved to work with children and vulnerable adults.

**Contact for further information**

If you would like further information about the study please contact the researcher:

hannah.dejong@postgrad.manchester.ac.uk
07843 161 302
Department of Clinical Psychology, School of Psychological Sciences, Zochonis Building,
University of Manchester M13 9PL

**What if something goes wrong?**

If you are concerned about any aspect of the study, please contact the researcher or
supervisor.

If you want to make a formal complaint about the conduct of the research you should contact
the Head of the Research Office, Christie Building, University of Manchester, Oxford Road,
Manchester, M13 9PL.
Using actigraphy to investigate circadian rhythm in young people with autistic catatonia.

You are being invited to take part in some research. This information sheet is to help you decide if you would like to take part.

**What is the research about?**

The research is about movement and activity levels in young people with autism.

**Who will take part in the research?**

About 15 young people will be asked to take part in the research. There may be other people at your school who are also taking part. All the young people who take part will be aged 11-17 years and have a diagnosis of autism.

**What would I have to do?**

If you take part in the research, I will with meet you and your mum or dad.

Your mum or dad will fill in some questionnaires about your autism and any difficulties you have with movement.

You will then be asked to wear an activity watch for about a week. The watches look like this:

![Activity Watch](image)

The watch will measure how much you are moving. You will need to wear the watch for the whole week, including at night time. It is waterproof so you can even wear it in the bath or shower.

During this week, I will ask you to fill in a diary showing what time you wake up and go to bed. Your mum or dad can help you fill this in.

**Do I have to take part?**

You only have to take part in the research if you want to. If you are not sure, you can talk to other people about it. You can also ask me if you have any questions about the research.

My name is Hannah DeJong. My email address is: hannah.dejong@postgrad.manchester.ac.uk
Appendix 6

Consent form
Using actigraphy to investigate circadian rhythm in young people with autistic catatonia.

CONSENT FORM

If you are happy to participate, please initial each item and sign the consent form below:

1. I confirm that I have read the attached information sheet about the above project and have had the opportunity to consider the information, to ask questions, and had my questions answered satisfactorily.

2. I understand that participation in the study is voluntary and that I/my child are free to withdraw at any time without giving a reason and without any detriment.

3. I agree to the use of anonymous quotes in any report or publications produced.

4. I understand that my data will be stored anonymously by the research team and may be used in future research.

5. (optional) I am willing to be contacted about future research that may be relevant to me or to my child.

I agree to take part in the above project

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Appendix 7

Evidence of project approval
15th April 2013

Dear Hannah

Research Ethics Committee 5 (Flagged Humanities) - Project Ref 12406

DeJong, Bunton, Hare: Using actigraphy to investigate circadian rhythm in young People with autistic catatonia (ref 12406)

I am writing to thank you for coming to meet with the University Ethics Committee 5 (flagged Humanities) on 11th March 2013 and for submitting the requested amendments to the project. This letter formally confirms approval for the above project and that no further changes are required to the documentation submitted to the committee.

This approval is effective for a period of five years and if the project continues beyond that period it must be submitted for review. It is the Committee’s practice to warn investigators that they should not depart from the agreed protocol without seeking the approval of the Committee, as any significant deviation could invalidate the insurance arrangements and constitute research misconduct. We also ask that any information sheet should carry a University logo or other indication of where it came from, and that, in accordance with University policy, any data carrying personal identifiers must be encrypted when not held on a university computer or kept as a hard copy in a location which is accessible only to those involved with the research.

Finally, I would be grateful if you could complete and return the attached form at the end of the project.

I hope the research goes well.

Yours sincerely

Jared Ruff
Senior Research Manager
Faculty of Humanities and Secretary to UREC 5 (Flagged Humanities)
0161 275 0288 Jared.ruff@manchester.ac.uk
Appendix 8

Example participant feedback
Dear [Name],

Thank you very much for taking part in my research project. I hope you enjoyed wearing the actiwatch.

I have included a copy of the graph that shows the data you collected. Tall black bars show that you were moving lots at that time. Shorter black bars mean you were moving less. The blue shaded parts show the times you were asleep.

If you or your parents have any more questions about the study or your graphs, please let me know. My email address and phone number are at the top of this letter.

Best wishes,

Hannah DeJong
Trainee Clinical Psychologist
Actiware Print Report

Analysis Name: New Analysis
Subject ID:
Date of Birth: 24/01/2014 16:38:00
Gender: Male
Activity Scale: 175980

Data Collection Start: 17/01/2014 08:00:00
Data Collection End: 24/01/2014 16:38:00

Activity Chart:
- Thursday 23/01/2014 (DAY 8)
- Friday 24/01/2014 (DAY 9)

Printed: 07/02/2014 10:24:27
Appendix 9

Report for schools
Report for schools

[SCHOOL] recently participated in a research study investigating circadian rhythms in young people with autistic spectrum conditions. The research was conducted by Hannah DeJong, a Trainee Clinical Psychologist at the University of Manchester.

15 students participated in the research, including [NUMBER] from [SCHOOL]. Participation involved wearing an actiwatch – a small sensor, worn on the wrist, which measures activity levels. The actiwatch data was used to examine circadian rhythms (i.e. daily patterns in activity, which are regulated by the ‘body clock’). A parent/guardian was also asked to complete a set of questionnaires for each student who participated. Only 8 of the students recruited were able to tolerate wearing the actiwatch. The findings described below are therefore based data from these 8 participants.

Each student who participated in the study received a graph of their actiwatch data. Parents/guardians were also given the option to discuss the data with the researcher.

The study showed that circadian rhythms in young people with ASD are highly variable. Several participants had unusual patterns of rest and activity, either involving very late sleep times or very early waking times. These patterns were often more extreme at weekends. The degree of individual variability and the changes at weekends suggest that people with ASD may have less stable and robust circadian rhythms than their peers. They may therefore be unusually reliant on external factors (e.g. imposed bed times, fixed routines) to maintain a stable daily pattern of rest and activity.

These findings have implications for supporting young people with ASD, for example by developing routines and environments that support stable circadian rhythms. As circadian rhythms were so variable across the group, it is likely that a highly individual approach will be needed. Many of the young people tolerated wearing the actiwatch extremely well and so this may be a helpful clinical tool to guide the development of intervention strategies.

This work has important implications because researchers believe that abnormalities in circadian function may underlie many of the symptoms of ASD. Future research using actigraphy will extend our understanding of circadian function in people with ASD, and may help to identify how circadian abnormalities affect other domains (e.g. social interaction, communication, movement problems).
I hope that taking part was an interesting experience for the staff, parents/guardians and students involved. I am grateful for the support offered by [SCHOOL], and particularly [TEACHER], in identifying young people to participate in the study and promoting the research.

---

Hannah DeJong
Trainee Clinical Psychologist
University of Manchester
Appendix 10

Initial information for parents
Research study: autism, movement difficulties and the ‘body clock’

Dear Parent/Guardian/Carer,

We are currently looking for young people and parents to take part in some research. The study is about movement difficulties in young people with autistic spectrum conditions.

Young people can participate in the research if they:
- are aged 11-17 years
- have a diagnosis of an autistic spectrum condition, e.g. autism, Asperger’s, ASD

Taking part in the study involves wearing an actiwatch for 1 week. An actiwatch is a small sensor worn like a wrist-watch that measures activity levels. Parents will also be asked to complete some questionnaires (approx. 20 minutes).

Everyone who participates in the study will receive individual feedback about their actiwatch data. This includes information about activity levels, sleep and circadian function (i.e. the ‘body clock’).

If you are interested in taking part in the study, or would like more information, please complete the slip below and return to school.

Many thanks,

Hannah DeJong
Trainee Clinical Psychologist

________________________________________

Child/young person’s name: ________________________________

☐ I would like to take part in the research.

☐ I would like more information about the research.

Parent/guardian/carer name: ________________________________

Signature: ________________________________________________

Contact telephone number: _________________________________