

## Diagnosis and Management of Mental Health Problems Among Individuals with Intellectual Disabilities and Autism Spectrum Disorder

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## Conflicts of Interest

- I have previously given talks on two occasions at events sponsored by Bristol-Myers Squibb. I have received honoraria in connection with both of these events.




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## Objectives

- To provide an overview of intellectual disability and its interface with mental health;
- To describe the characteristics of ASD, including diagnosis and comorbidities;
- To provide a more detailed discussion of challenging behaviours and their management in these two populations.

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## 'Developmental Psychiatry'




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## Part I

Intellectual Developmental Disorder

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## MR (now IDD): Diagnostic Criteria

- DSM-IV TR
  - Significant sub-average intellectual functioning on a standardized test of intelligence (IQ < ~70-75);
  - Significant limitation in two or more areas of everyday adaptive function (communication, self-care and so forth);
  - Onset during the developmental period (<18y).

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### Epidemiology of Intellectual Developmental Disorder

- 2-2.5% of the population have an IQ less than 70;
- 'Administrative prevalence' of IDD in the population is 0.4-1%:
  - Canada (Bradley et al., 2002): 7.2/1000
  - Ireland (inc. NI, McConkey et al., 2006): 6.3/1000
  - Australia (Leonard et al., 2003): 14.3/1000
  - USA (Murphy et al., 1995): 12/1000
- Prevalence in developing countries shows significant variation (from 9 – 156/1000)
- Male to Female ratio approx. 1.3:1

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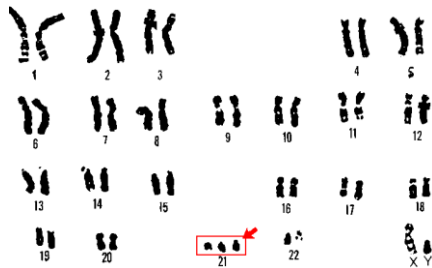
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### Diagnosis?




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### Diagnosis?



Image taken from Wikipedia, Oct 2013

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## Epidemiology of 'dual diagnosis'

	Cooper et al, 2007 <sup>1</sup>	Corbett, 1979 <sup>2</sup>
Schizophrenia	4.4% (DSM IV 3.4%)	6.2%
Bipolar disorder	0.5% (not known)	1.3%
Affective Disorder	6.6% (DSM IV 3.6%)	4.0%
Anxiety disorder	3.8 % (DSM IV 2.4%)	NA
OCD	0.7% (DSM IV 0.2%)	NA
'Any' diagnosis	40.9% (DSM-IV 15.7%)	46.3%
"Problem behaviour"	22.5% (DSM IV 0.1%)	25.4%

<sup>1</sup>Cooper, SA et al., *British Journal of Psychiatry*, 190: 27-35.

<sup>2</sup>Corbett, J. A. (1979) Psychiatric morbidity and mental retardation. In *Psychiatric Illness and Mental Handicap* (eds F. E. James & R. P. Snaith), pp. 11–25. Gaskell.

## Factors associated with psychiatric diagnosis ('Any')

- Cooper et al. (2007):
  - Severe ID;
  - Profound ID;
  - Life events in previous 12 months;
  - Living with paid carer;
  - Female;
  - Urinary Incontinence;
  - Being mobile;
  - Not having physical disability.

## Significance of Epilepsy

- Epilepsy diagnosed among 30% of those with IQ less than 50, and 15% of those with mild IDD (i.e. IQ between 50 and 70).
- Association between epilepsy and psychosis:
  - Usually post-ictal;
  - Inter-ictal and ictal psychosis also described.
- Association between epilepsy and mood disorders also described (lifetime 15-45%).
- Also specific association with behaviour disorders.
- Anticonvulsant medication can impact on mood and behaviour (e.g. Vigabatrin & Levetiracetam).

## Psychosis in Epilepsy

- Usually post-ictal
  - Usually in focal (partial) seizures;
  - Often after a cluster of particularly severe seizures;
  - Usually florid;
  - Typically resolves after one week;
- Sometimes inter-ictal:
  - Phenomenologically indistinguishable from sz;
- Aetiology of psychosis may be related to concepts of 'forced normalization' or 'kindling'.
- FH of schizophrenia does not increase risk.

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## Significance of other medical disorders

- Medical factors can impact on mood and behaviour, and may be overlooked, particularly among non-verbal individuals.
- Constipation and UTI common causes of behavioural disturbance.
- Allergies, rashes, pain (e.g. headache) are often associated with change of behaviour.
- Hypothyroidism not infrequent cause of depression.
- Cognitive decline (AD) in Down's Syndrome can present with behavioral deterioration.

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## Significance of Autistic Disorder

- ASD is itself associated with significant psychiatric co-morbidity irrespective of IQ;
- ASD can also present with behavioural deterioration as a result of factors such as:
  - Sensory over (or under) stimulation;
  - Communication difficulties;
  - Change of routine, unpredictability in their environment;
  - EF and problem solving difficulties.

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### Significance of Genetic Syndromal Diagnoses

- The concept of 'behavioural phenotype' (Nyhan, 1972)
- "A behavioural phenotype refers to those aspects of an individual's psychiatric, psychological, cognitive, emotional & behavioural functioning which can be attributed to an underlying, discrete, usually biological (including genetic) abnormality which has occurred early in development." (O'Brien, 2007; Turk, 2007).

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### Examples of Behavioural Phenotypes

- Down Syndrome
  - Depression
  - Obsessional slowness
  - Alzheimer's Disease
- Prader-Willi Syndrome
  - Overeating behaviour
  - OCD
- Fragile X syndrome
  - ASD
  - Social Anxiety Disorder
  - ADHD
- Smith-Magenis Syndrome
  - Onychotillomania
  - Polyembolokoilamania

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### Diagnosing

- Schizophrenia will be difficult to diagnose in a nonverbal individual (say, IQ<50);
- 'Pfropfschizophrenie' in mild IDD;
- Mood and anxiety disorders can be diagnosed at any level of intellectual ability;
- The DSM-IV (and DSM-5) criteria are, on the whole, adequate for psychiatric diagnosis in this population;
- DM-ID provides an alternative classification scheme that is widely used.

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## DM-ID example: Major Depressive Episode

DSM-IV	DM-ID
Five or more symptoms, 2 wk period. At least one symptom depressed mood or anhedonia.	Four or more symptoms, 2 wk period. At least one symptom depressed mood, anhedonia or irritability.

•Otherwise symptoms unmodified;

•Importantly, symptoms may be reported by observer rather than described by the individual;

•Ultimately, diagnosis will be based on clinical judgement.

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## Part 2

### Autism Spectrum Disorder

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## The historical roots of ASD



Emil Kraepelin, 1856-1926



Leo Kanner, 1894-1981




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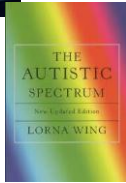
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## DSM-5 and beyond



- Our current conceptualization is the result of Wing's description of a series of cases in 1981.
- Most cases on the 'spectrum' bear no relation to those cases described by either Kanner or Asperger.

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## Diagnostic Concepts:

Autism and Pervasive  
Developmental Disorders




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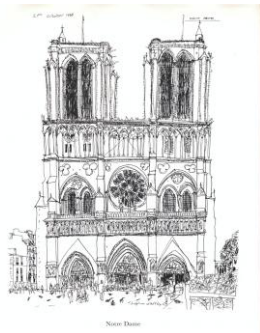
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## Unusual Drawing Ability

Stephen Wiltshire




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## Diagnostic Features

- Social problems:
  - Social reciprocity; eye-contact, smile, directing attention, greeting, empathy, offering/asking for comfort
  - Peer relations; interest, initiative, sharing, best friend, reciprocity
  - Imitation
- Communication:
  - No babbling
  - Speech delay; words and phrases
  - Poor conversation; unusual speech patterns; echolalia, pronoun reversal, made up words,
  - Gestures, pointing, nodding etc
- Repetitive and stereotyped behaviour:
  - Circumscribed interests
  - Resistance to change

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## The vagueness of diagnostic characteristics

"At school, he was observed to be both quiet and timid. Although largely reserved and uncommunicative in grade school he did have a small number of friends. From an early age, he manifested an interest in animals. He initially collected large insects, dragonflies and butterflies which he placed inside jars. He described a curiosity as to how each animal 'fitted together'. From his freshman year he was seen by his peers as a loner with few friends. However, although largely uncommunicative, he was observed by staff to be a polite student who was known to be highly intelligent. He was known to regularly stage pranks, some of which were done to amuse his classmates, others apparently to simply attract attention".

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## ...may lead to phenotypic heterogeneity

- "At school, he was observed to be both quiet and timid. Although largely reserved and uncommunicative in grade school he did have a small number of friends. From an early age, he manifested an interest in animals..."




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## How Common Is It?

- Historical:
  - Autistic Disorder; 13 per 10,000.
  - AS and PDDNOS; 2.6 and 20.8 per 10,000 respectively.
- Current:
  - ASD in 1 in 88 children (USA).
- Rates have increased over time, although no evidence of an "epidemic".
- Male to Female 4:1 approaching 1:1 among lower IQs.
- Reported worldwide.
- No correlation with social class or ethnicity.

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## Is the frequency increasing?

- No question that more cases are being identified but is there a 'real' increase?
- Changes in definition;
- Better diagnosis at both 'ends' of the spectrum;
- Growing awareness of the condition;
- Educational implications of label (for services);
- Diagnostic substitution.

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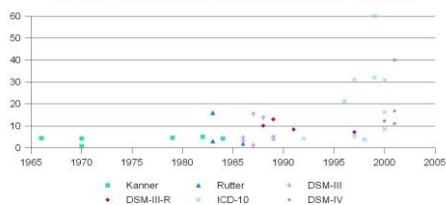
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## Epidemiology of Autism

Rates per 10,000 children  
Changes in rates AND changes in criteria over time




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## The aetiology is principally genetic

- Family and twin studies (Rutter, Bolton and colleagues, 1977, 1994; Hallmayer, 2011).
- Single gene disorders (Rett Syndrome, Tuberous Sclerosis, Fragile X).
- Microdeletion and duplication syndromes (e.g. 16p11.2).
- Copy number variation (gains or losses of large chunks of DNA, ranging from 1kb to 5MB in size):
  - The focus is on rare CNVs (<1% population freq.)
  - Hotspots (15q11-13);
  - Some CNVs are inherited from phenotypically normal parents;
  - CNVs often occur *de novo*.

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## Is there evidence for non-genetic factors?

- A lower heritability estimate calculated in recent years supports the role of shared environment.
- There is currently little or no evidence for any one environmental factor, although the quality of research is often poor.
- Specifically, no evidence whatsoever for:
  - MMR,
  - Thiomerosal.
- Immune factors are a growing area of interest, and evidence looking stronger.
- Possibility of a role zinc deficiency, but mediocre quality of research.
- Paternal age has emerged from genetic studies as another possible risk factor.

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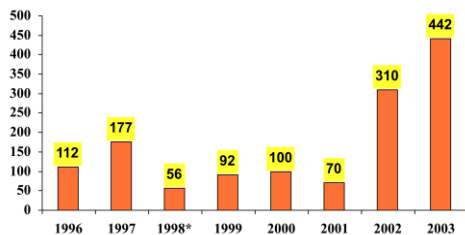
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## Measles in the UK 1996-2003



1998 publication date of MMR study, 2003 data provisional, note that UK has 10X number of US measles cases but is 1/4<sup>th</sup> size

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JOURNAL OF THE AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY  
VOLUME 53 NUMBER 2 FEBRUARY 2014

- Depression and anxiety disorders probably occur at frequencies greater than general population:
  - Among children mood and anxiety symptoms and disorders certainly more common (e.g., Ghaziuddin et al., 1998, Hurlig et al., 2009, White et al., 2009);
  - Among adults less data, but case series of Wing (1980), Tantam (1991) and Howlin (2000) all report high rates of depressive disorders;
  - Frequency does not correlate with IQ or ADI scores (Kim et al., 2000);
  - Depression: relationship with life events & family history (Ghaziuddin, 1995, 1998).
- Psychotic disorders probably occur at frequencies no greater than general population (although less clear, e.g. Tantam and Wolff's series).
- Co-morbidity with other developmental disorders (e.g. tic disorders, attention related disorders) definitely occur frequently.

- Mutism, akinesia and catalepsy;
- Includes other less serious posture, movement and speech disorders;
- Relatively common among individuals with ASDs (e.g. one study found prevalence of 17%, Wing & Shah, BJ Psychiatry, 2000);
- Conceptually may be exacerbation of autism rather than psychosis per se;
- No clear evidenced-based treatments, but bzps, antipsychotics and ECT have all been used.

## Other Conditions

- Tics and ASDs - cases have been reported:
  - Gillberg & Rantam, 1992; Kerbeshian & Burd, 1986; Littlejohns, et al. 1980;
  - Volkmar et al., 1996; Baron-Cohen et al., 1999;
  - Unclear whether rates are significantly elevated nor if outcome and response to treatment differs.
- Attention and Motor control and ASDs:
  - There are no strong data on this;
  - Rates certainly look elevated, but whether this is true comorbidity is unclear.

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## Part 3

Assessment and management of mental health comorbidity and challenging behaviours

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## 'Challenging Behaviour'

- The most common 'presenting complaint' is 'behaviour' and it is the task of the psychiatrist to determine the aetiology of the behaviour; mental health or otherwise;
- 'Socially unacceptable behaviour that causes distress, harm or disadvantage to the person themselves or to others [...] and usually requires some intervention' (Deb, 2009)

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## Differential Diagnosis of Behaviour

- Physical illness
  - Constipation;
  - UTIs;
  - Pain;
  - Allergy.
- Psychiatric illness
  - Any of the psychiatric disorders may present in this way.
- Psychological factors
  - Poor problem solving skills;
  - Inability to regulate emotions in context of life events.
- Sensory impairments:
  - Visual, auditory;
  - Communicative (receptive and expressive).
- Social factors
  - Overstimulation;
  - Boredom;
  - Carer related;
  - Contagion.

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## Reasons for Co-morbidity

- Predisposing
  - Biological (Genetic, neurochemical, neurofunctional)
  - Physical illness (e.g. epilepsy)
- Precipitating
  - Life events
  - Routine: Change/Disruption of routine
  - Communication: e.g. misunderstandings
  - Social: e.g. isolation, rejection
  - Physical illness
- Perpetuating
  - Poor 'illness reporting'/ diagnostic overshadowing
  - Employment status & lack of social support
  - Expressed emotion
  - Physical illness

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## Approach to Assessment

- Best not to make assumptions about a person's level of functioning based on appearance or behaviour.
- Make a judgement early on regarding the relative merits of including the individual in the assessment (from a safety point of view).
- In reality, much of the historical information may be obtained by an informant, but most people with ID dislike being excluded (for understandable reasons), and observation is a crucial component of the evaluation.
- Be aware of the caregiver's agenda (why have they presented now?).
- An appropriate environment will facilitate the assessment.
- Many people with IDD are nervous about the medical profession and if you do not attend to this distress you risk disengagement by the patient or potentially a worsening of their symptoms.
- Remember: challenging behaviour is the presenting complaint, not the diagnosis.

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## Assessment specifics

- Get a clear account of the presenting complaint, associated symptoms, and the 'predisposing, precipitating and perpetuating' context.
- Ask for supporting documentation (sleep and behavioural charts).
- Be certain that you are getting a reliable history (and phone group home, for example, if necessary).
- Use structured assessments if necessary (Aberrant Behaviour Checklist, PAS-ADD).

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## Approach to Medical Management

- In the absence of a clear-cut diagnosis, medication to 'treat' behaviour is 'off label'.
- When there is a clear diagnosis (such as depression etc) management should proceed in the same way as in the population at large (with some caveats).
- There are a very limited number of studies of psychotropic medication use in this population, and therefore for all psychotropic medication:
  - start with low doses of all medications;
  - titrate more slowly.

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## Treatment approaches

- Generally no need to rush in with treatment:
  - Some symptoms resolve spontaneously;
  - Symptoms may change over time and facilitate a clearer diagnosis.
- Start low, go slow;
- Aim for mono-pharmacology;
- Careful consideration of interactions;
- Careful considerations of potential side effects (e.g. seizure threshold lowering capacity);
- If it doesn't work, stop it and try something different.

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## Integrate behavioural/education and drug treatments

- Be a good 'detective':
  - Distribution of symptoms over time and space.
- Do NOT expect drug therapy to make up for an inadequate or inappropriate program;
- Be realistic about expectations and side effects:
  - 'Minor side effects' may cause a lot of distress
- Focus on specific target symptoms:
  - Source of the greatest distress or impairment;
  - Prioritize;
  - Monitor.
- Behavioral and pharmacological interventions are NOT incompatible.

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## Management – The acute situation

- There are no specific data pertaining to the use of rapid tranquillization in individuals with IDD.
- Therefore avoid if at all possible.
- You can often 'talk down' a difficult situation, and then provide specific advice on non-psychotropic management to the patient and their carer(s).
- If unavoidable, need to be aware of, and prepared to manage, potential medical complications (e.g. respiratory compromise with benzodiazepines and NMS with antipsychotics).
- Try oral first, e.g. Haloperidol 2.5mg, Risperidone (orodispersable) 1mg, or Olanzapine (orodispersable) 5mg are three options.
- Quetiapine (50mg in first instance, higher if not neuroleptic naïve) is a reasonable alternative.
- Benzodiazepines can be added, but should not be first line because of risk of worsening agitation and lack of RCT for their use.
  - E.g. Lorazepam 1-2mg oral

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## Medical Management of Behaviour

- Most evidence with Haloperidol, Risperidone and Aripiprazole;
  - Risperidone and Aripiprazole both strong evidence from RCT for management of 'irritability' in ASD (children & adolescents), and therefore should be first line in this population.
  - Haloperidol also evidence from RCT in this population.
  - Risperidone and Haloperidol have strongest evidence in the IDD population (three RCT).
  - However, all atypical antipsychotics are reasonable options.

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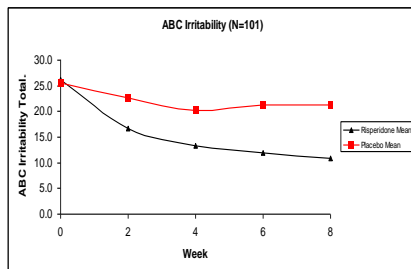


## Pharmacological Interventions: RUPP Risperidone Study

(RUPP Network McDougle, Volkmar & Scahill, 2000-2005)

- Double blind, placebo control study
  - Largest controlled study of effective drug treatment to date
  - N=101 (Risperidone N=49, Placebo N=52)
  - Mean age 8.8 years,
  - Targets: aggression, tantrums, self-injury
  - Trial 8 weeks parallel groups, extension
- Outcome measures: parent/teacher/clinician report

## RUPP Autism Network: Irritability Scale



## Risperidone, haloperidol, and placebo in the treatment of aggressive challenging behaviour in patients with intellectual disability: a randomised controlled trial

Peter Tyrer, Patricia C Oliver-Africano, Zed Ahmed, Nick Bouras, Shervia Cooney, Shoumitra Deb, Deslan Murphy, Monica Hare, Michael Mead, Ben Reece, Kofi Kramo, Satyeeschi Bhaumik, David Harley, Adrienne Regan, David Thomas, Bharti Rao, Bernard North, Joseph Eliathos, Sharmshad Karatada, Anju Soni, Mike Crawford

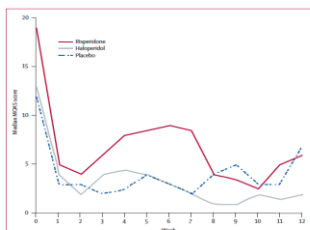


Figure 2: Median aggression scores on the modified overt aggression scale (MOAS) during the first 12 weeks of the trial

www.thelancet.com Vol 371 January 5, 2008

### Psychopharmacology: recommendations

- Risperidone and aripiprazole can be used as an adjunct to behavioural interventions in the management of dysregulatory behaviours among children and adults with ASD.
- Less evidence for other antipsychotics but no reason why they cannot also be used.
- No evidence for the efficacy of SSRIs in the management of ritualistic patterns of behaviour, and so use as a last resort in more severe cases
- No reason to believe that any of the psychotropics will be any less efficacious in this population in the treatment of primary mental disorders (i.e. major depressive disorder, GAD, sz and so forth).

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### Medical management of behaviour (continued)

- There is no evidence to support the use of SSRIs or other antidepressants/anxiolytics in the management of behaviour.
- There is no evidence to support the use of mood stabilizers in the management of behaviour (although historically Lithium used in this population for aggressive behaviour, and there is evidence from two RCTs).
- Benzodiazepines (such as lorazepam & clonazepam) often used but "without good evidence".
- Propranolol commonly used and has some evidence for efficacy.
- Naltrexone rarely used, but also has some evidence for efficacy, primarily in SIB.

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### Management of mental disorders

- Specific mental disorders can be treated according the evidence in the population at large, but doses need to be low and titration slow.
- Sleep problems common in this population, but advice re: over-the-counter preparations recommended (Benadryl, Melatonin). In severe cases, trazodone, zolpidem and chloral hydrate are reasonable options.

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## Management – Treatment of Behaviour

- Behavioural therapy is often used, correctly so, as first line management of challenging behaviour. However, the evidence for its efficacy is lacking.
- Strategies include:
  - Management of all known risk factors;
  - Provision of a safe environment;
  - 'Toolbox' of strategies to alleviate distress;
  - Consequences;
  - Positive reinforcement.

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## Understanding single case 'cures'

- Intrinsic limitations
  - case reports and the news media
  - Mark Twain's 3 kinds of stories
  - Bias for positive reports
  - Minimal attention to unrelated but (important) issues
  - Typically little independent assessment
  - Regression to the mean (fluctuation over time)
  - Some children will do well without (or despite) treatment




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## Alternative Treatments

- Why there are so many?
- Open-mindedness and communication with families is important
- However, treatments should have an empirical basis and reasonable skepticism should be used
- Rules of thumb relative to RISKS
  - Costly (\$, time, emotion)
  - Understanding claims and "cures"
  - Risk in removing child from proven interventions

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## Case 1: Mr A

- Mr A is a 17 year old young adult with autistic disorder and moderate to severe mental retardation. He is admitted for short term assessment because of increasing agitation and self-injury.
- How would you proceed?

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## Case 1: Mr A

- Additional information regarding behaviour:
  - History of behaviour: self-injury (slapping face) and aggression since the age of 8 years.
  - Pattern of behaviour: "no clear pattern", but worse in morning, at time of class transition, and during recess.
  - Alleviating factors: From parents: "nothing helps...anything we try just makes it worse...we try to calm him".
  - Current episode over last two weeks; prior to this "fine for the last 12 months or so".
  - Context for behaviour: No major life events reported.
  - No problems with biological parameters, although has been waking early of late.

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## Case 1: Mr A

- Additional information regarding living circumstances:
  - Lives with parents, and respite two nights per week.
  - Has one sibling, aged 19 years who has just left to "travel the world".
  - Parents generally healthy but mother has had to go into hospital for some "investigations...but 'A' doesn't know".
  - In full time education.
  - The regular transport to school broke down and he has been getting a taxi for the last week.
- What is your differential diagnosis?

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## Case I: Mr A

- Additional information regarding psychiatric history:
  - Has been hospitalised several times for aggression towards others.
  - Many different antipsychotics have been tried, both conventional and atypical. Currently maintained on Fluoxetine 40mg, Risperidone 6mg daily, and Chlorpromazine 50mg up to tid prn.
  - No mental health diagnosis ever given.
  - No FH of mental health problems.

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## Case I: Mr A

- Differential diagnosis:
  - Challenging behaviour in context of autism
  - Medication side effects (akathisia)
  - Peri-ictal agitation
  - Adjustment disorder
  - Anxiety Disorder
  - Depressive disorder

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## Mr A: Aetiology

- Biological
  - Genetic: none known
  - Medical: epilepsy
  - Developmental: MR, autism
  - Medication: high doses of several psychotropics
- Psychological
  - Cognitive: executive dysfunction, emotional dysregulation.
  - Communication: impaired ability to express himself.
  - Temperament
- Social
  - Support
  - Stressors: mother's illness, sibling leaving, transport issues.
  - Quality of Life

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## Case 1: Mr A

- Examination:
  - Refuses to let you in his room, stands at the door, restless, can't stand still, verbalising 'no' repetitively. Pushes you away, starts howling loudly. You decide to end the interview at this point.
- Investigations
  - Blood tests all in normal range, although triglycerides a little on the high side.
- What is your preferred diagnosis?

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## Case 1: Mr A

- Medical management of his behaviour/anxiety:
  - Risperidone reduced and ?stopped
  - Consider adding B-blocker, clonazepam or cyprohepatidine
  - Lorazepam prn added
  - Consider alternative antipsychotic:
    - ?quetiapine
    - ?aripiprazole

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## Summary

- The management of the person with an IDD in the first instance requires the establishment of a mutually comfortable doctor-patient relationship (should go without saying) and a systematic approach to assessment.
- Despite limited evidence and poor data, there is a place for the use of psychotropic medication (principally antipsychotics) in the management of behaviour in IDD and ASD in the absence of a psychiatric diagnosis as part of a wider treatment strategy.
- Mental disorders should be managed as in the population at large, but good data are lacking, and the general heuristic is 'start low and titrate slow'.

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**THANK YOU!**  
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