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Interventions based on the Theory of Mind cognitive model for autism spectrum disorder (ASD) (Protocol)

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Interventions based on the Theory of Mind cognitive model for autism spectrum disorder (ASD)

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effect of interventions based on the Theory of Mind model for autism spectrum disorders.
BACKGROUND

Description of the condition

Autism spectrum disorder (ASD) is a term which refers to a range of lifelong neurodevelopmental conditions comprising autism, atypical autism, pervasive developmental disorder - not otherwise specified (PDD-NOS), and Asperger syndrome (AS) (APA 1994; WHO 1993). The disorders are all diagnosed using the same set of behavioural criteria, namely atypicalities in interaction, language and communication, and imagination (Wing 1979). The diagnosis of ‘core’ autism includes serious impairments in each of these domains, which are apparent as a lack of understanding of social interaction and shared attention and problems with the social aspects of communication. Although some people with autism may be fairly sociable, they usually lack the skills to create successful interactions and relationships. Impairments in the imagination domain are signalled by repetitive behaviours or restricted interests, which further impede life in a social environment. All of these difficulties make it very hard for people with autism to be successful members of society and can present very serious challenges to parents, teachers and other professionals.

The other diagnostic categories within the autism spectrum incorporate the same types of behaviours, but these are present in different combinations. The exception is Asperger syndrome, for which the individual must have had a normal onset of language, though there is currently some debate about whether this diagnostic requirement should be maintained (Frith 2004; Leckam 2007; Mayes 2003).

Prevalence estimates of ASD in children have been rising significantly in recent years with the most recent large-scale study recording a prevalence of 116.1 per 10,000 (Baird 2006). For the diagnosis of core autism, prevalence is estimated at 24.8 per 10,000 (Baird 2006). This represents a fivefold increase on previously published figures, which estimated autism prevalence at about 5 per 10,000 (Fombonne 2001). While there are methodological differences between prevalence studies, the rising prevalence of ASD has been well-documented across Western countries including Europe, Australia and the USA (for example, Atladottir 2007; Kogan 2009; Nassar 2009; Williams 2006; Yeagin-Allsopp 2003).

There has been significant debate about the cause of the recent rise in prevalence of ASD, but the influence of increased awareness of the disorder among health professionals and the community at large, and the role of diagnostic substitution, should not be underestimated (Atladottir 2007; Croen 2002). There are other candidate explanations, including the possibility of environmental causes of the rising incidence, though there is as yet no good empirical evidence for these (Rutter 2005). Baird et al conclude that “Whether the increase is due to better ascertainment, broadening diagnostic criteria, or increased incidence is unclear” (p 210).

Within the disorder there is a male to female ratio of 4:1 or 5:1 (Baird 2006; Kogan 2009), as noted in the set of case studies which defined the condition for the first time (Kanner 1943). ASDs have this feature in common with most other neurodevelopmental disorders (such as attention deficit hyperactivity disorder, dyslexia, dyspraxia). There is no empirical evidence for systematic differences between male and female individuals with ASD.

Theory of Mind

The term ‘Theory of Mind’ (ToM) describes the ability to understand another’s thoughts, beliefs and other internal states, and was originally applied to the study of non-human primate cognition (Premack 1978). The term has since been developed in a number of different directions (for example, Carruthers 1996) including in research into ASD. The first application of the term in ASD research was in an experiment which used false-belief paradigms to explore ToM in children with autism (Baron-Cohen 1985). In this study, children were presented with a scenario in which a doll, Sally, believed her marble was in the basket where she left it. However, the child and experimenter knew that while Sally was elsewhere, another doll had moved the marble into a box. The key question was “Where will Sally look for her marble?” Typically-developing children from the age of four years, sometimes earlier, can correctly ascertain that Sally will look in the basket; she holds a false belief about the location of the marble (Wellman 2001). Children with ASD are much less likely to give a correct answer to this question at age four years. They normally claim that Sally will look in the box, in accordance with reality.

Research into ToM in children and adults with ASD has been prolific over the last 25 years (for example, Baron-Cohen 2000a). While the details are subject to debate, it is widely accepted that people with ASD do not possess a fully-functioning theory of mind; even high-functioning adults with ASD struggle with complex ToM tasks (Donnet 2004). ToM has been placed in a developmental context, consisting of a range of precursor skills including following eye-gaze, establishing joint attention, imitation, pretend play and emotion recognition (Baron-Cohen 1995; Charman 2000; Melzoff 1993; Ruffman 2001; Wellman 2000). ToM then also links to subsequent social and communicative skills including the development of language (Garfield 2001; Tager-Flusberg 2000). As a result, failures of ToM are thought by many to be central to explaining the difficulties experienced by people with ASD (though not a sufficient explanation). Therefore ToM and its precursor skills are targets for interventions.

Description of the intervention

A ‘Theory of Mind intervention’ is a treatment or therapy which is explicitly or implicitly based on the Theory of Mind (ToM) cognitive model of ASD. ToM interventions target those skills which are either potential components or precursors of ToM (Swettenham 2000). One example of an intervention targeting such skills is using ‘thought-bubbles’ to teach children with ASD to understand others’ thoughts and beliefs by illustrating these in
bubbles (as in a cartoon) (Parsons 1999). Likewise, interventions targeting a range of social behaviours grouped together, such as general ‘social skills’ training, may also be described as targeting ToM. Specific precursor skills can also be taught, such as helping a child to make eye-contact to accompany pointing to an object of interest (joint attention). More detail on which interventions are eligible for inclusion in this review is given in the Methods section, but we will only consider interventions which explicitly target ToM skills.

ToM interventions can be contrasted with other types of treatment-as-usual for ASD. Many such intervention models focus on behaviour management and personal skills training, using a basic conditioning model for learning (repetition, rewarding good behaviour, ‘punishing’ bad behaviour such as tantrums). In addition, most treatment-as-usual for ASD occurs within a fairly strict timetable as people with ASD tend to feel more comfortable following familiar routines in a consistent environment and respond very poorly to change.

**How the intervention might work**

In a chapter reviewing evidence for the possibility of teaching ToM to individuals with autism, Swettenham states (p 442) that “a successful method for teaching theory of mind may alleviate the impairments in social interaction that are so debilitating in autism” (Swettenham 2000).

The ToM model of autism suggests that the social and communicative difficulties that are characteristic of the syndrome stem from a failure to develop an intact ToM. Certainly there is evidence that ToM is correlated with real-life social skills (Frith 1994) and symptomatology (Joseph 2004). Certain ToM precursor skills also have a direct relationship with symptoms (Mundy 1994). Therefore, training in ToM, or in the precursor or component skills of ToM, should alleviate the social and communicative difficulties experienced by individuals with the disorder. For example, a targeted joint attention intervention for autism produced improvements in responsiveness to joint attention opportunities and also improved sharing and language (Kasari 2006; Kasari 2008), indicating that ToM interventions have consequences for wider developmental abilities.

It is possible that interventions targeting different ToM skills will produce different types of change in participants and the extent of change may vary. The method of delivery of the intervention may also produce different outcomes. For example, one might expect an intervention delivered by a trained therapist to have greater impact than one delivered by parents. An intervention taught in school may have a different impact to one delivered in the home. The duration of the intervention may also be significant. Deficits in ToM and related skills vary with age (Happe 1995), IQ (Bowler 1997; Happe 1994; Ozonoff 1991a), specific diagnosis (Bowler 1992; Ozonoff 1991b) and verbal ability (Garfield 2001; Happe 1995). As a result, the specific skill being targeted, the method of intervention delivery, its duration and individual differences between participants in ToM intervention studies will be important factors for consideration and for statistical analysis in this review.

**Why it is important to do this review**

To date, there is no comprehensive review of ToM interventions for autism, despite the fact that the first study attempting to teach ToM to individuals with autism was published in 1995 (Ozonoff 1995). This review will be of relevance to both the clinical and academic research communities since ToM interventions not only have the potential to benefit people with ASD but also provide a unique and rigorous way to test the theoretical model on which they are based.

**Objectives**

To assess the effect of interventions based on the Theory of Mind model for autism spectrum disorders.

**Methods**

**Criteria for considering studies for this review**

**Types of studies**

All relevant randomised and quasi-randomised controlled trials (defined as trials in which allocation was made by, for example, alternate allocation or allocation by date of birth).

**Types of participants**

Participants of any age with a diagnosis of an ASD, including autism, atypical autism, Asperger’s syndrome, and PDD-NOS, according to either ICD-10 or DSM-IV criteria. All diagnostic categories will be included since the validity of differentiating between categories on the spectrum is not well established (Klin 2005). Furthermore, the ToM cognitive model does not distinguish, on a qualitative basis, between different forms of ASD. Participants must have received a ‘best estimate’ clinical diagnosis. That is, at a minimum, diagnosis by a multidisciplinary clinical team using standard procedures with reference to the international classification systems. Use of a particular diagnostic tool, such as the Autism Diagnostic Observation Schedule (ADOS) (Lord 1999) or the Autism Diagnostic Interview (ADI-R) (Lord 1994), is desirable but not required. Co-morbid cases will also be included since these individuals are just as needful of intervention for their specifically autistic difficulties.

Interventions based on the Theory of Mind cognitive model for autism spectrum disorder (ASD) (Protocol)
Types of interventions
Interventions eligible for inclusion in this review will:
1. explicitly state that they are designed to teach ToM, or
2. explicitly state that they are designed to teach precursor skills of ToM, or
3. explicitly state that they are based on or inspired by ToM models of autism, or
4. explicitly state that they aim to test the ToM model of autism.
The following kinds of interventions will not be included in this review:
1. interventions which do not meet the criteria given above
2. medical interventions (e.g. risperidone for aggression in ASD)
3. dietary interventions (e.g. gluten-free and casein-free diets)
4. interventions which target a particular behaviour rather than a cognitive skill (e.g. over-sensitivity to light modified using colour spectacles; sleep difficulties modified using applied behavioural analysis)
5. language-focused interventions (e.g. to make requests using the Picture Exchange Communication System or spoken single words).
ToM interventions will be compared with the following conditions, where these are used.
1. Treatment-as-usual / wait list control
2. 'Placebo' interventions, for example a 'contact control' intervention with no therapeutic content.
All 'doses' (that is the number and length of treatment sessions per week), durations and methods of delivery (professional, parent led etc) will be considered.

Types of outcome measures
Outcome measures do not form part of the criteria for inclusion of studies in the review.

Primary outcomes
Primary outcomes will be at a participant symptom level, measured using standardised diagnostic assessments or clinical report. Outcomes will be in each of three symptom domains that are used in clinical diagnosis and are followed by most diagnostic tests for autism. These are as follows, with examples of outcomes in each category as measured by the ADOS (Lord 1999) or ADI (Lord 1994).
1. Communication: overall level of non-echoed language; stereotyped or idiosyncratic use of words or phrases; pointing; gestures; conversation
2. Social function: unusual eye-contact; facial expressions directed to others; spontaneous initiation of joint attention; shared enjoyment in interaction; quality of rapport
3. Flexibility and imagination: imagination or creativity; unusual sensory interests; unusually repetitive interests or stereotyped behaviours; compulsions or rituals

Secondary outcomes
In addition, the following secondary outcomes will be included.

Participant
- Intervention-specific: change in targeted cognitive skill, such as false belief understanding
- Change in participant behaviour or quality of interpersonal interaction, or both, measured by direct observation.

Parent, teacher or other individual in caring or educational relationship to the participant
- Change in participant behaviour and skills or deficits such as: adaptive skills; school success; challenging behaviours; social participation, measured by parent, teacher or other report
- Acceptability of intervention (time, cost).

Other
- Other process measures e.g. rate of drop-out
- Economic data e.g. financial cost of intervention; time commitment required.

Main outcomes for 'Summary of findings' table
The main outcomes for likely inclusion in the 'Summary of findings' table will be:
- symptom level, communication domain;
- symptom level, social interaction domain;
- symptom level, flexibility or imagination domain;
- general communicative ability (e.g. vocabulary);
- 'Theory of Mind' ability (e.g. false belief test score).

All outcomes will be organised into three time points: immediately post-treatment; in the medium term (up to six months post-treatment); and long term (12 months post-treatment). The 'Summary of findings' table will include an estimate of assumed control group risk. This will be estimated from a study which is considered by the authors to be representative of the review's target population and which presents a low risk of bias and high methodological and reporting standard.

Search methods for identification of studies

Electronic searches
Relevant trials will be identified by searching the following electronic databases: the Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; CINAHL; PsycINFO; ERIC; Applied Social Sciences Index and Abstracts (ASSIA); Social Services Abstracts; metaRegister of Controlled Trials (including ClinicalTrials.gov), and Autism Data. The search terms that will be used to search MEDLINE, and amended where necessary to search the other listed databases, can be found in Appendix 1. No language or date restrictions will be applied to the searches.

Searching other resources
In addition to searches of electronic databases, the following search techniques will be used. Key authors in the field will be contacted directly and asked to provide any relevant published, unpublished or in-progress data. The bibliographies of key articles will be searched for citations of papers not found electronically. Finally, searches will be made of the online databases of journals which regularly publish work on this topic, such as the Journal of Autism and Developmental Disorders and Autism; and of the proceedings of relevant conferences, such as the International Meeting for Autism Research.

Data collection and analysis

Selection of studies
All citations sourced from the search strategy will be transferred to EndNote, a reference management programme. Initial screening of titles and abstracts by an experienced research assistant (RA) will eliminate all those citations obviously irrelevant to the topic, for example, prevalence studies, studies not relating to autism spectrum disorders, single case studies. Thereafter, two review authors (SFW and IM) will assess and select studies for inclusion from the group of superficially relevant studies. In the event of disagreement, resolution will be reached in discussion with the third author (HM).

Data extraction and management
SFW and RA will independently extract data from selected trials using a specially designed data extraction form. Extracted data will consist of methods (dose and frequency of intervention); diagnostic description of participants, and type of intervention, including target, intensity, duration and method of application (parent-mediated, therapist, school-based etc.). Data will be extracted independently by two review authors (SFW and IM) and disagreements will be resolved by negotiation with a third author (HM).

Assessment of risk of bias in included studies
SFW and RA will assess the risk of bias in studies to be included in the following domains: sequence generation; allocation concealment; blinding; incomplete outcome data; selective outcome reporting; other sources of bias. We will use the Cochrane Collaboration tool for assessing risk of bias in these areas. The process will involve recording the appropriate information for each study (for example describing the method used to conceal allocation in detail) and evaluating whether there is risk of bias in that area (for example, was allocation adequately concealed?). We will allocate studies to categories according to our evaluation of each area or potential risk of bias.

A. Low risk of bias.
B. Moderate (or unclear) risk of bias.
C. High risk of bias.

Only studies where the assessment of risk falls into categories A or B will be included in subsequent analyses. Studies with quasi-random allocation to treatment condition will be included. Risk of bias will be assessed by two independent review authors (SFW and IM) and disagreements will be resolved by negotiation with a third review author (HM).

Measures of treatment effect

Binary and categorical data
Most data from the expected outcome measures are likely to be expressed as scores from continuous scales. Where categorical data are reported, these outcomes are most likely to be binary (for example, clinical improvement versus no clinical improvement or false belief pass versus false belief fail).

Outcomes are unlikely to be expressed as categorical data with more than two categories. However, in the event that data are reported as a small number of ordinal categories, these data will be converted to binary outcomes. For example, in the event that participants are categorised as: no clinical improvement; small clinical improvement; large clinical improvement, the groups will be converted to two groups (improvement versus no improvement), ideally by recourse to the original dataset. If that is not available, we will combine two groups as appropriate, according to the original group characteristics.

For all binary outcomes, the risk ratio with 95% confidence intervals will be calculated from meta-analysis. Categorical data expressed as a large number of ordinal categories will be treated as continuous data and analysed as described below.

Continuous data
Where standardised assessment tools generate a continuous score as the outcome measure, and means and standard deviations are reported or provided by the authors, comparisons will be made...
between the means of these scores. Where possible, mean difference will be calculated as the summary statistic by meta-analyses. Where measures are on different scales but those scales are clinically homogeneous, meta-analyses will use standardised mean difference; using Hedges g with a small sample correction if required (Hedges 1985). The meta-analysis will combine all three types of effect sizes by transforming them to a single effect-size metric. We will convert raw mean differences to standard mean differences.

Unit of analysis issues

It is possible that cluster-randomised trials will be included in this review. In this case, the authors will use a summary measure from each cluster and conduct the analysis at the level of allocation (that is sample size = number of clusters). However, if there are very few clusters this would significantly reduce the power of the trial, in which case the authors will attempt to extract a direct estimate of the risk ratio using an analysis that accounts for the cluster design, such as a multilevel model, a variance components analysis or generalized estimating equations (GEEs). Statistical advice will be sought to determine which method is appropriate for the particular trials to be included.

Dealing with missing data

Missing data will be assessed for each individual study. Where a loss of significant quantities of participant data is reported such that the review authors agree that the conclusions of the study are compromised, trial authors will be contacted. If no reply is forthcoming or full data are not made available, these studies will not be included in the final analysis.

For included studies reporting drop-out, we will report the number of participants included in the final analysis as a proportion of those participants who began the intervention. Reasons for missing data will be reported (that is whether data are missing at random or not). If data are missing at random, the remaining data will be analysed and the missing data ignored. Where data are not missing at random, we will impute the missing data with replacement values (last observation carried forward or the treatment-group mean) and treat these as if they were observed. The extent to which the results of the review could be altered by the missing data will be assessed and discussed.

If summary data are missing, trial authors will be contacted. If no reply is forthcoming or the required summaries are not made available, the authors will include the study in the review and assess and discuss the extent to which its absence from meta-analysis affects the review results.

Assessment of heterogeneity

Consistency of results will be assessed visually and by a Chi² test. If the meta-analysis includes only a small number of studies, or where studies have small sample sizes, a P value of 0.10 will be applied for statistical significance. In addition, since Chi² can have low power when only few studies or studies of a small sample size are available, we will use the I² statistic to calculate the degree to which heterogeneity is having an impact on the analysis (Higgins 2008).

Assessment of reporting biases

If sufficient studies are found, funnel plots will be drawn to investigate any relationship between effect size and sample size. Such a relationship could be due to publication or related biases, or due to systematic differences between small and large studies. If a relationship is identified, clinical diversity of the studies will be further examined as a possible explanation. Every attempt will be made to obtain unpublished data and data from conference proceedings.

Data synthesis

Data synthesis will be performed using RevMan. We will assess continuous and binary data. Assuming that two or more studies that are suitable for inclusion are found, and that the studies are considered to be homogeneous, a meta-analysis will be performed on the results. A random-effects model analysis will be performed since we do not assume that each study is estimating exactly the same quantity.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis will be undertaken if clinically different interventions are identified, or there are clinically relevant differences between participant groups. Anticipated clinically relevant differences are:

1. intervention delivery type (e.g. therapist, parent-mediated, school-based) and length
2. intervention target skill (e.g. ToM as a whole, joint attention, emotion recognition, false belief understanding)
3. participant age (e.g. pre-school, young children, adolescents, adults), IQ (low versus normal or high), specific diagnosis and verbal ability.

Sensitivity analysis

Sensitivity analysis will be conducted to assess the impact of study quality on the results of the meta-analyses. For example, we will test to see if studies with high rates of loss to follow up or inadequate blinding are more likely to show positive outcomes and also to assess the impact of imputing missing data.

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Atladottir 2007

Baird 2006

Baron-Cohen 1985

Baron-Cohen 1995

Baron-Cohen 2000a

Bowler 1992

Bowler 1997

Carruthers 1996

Charman 2000

Creen 2002

Fombonne 2001

Firth 1994

Firth 2004

Garfield 2001

Happe 1994

Happe 1995

Hedges 1985

Higgins 2008

Joseph 2004

Kanner 1943

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Kasari C, Paparella T, Freeman S, Jahromi LB. Language outcome in autism: randomized comparison of joint

Klin 2005


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Leekam 2007


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Lord 1999


Mayes 2003


Melzoff 1993


Mundy 1994


Nassar 2009


Ozonoff 1991a


Ozonoff 1991b


Ozonoff 1995


Parsons 1999


Ponnet 2004


Premack 1978


Ruffman 2001


Rutter 2005


Swettenham 2000


Tager-Flusberg 2000


Wellman 2000


Wellman 2001

WHO 1993

Williams 2006

Wing 1979

Yeargin-Alsopp 2003

* Indicates the major publication for the study

APENDICES

Appendix 1. MEDLINE search strategy
1 exp Child Development Disorders, Pervasive/
2 pervasive developmental disorder$.tw.
3 PDD.tw.
4 childhood schizophrenia.tw.
5 autis$.tw.
6 kanner$.tw.
7 asperger$.tw.
8 (language adj3 delay$).tw.
9 (speech adj3 disorder$).tw.
10 or/1-9
11 randomized controlled trial.pt.
12 controlled clinical trial.pt.
13 randomi#ed.ab.
14 placebo$.ab.
15 drug therapy.fs.
16 randomly.ab.
17 trial.ab.
18 groups.ab.
19 or/11-18 (2574360)
20 exp animals/ not humans.sh.
21 19 not 20
22 10 and 21
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CONTRIBUTIONS OF AUTHORS

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<tr>
<th>Draft the protocol</th>
<th>S Fletcher-Watson</th>
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<tr>
<td>Develop a search strategy</td>
<td>S Fletcher-Watson</td>
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<tr>
<td>Select which trials to include (2 people + 1 arbiter in the event of dispute)</td>
<td>S Fletcher-Watson, I Manola, Arbiter: H McConachie</td>
</tr>
<tr>
<td>Extract data from trials (2 people)</td>
<td>S Fletcher-Watson, I Manola</td>
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<tr>
<td>Enter data into RevMan (Cochrane software)</td>
<td>S Fletcher-Watson</td>
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<td>Carry out the analysis</td>
<td>S Fletcher-Watson</td>
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<td>Interpret the analysis</td>
<td>S Fletcher-Watson, H McConachie</td>
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<tr>
<td>Draft the final review</td>
<td>S Fletcher-Watson, H McConachie</td>
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<tr>
<td>Keep the review up to date</td>
<td>S Fletcher-Watson</td>
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None

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