International multicentre randomised controlled trial of improvisational music therapy for children with autism spectrum disorder: TIME-A study

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Declared competing interests of authors: The institutions of most of the authors have received funding from the National Institute for Health Research Health Technology Assessment programme for other studies. Christian Gold received funding from the Research Council of Norway during the conduct of the study. Christian Gold, Claire Grant, Helen Odell-Miller, Sarah Faber, Karin Antonia Mössler, Stephan Sandford, Anna Maratos and Monika Geretsegger are clinically trained music therapists.

Published October 2017
DOI: 10.3310/hta21590

Scientific summary

The TIME-A study

Health Technology Assessment 2017; Vol. 21: No. 59
DOI: 10.3310/hta21590

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

One out of every 100 children have autism spectrum disorder (ASD). The core features of the condition are persistent impairment in reciprocal social interaction and social communication, together with restricted, repetitive patterns of behaviour, interests or activities. ASD are associated with an increased risk of poor mental health, social exclusion and reduced quality of life. The costs associated with ASD in the UK are estimated to be > £28B per year.

The evidence base for effective early intervention is weak. Recent guidance from the National Institute for Health and Care Excellence (National Institute for Health and Care Excellence. *Autism: Management and Support of Children and Young People on the Autism Spectrum. Clinical Guideline 170*. London: National Institute for Health and Care Excellence; 2013) emphasised advice, education and support for parents and efforts to adjust the child's environment to minimise the impact of their difficulties.

A systematic review in 2014 (Geretsegger M, Elefant C, Mössler KA, Gold C. Music therapy for people with autism spectrum disorder. *Cochrane Database Syst Rev* 2014;**6**:CD004381) identified 10 small randomised controlled trials (RCTs) of music therapy (involving 165 participants) and found evidence of improvements in social interaction and communication. The authors concluded that music therapy may help children with ASD, but highlighted differences in delivery between trials and normal clinical practice. In clinical practice, most children received weekly sessions, but trials have generally tested more frequent sessions. Another limitation is that the trials examined the impact of music therapy only while it was being delivered. No trials have tested if any benefits persist once treatment stops.

The TIME-A study is an international multicentre RCT funded by the Research Council of Norway to investigate the clinical effectiveness of improvisational music therapy (IMT) for children with ASD. We obtained funding for recruitment in England.

Objectives

To examine whether or not adding IMT improves children's social affect and social responsiveness, and to explore whether or not any benefits are influenced by how often the treatment is offered. In the National Institute for Health Research (NIHR)-funded arm, we also explored if music therapy was associated with reduced stress and improved mental well-being of parents.

Methods

Study design

A three-arm, international, multicentre, Phase III RCT. Researchers conducting assessments were masked to allocation status, but participants, their families and staff involved in their care were not.

Setting

State-funded, voluntary and private sector-funded health, educational and social care services in Australia, Austria, Brazil, Israel, Italy, Korea, Norway and the USA. Participants for the NIHR-funded arm of the study were recruited from schools and NHS clinics in Bedfordshire, Cambridgeshire, Essex and London.

Target population

Children aged between 4 years and 6 years and 364 days (i.e. > 4 years but < 7 years) with a clinical diagnosis of ASD that was confirmed using the Autism Diagnostic Observation Schedule (ADOS), and two of the three domains of the Autism Diagnostic Interview-Revised (ADI-R). We excluded children who were already receiving music therapy or had done so within the past 12 months, children with severe sensory disorder and those whose parent or guardian was unable or unwilling to provide written informed consent to participate.

Health technologies being assessed

Parents/guardians (referred to as 'parents' in the remainder of this report) of all participants were offered enhanced standard care (ESC) by adding three sessions of advice and support to the care they would otherwise have received. Half of all children were also offered IMT for 5 months, either three times per week (high frequency) or once per week (low frequency). All music therapy sessions were 30 minutes long and delivered in accordance with consensus guidelines.

Measurement of outcomes

The primary outcome was the child's social affect at 5 months using the social affect scale of the ADOS. Higher scores indicated greater impairment. Secondary outcomes included social affect measured at 12 months and social responsiveness reported by parents using the Social Responsiveness Scale (SRS) at 5 and 12 months. Following feedback from parents of children with ASD in England, we also assessed parental stress, using the Parenting Stress Index – Short Form (PSI-SF), and parental well-being, using the short version of the Warwick–Edinburgh Mental Well-Being Scale, at 5 and 12 months in the NIHR-funded English arm of the trial. Higher scores on the PSI-SF indicated higher levels of stress, and higher scores on the Warwick–Edinburgh Mental Well-Being Scale indicated higher levels of mental well-being.

Study logistics

Potential participants were identified by teachers and staff working in schools who deliver specialist education to children with developmental problems, and by clinical staff in health centres. Parents who gave verbal consent to meet a researcher were given written and verbal information about the study. Those willing to take part were asked to provide written informed consent to assess eligibility and to complete baseline assessments.

Those meeting the eligibility criteria were randomised by a remote service (based in Norway) using an allocation ratio of 1 : 1 : 2 (high-frequency music therapy : low-frequency music therapy : ESC alone). We used block randomisation with randomised block sizes of four or eight, stratified by study centre.

Follow-up assessments were conducted 5 and 12 months after randomisation by a researcher who was masked to the participant's allocation status.

Sample size

We estimated that a sample of 235 participants would provide 90% power to detect a medium effect size of the intervention in the social affect score of the ADOS at 5 months, with a 5% level of statistical significance. To take account of clustering and loss to follow-up, we set out to recruit a minimum of 300 children and their families. We aimed to recruit 100 participants in the NIHR-funded arm of the trial to help the international study to achieve the required sample.

Data analysis

All primary analyses were by intention to treat using two-sided tests and a 0.05 level of statistical significance. The primary analysis compared changes in the social affect score of the ADOS between baseline and 5 months in the pooled active arms and controls randomised to ESC. Following assessment of normality, treatment effects were analysed using generalised estimating equations that allow for analysis of longitudinal data while accounting for correlations among the repeated observations for each participant. Generalised estimating equation analyses were also used to examine dose–effect relationships and to explore possible confounding effects of site or relevant subgroups, such as age and gender.

Results

Between November 2011 and November 2015, 702 children were assessed for eligibility, of whom 315 were excluded ($n = 109$ ineligible; $n = 206$ declined) prior to the baseline assessment, and another 23 were found ineligible and not randomised. Among the 364 remaining participants, 182 were allocated to IMT plus ESC (90 to high-frequency sessions and 92 to low-frequency sessions) and 182 were allocated to ESC alone. Participating children had a mean age of 5 years and 4 months (standard deviation 0.9 years) and 302 (83.0%) were male. In total, 316 (86.8%) were followed up 5 months later. Among the 182 participants randomised to IMT, 171 (94.0%) received it. The median number of sessions attended was 19 (35 in those offered high-frequency therapy and 15 in those offered low-frequency therapy).

No difference in the primary outcome was found between trial arms. The mean change in social affect scores at 5 months between the active and control arms of the trial was 0.06 [95% confidence interval (CI) –0.70 to 0.81]. The mean difference in change in parent-reported SRS score between those randomised to IMT and ESC was –3.64 (95% CI –7.72 to 0.94; $p = 0.90$).

A total of 81 participants were recruited in the NIHR-funded arm of the trial. All 41 (100%) children randomised to IMT in the NIHR-funded arm of the trial received it. The median number of sessions attended was 43 in the high-frequency group and 15 in those randomised to the low-frequency group.

The outcomes of participants in the NIHR-funded arm of the trial did not differ from those in the international study. Parents of children who were randomised to music therapy reported less distress at 12 months (difference of –3.73%, 95% CI –2.39 to – 10.86; $p = 0.007$); no differences were seen in parental mental well-being. Further details of the results of the study have been published in the *Journal of the American Medical Association* (Bieleninik L, Geretsegger M, Mössle K, Assmus J, Thompson G, Gattino G, *et al.* Effects of improvisational music therapy versus enhanced standard care on symptom severity among children with autism spectrum disorder: the TIME-A randomized clinical trial. *JAMA* 2017;**318**:523–4).

Implications for health care

Many children with ASD enjoy music and engage well with music therapy. However, adding IMT to other treatments received by children aged 4–7 years with ASD does not appear to improve the core symptoms of this disorder.

Recommendations for future research

Future research should examine alternative methods for delivering music-focused interventions for children with ASD.

Trial registration

This trial is registered as ISRCTN78923965.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the NIHR.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.236

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 12/167/95. The contractual start date was in June 2014. The draft report began editorial review in April 2017 and was accepted for publication in August 2017. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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