ORIGINAL ARTICLE

Auditory integration training and other sound therapies for autism spectrum disorders: a systematic review

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Objectives: To determine the effectiveness of auditory integration training (AIT) or other methods of sound therapy in people with autism spectrum disorders (ASD).
Study design: A systematic review was carried out of randomised controlled trials (RCTs) of adults or children with ASD. Meta-analysis was attempted.
Results: Six RCTs of AIT, including one crossover trial, were identified, with a total of 171 participants aged 3–39 years. 17 different outcome measures were used, with only two outcome measures used by three or more studies. Meta-analysis was not possible owing to very high heterogeneity or presentation of data in unusable forms. Three studies did not show any benefit of AIT over control conditions. Three studies reported improvements at 3 months in the AIT group for total mean scores of the Aberrant Behaviour Checklist (ABC), which is of questionable validity. Of these, one study also reported improvements at 3 months in the AIT group for ABC subgroup scores. No significant adverse effects of AIT were reported.
Conclusion: At present there is not sufficient evidence to support its use.

Autism spectrum disorder (ASD), or autism, refers to a wide spectrum of associated cognitive and behavioural disorders. Core features include impairments in socialisation and verbal and non-verbal communication, and restricted patterns of behaviour and interests.[1] Currently, educational, communication and behavioural methods remain the mainstay of treatment.[2] However, given the heterogeneity of ASD and the knowledge that there is no single known aetiology, a range of interventions and treatments have been developed. Treatments to overcome variations in auditory sensitivity commonly encountered in people with autism have been developed and are collectively called auditory integration therapies. They include auditory integration training (AIT), the Tomatis method and Samonas sound therapy.

AIT (Berard's method) was first developed in France in 1982.[3] Berard postulated that abnormal sensitivity or insensitivity to certain frequencies of sound waves, regardless of overall hearing ability, was associated with a range of behaviour and learning problems,[4] and that his technique of AIT would bring about a ''re-education'' of the hearing process. The technique gained wide popularity after the publication of Stehli's book,[5] *The sound of a miracle. A child's triumph over autism*, which reported the complete recovery of her daughter, Georgie (diagnosed with autism and schizophrenia), after 10 h of training in Berard's clinic. AIT involves 10 h of listening to electronically modified music delivered by headphones during two half-hour daily sessions over 10 days. The AIT device uses filtering to dampen peak frequencies to which the person is ''hypersensitive'', and delivers sounds modulated by random dampening of high and low frequencies and intensities.[4]

Tomatis sound therapy uses electronically modified human voice and music, delivered through an ''electronic ear''.[6] Samonas sound therapy involves listening to compact disc recordings of filtered music, voice and sounds of nature through headphones. The therapy was developed by Steinbach, using the work of Tomatis.[7]

In practice, all three methods of auditory integration require listening to electronically modified music for varying periods of time and are intended to ameliorate auditory processing defects and improve concentration. Therapists seem to be practising their own version of these methods and may modify treatment to suit the individual patient. This raises theoretical concerns as to whether such methods are comparable, owing to the variation in intensity and time.

This systematic review aimed to identify, evaluate and, if appropriate, combine any evidence of the effects of AIT or other methods of delivering sound therapy in people with autism.

METHODS

Inclusion and exclusion criteria

We included randomised controlled trials (RCTs) of adults or children with ASD. ASD included pervasive developmental disorders that were described in DSM-IV[8] and ICD-10[9] or diagnosed using a standard diagnostic instrument. They excluded child disintegrative disorder and Rett disorder. Types of interventions included were auditory integration therapy (AIT) or other sound therapies that involve listening to music modified by filtering and modulation, where filtering entails attenuating sounds at selected frequencies and modulation refers to random alternating of high and low sounds.[4] Control groups could be those having no treatment, on the waiting list, or having the usual therapy or placebo equivalent.

Standardised measures dealing with core features of autism, cognitive ability, auditory sensitivity and processing, quality of life and behaviour were considered to be suitable outcomes, and information about short-term, medium-term and long-term outcomes was sought. Available information regarding adverse events was noted.

Abbreviations: ABC, Aberrant Behaviour Checklist; AIT, auditory integration training; ASD, autism spectrum disorders; RCT, randomised controlled trial

Identification of trials

We searched the Cochrane Central Register of Controlled Trials (Cochrane Library Issues 3 and 4, 2004), Medline (1966–February 2005), Embase (1980–February 2005), Cinahl (1982–March 2005), PsycINFO (1887–March 2005), Eric (1965–July 2004), Lilacs (1982–March 2002) and the Health Technology Assessment database using the search terms listed in box 1. There were no language restrictions for the search. The Lilac database search was completed in English, Spanish and Portuguese.

Search terms were modified to meet the requirements of individual databases. The search strategy was developed to maximise sensitivity. Reference lists of identified trials and review articles were searched for further relevant publications. Authors of the included trials were contacted about their research. We did not write to other known experts.

Quality assessment

Titles and abstracts from the search were screened independently by two reviewers. Articles that appeared to fulfil the inclusion criteria were retrieved for full-text assessment and data extraction. Studies under consideration were independently evaluated for methodological quality by three reviewers. Each reviewer assigned each study to a quality category based on allocation concealment, as described in the *Cochrane Reviewers' Handbook* 4.2.2[10] (box 2). Study quality was also assessed on the basis of intention-to-treat analysis, standardisation and blinding of outcome assessment, and percentage lost to follow-up. Study quality was not scored on an additive basis.

Data management

Data extraction forms were developed to collect information about study location, methods, participant characteristics (eg, age, sex), frequency of AIT or other forms of sound therapy and outcome measures. Data were extracted by two independent reviewers, and disagreements were resolved by negotiation with a third reviewer. Information from authors was obtained, detailing methods of diagnosis of the participants, randomisation and recruitment. Only one study[11] published outcomes suitable for meta-analysis. All other authors were asked to provide summary statistics suitable for meta-analysis or de-identified raw data.

Box 1 Search terms

1 CHILD-DEVELOPMENT-DISORDERS-PERVASIVE*:ME *OR*
2 SPEECH-DISORDERS*:ME *OR*
3 AUTIS* *OR*
4 (PERVASIVE and (DEVELOPMENTAL and DISORDER*)) *OR*
5 PDD *OR*
6 (LANGUAGE next DELAY*) *OR*
7 (COMMUNICAT* next DISORDER*) *OR*
8 (SPEECH next DISORDER*)) *OR*
9 (CHILDHOOD next SCHIZOPHRENIA) *OR*
10 KANNER* *OR*
11 ASPERG* *OR*
12 ((ACOUSTIC or AUDITORY) and STIMULAT*) *OR*
13 (AUDITORY and ((DISCRIMINAT* or PERCEPTION*) or TRAIN*)) *OR*
14 (AURAL next LEARN*) *OR*
15 ((HEARING or SOUND) and THERAP*) *OR*
16 (LANGUAGE near ACQUI*) *OR*
17 (LISTEN* near COMPREHEN*) *OR*
18 (PERCEPTUAL near IMPAIR*) *OR*
19 (SENSORY next INTEGRAT*) *OR*
20 TOMATIS or SAMONAS

Box 2 Allocation concealment criteria[10]

(A) Adequate: concealment of the allocation, eg by telephone randomisation, or by the use of consecutively numbered, sealed, opaque envelopes

(B) Unclear: uncertainty about whether the allocation was adequately concealed, eg where the method of concealment is not reported

(C) Inadequate: allocation was definitely not adequately concealed, eg open random number lists or quasi-randomisation such as alternate days, odd/even date of birth, or hospital number

(D) Allocation not used as a criterion to assess study validity

Statistical analysis

All outcome data reported in included papers were continuous. Our initial intention was to undertake meta-analyses, using mean difference and standard deviation to take into account differences between treatment and control groups at baseline. These data were not provided by authors. Where data were available, point estimates and standard errors were calculated from t test scores and post intervention means using comprehensive meta-analysis software (Biostat). Assessment of suitability of data for meta-analysis and attempted meta-analysis was carried out using Review Manager V.4.2.2.

Consistency of results was assessed visually and by examining I^2,[12] a quantity which describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error. This was supplemented with a test of homogeneity to determine the strength of evidence that the heterogeneity was genuine. Where heterogeneity was found, the authors looked for an explanation.

Meta-analysis of Aberrant Behaviour Checklist (ABC) subscores was attempted using inverse variance and a random effects model with 95% confidence intervals. No other meta-analysis was attempted because studies used different outcome measures, or because data were not available in a usable form.

Although the authors intended to use funnel plots to investigate any relationship between effect size and study precision, the number of studies was too small and the outcome measures used were too inconsistent for this method to be viable.

As meta-analysis was not possible, neither sensitivity analysis nor subgroup analysis could be used to assess the effect of study quality, participant inclusion criteria or differences in treatment of administration.

RESULTS

Search results

The electronic search yielded 377 titles and abstracts. Figure 1 outlines the study selection process. Six RCTs fulfilled the inclusion criteria: four RCTs from the electronic search and two from reference lists and unpublished data. No trials that used sound therapies other than AIT included participants with ASD.

Characteristics of the studies included

The number of participants in the six studies included[11–17] ranged from 10 to 80; most studies had 20 or fewer participants (table 1). Diagnostic definitions of autism varied between trials (table 1). The participants in the trial by

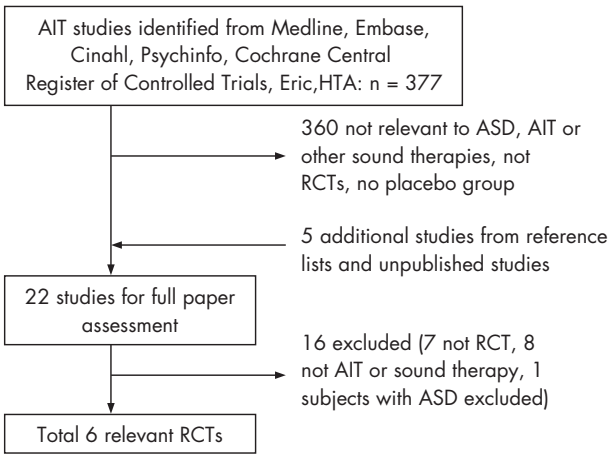

Figure 1 Flow chart outlining the study selection process. AIT, auditory integration training; ASD, autism spectrum disorder; HTA, Human Technology Assessment; RCT, randomised controlled trial

Zollweg *et al*[16] included 21 people with cognitive impairment and nine people with autism. Communication with the author confirmed that all 30 participants would have fulfilled DSM-IV criteria for an ASD; however, some had arrived in the institution before the introduction of DSM-IV. Clinicians associated with the participants at the time reaffirmed this (Zollweg W, 15 August 2002).

The treatment period was uniform for all trials, consisting of AIT for 10 consecutive days, with two 30 min sessions per day. Studies used different machine models and types of music. Control conditions were the same for five studies—namely, listening to unmodified music through headphones for the same time period as for the treatment group. In one study,[15] the music was played directly in the room for the control group, with non-functional headphones.

A total of 17 different outcome measures were used in the studies. Five of the trials used the ABC[19] as an outcome measure. Three studies[11 15 16] presented total and subgroup scores, with the remaining two[14 17] presenting total scores only. Three trials used Fisher's Auditory Problems Checklist—Parent,[20] and two trials used Conners' Rating Scales—Parent,[21] Leiter International Performance Scale[22] or pure tone discomfort test. The 12 other outcomes were each used by only one study.

Methodological quality of included studies

Although all six studies stated that participants were randomised, no information about methods of randomisation or allocation concealment was reported in five of the papers. After contact with the authors (S Edelson, 21 September 2002, 9 May 2003; O Mudford, 5 September 2002; W Zollweg, 15 August 2002; and S Bettison, 16 September 2002) allocation concealment was deemed inadequate for all of the studies (box 2). In four of the included studies,[11 13 14 17] the principal investigators were not blinded to the intervention but had little or no interaction with the outcomes assessors (as described in the study or confirmed by personal

Table 1 Characteristics of the studies included

Study	Trial type	Method of randomisation	Blinding	Duration of follow-up (months)	Diagnostic criteria	Age (years)	Follow-up	AIT interventions	Control condition
Bettison,[13] n = 80	Parallel RCT	Random numbers table	Outcome assessors blinded, investigators not blinded	12	Autism or Asperger's syndrome diagnosed by an independent agency	3–17	No loss to follow-up	2×30 min sessions for 10 consecutive days	As for AIT but music unmodified
Edelson *et al*,[14] n = 18	Parallel RCT	Telephone number	Outcome assessors blinded, investigator not blinded	3	Autism diagnosed by an independent agency and Rimland Diagnostic E-2 checklist[18]	4–39	Data from one control participant excluded due to no match in the AIT group	2×30 min sessions for 10 consecutive days	As for AIT but music unmodified
Mudford *et al*,[15] n = 16	Crossover RCT	Geographically divided into groups, then into subgroups alphabetically, by the first letter of their name	Investigators and outcome assessors blinded	14	Diagnosis: autism (DSM-IV or ICD-10 criteria)	5.75–13.92	5 lost to follow-up due to lack of cooperation, safety issues, transport problems	2×30 min sessions for 10 consecutive days	As for AIT, but headphones non-functional and unmodified music played in the room (not through AIT device)
Rimland and Edelson,[11] n = 17	Parallel RCT	Last 2 digits of telephone number	Outcome assessors blinded, investigator not blinded	3	Autism diagnosed by an independent agency and Rimland Diagnostic E-2 checklist[18]	4–21	1 lost to follow-up due to transport problems	2×30 min sessions for 10 consecutive days	As for AIT but music unmodified
Veale,[17] n = 10	Parallel RCT	Last 2 digits of telephone number	Outcome assessors blinded, investigator not blinded	3	Autism diagnosed by an independent agency	6–10 (approximately)	No loss to follow-up	2×30 min sessions for 10 consecutive days	As for AIT but music unmodified
Zollweg *et al*,[16] n = 30	Parallel RCT	Random numbers table	Investigators and outcomes assessors blinded	9	Cognitive impairment including ASD diagnosed by an independent agency	7–24	28 analysed for ABC at 9 months, 22 analysed for loudness discomfort, 14 analysed for pure tone thresholds	2×30 min sessions for 10 consecutive days	As for AIT but music unmodified

ABC, Aberrant Behaviour Checklist; AIT, auditory integration training; ASD, autism spectrum disorder; DSM-IV, Diagnostic Manual of Mental Disorders (4th edn); ICD, International Classification of Diseases; RCT, randomised controlled trial.

communication with the authors). The investigators were not blinded as they needed to set and give treatment.

The number of participants lost to follow-up varied (table 1). There were considerably fewer participants for audiological and sound sensitivity data for two trials[14 16] owing to the difficulty in obtaining reliable scores in the patient population. Intention-to-treat analysis was not used in the four trials in which there was loss to follow-up.[11 14–16]

Five of the trials were of a parallel design and one[15] was a crossover study. The crossover study included a washout period of at least 4 months between treatments. It is not certain whether the washout period was adequate.

Outcome measures

All trials used at least one standardised behaviour scale outcome. Of the five studies[11 14–17] that used the ABC,[19] all published total scores, including group means or difference scores. The ABC consists of five subgroup scores. The tool is not designed to calculate a total or grand mean score; therefore, a meta-analysis of total ABC scores was not carried out (communication with Dr Michael Aman, 24 June 2003, 2 December 2004). Meta-analysis of changes in the ABC subgroup scores 3 months post intervention was attempted for two eligible studies.[11 16] Inconsistency between these studies was extremely high (I^2 ranging from 55.4% for hyperactivity to 87.8% for stereotypic behaviours subgroups); therefore, meta-analysis was deemed inappropriate. This inconsistency may have been due to the many differences between the studies, notably participant characteristics and data collection.

The largest trial[13] by Bettison did not use the ABC as an outcome measure and instead used the Autism Behavior Checklist,[23] which is part of a broader tool, the Autism Screening Instrument for Educational Planning.[24] Using this instrument, Bettison reported improvement in both groups, but no significant between-group differences were found when the effects of group and time and their interaction were analysed. One study[11] reported a significant improvement ($p<0.05$) in Fisher's Auditory Problems Checklist[20] scores for the treatment group at the 3-month follow-up. Veale[17] reported no significant improvement for the Conners' Rating Scales—Parent,[21] the Fisher's Auditory Problems Checklist or the ABC, only a ''trending towards positive therapeutic effects'' at the 3-months follow-up. Mudford *et al*[15] used direct observational data in addition to behaviour rating scales.[15] Overall, combined data from parents, teachers and observers did not show a benefit with AIT. No other measures of behavioural problems were used by more than one study or reported in suitable form for meta-analysis.

Mudford *et al* did not report marked cognitive improvements for either the AIT or control groups after 14 months of follow-up, whereas Bettison described improvement in both groups at 6 and 12 months. All data were presented as group mean scores before intervention and after intervention.

Sound sensitivity outcome measures differed between trials and were non-standardised, and meta-analysis was not possible.

Two of the trials[11 13] sought to measure the adverse effects of therapy. Minor physical complaints were reported by parents in both groups for both studies, and no significant differences were found between treatment and control groups. Mudford *et al*[15] mentioned minor side effects reported anecdotally by parents at the end of the study. Three studies[14 16 17] did not report the recording of adverse events in their trials. No study reported specific deterioration in behaviour measured on a standardised test.

DISCUSSION

In this systematic review, data synthesis was limited by statistical and clinical heterogeneity. Studies reported a disparate range of clinical outcomes, many of which were used by only one study each. Variation in statistical methods between studies was common, and data were presented in forms that could not be converted for use in meta-analysis software. The largest studies[13 16] did not report a difference between treatment and control conditions. A power analysis to calculate sample size was carried out in only one study[13] (using two standardised behavioural checklists) and included a total of 80 participants. One small crossover trial[15] also reported no long-term benefits of AIT. Although three small trials[11 14 17] reported an improvement in ABC scores in the AIT group at 3 months, the clinical relevance of these results is uncertain, because the total score of the ABC is not, according to the person who developed the instrument, a clinically meaningful outcome.[19] The author of the instrument has stated that the use of a ''total aberrant score'' is incorrect and inconsistent with the instrument's design. Results should be presented as the five subscale scores.[19] The only trial that used such subscales[11] did note a statistically significant improvement in ABC subscale scores in the AIT group at 3 months. The age range of participants was wide in this review. It was not possible to analyse the results for different age groups, nor was this discussed in any of the studies. Given that language skills are best acquired in young children, it is possible that greater improvements would be seen in a younger sample or that improvement in language in younger participants might be blinded by fewer gains in a generally older sample. Likewise, duration of follow-up for a lifetime condition such as autism is important. Follow-up in trials included in this review did not exceed 14 months.[15]

Berard[4] did not specify the outputs intended for AIT. However, questions have been raised on the potential harms of AIT,[25] particularly regarding whether output levels of the machines exceed safe limits. Lucker[25] concluded that AIT will not put listeners at risk of hearing loss, provided practitioners use lower rather than maximal settings on the equipment. Four of the trials described the output used for their machines[13–16] and described compliance with manufacturers' recommendations or adjustment to comfort level.

A statement issued by the American Academy of Pediatrics[26] in 1998 suggested limitation of the use of AIT to research protocols only, based on the available information at the time. This included concerns about the validity and theoretical basis of the therapy.[27] Recent reviews[28 29] have reached similar conclusions. AIT continues to be practised worldwide,[30] despite evidence that shows it to be still an experimental treatment at best, and one which may be only available at a considerable cost to the family.

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permission): Sinha Y, Silove N, Wheeler D, Williams K. Auditory integration training and other sound therapies for autism spectrum disorders. *Cochrane Database Syst Rev* 2004;(1):CD003681 (see www.thecochranelibrary.com). The Cochrane version of this review will be updated as new evidence emerges, and in response to comments and criticisms. The results of a Cochrane review can be interpreted differently, depending on people's perspectives and circumstances. Please consider the conclusions presented carefully. They are the opinions of review authors, and are not necessarily shared by The Cochrane Collaboration.

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ARCHIVIST

Nitric oxide to prevent bronchopulmonary dysplasia

There is animal evidence that inhaled nitric oxide (NO) reduces lung inflammation, improves surfactant function, attenuates hyperoxic lung injury, and promotes lung growth. It is hoped, therefore, that it might prevent bronchopulmonary dysplasia (BPD). Trials in preterm infants with respiratory failure have, however, given inconclusive results. Now two US multicentre trials have provided some support for treatment with inhaled NO.

In a 21-centre trial (*New England Journal of Medicine* 2006;**355**:343–53; see also editorial, ibid: 404–6) 582 infants (birthweights 500–1250 g, mean gestational age 26 weeks) on mechanical ventilation (or on nasal CPAP if birthweight <800 g) were randomised at age 7–21 days to inhaled NO or placebo for at least 24 days. NO was given in an initial concentration of 20 ppm, gradually decreasing. The rates of survival to 36 weeks postmenstrual age without BPD were 44% (NO) vs 37% (placebo), a significant difference. The results were similar in infants above or below 800 g birthweight but the study was not powered to detect weight-group differences in outcome. A post hoc analysis showed that the benefits only applied to infants aged 7–14 days at randomisation. The NO group left hospital sooner and spent less time on supplemental oxygen. There were no short-term serious adverse effects of NO.

In a 16-centre trial (ibid: 354–64) 793 ventilated infants (gestational age 34 weeks or less, birthweight 500–1250 g) were randomised within 48 hours of birth to a lower dose of NO (5 ppm) for 21 days or until extubation. Only infants with birthweights of 1000 to 1250 g had a significant reduction in death or BPD (39% vs 64%) or BPD alone (30% vs 60%) with NO but the incidence of intracranial haemorrhage, periventricular leukomalacia, and ventricular enlargement was reduced by NO in the whole cohort.

In these trials inhaled NO was associated with no evidence of harm and may have prevented BPD, especially among the larger infants. The time of starting treatment and the dose of NO were different in the two trials. The editorialist points out that NO is probably not effective in preventing death or BPD in the sickest and smallest infants, longer follow up is needed before it can be said to be safe, and it is expensive. She advises that this use of inhaled NO should still be restricted to clinical trials.