Phonics Training Improves Reading in Children with Neurofibromatosis Type 1: A Prospective Intervention Trial

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Objective To examine the efficacy of a phonics-training program in children with neurofibromatosis type 1 (NF1) and reading difficulties.

Study design Thirty children (7-12 years of age) with NF1 completed a double-baseline, 24-week intervention trial. Literacy outcome measures were assessed at 4 time points: (1) at baseline; (2) after an 8-week no-treatment period; (3) immediately post-treatment; and (4) at follow-up 8 weeks post-treatment. Repeated-measures ANOVA were conducted to examine change over time for all outcome measures, and significant main effects were explored with planned comparisons. Predictors of treatment effects were examined by linear regressions.

Results Ninety percent of participants completed the intervention. Intervention-specific improvements were observed across a range of literacy outcomes, including reading accuracy (nonword reading, Cohen $d = 1.10$; regular-word reading, Cohen $d = 0.32$), letter-sound knowledge (Cohen $d = 0.80$), blending (Cohen $d = 0.88$), repetition of nonsense words (Cohen $d = 0.94$), phonemic decoding fluency (Cohen $d = 0.55$), and reading comprehension (Cohen $d = 0.31$). Improvements were maintained 8 weeks post-treatment. Age ($P = .03$) and working memory ($P = .02$) significantly influenced efficacy, with greatest improvements observed in older children with stronger verbal working memory capacity.

Conclusions Home-based, computerized reading intervention was effective in improving the reading and reading-related abilities of children with NF1 and reading difficulty. *(J Pediatr 2016;177:219-26).*

Trial registration Australian and New Zealand Clinical Trials Registry: ACTRN12611000779976

Neurofibromatosis type 1 (NF1) is an autosomal-dominant genetic disorder with a birth incidence approximating 1 in 2700.[1] Although NF1 is characterized by a diverse range of cutaneous and neoplastic manifestations,[2] the most common complication in childhood is cognitive impairment.[3] While intelligence is typically within normal limits, specific cognitive deficits are demonstrated in up to 80% of children, with executive dysfunction, reduced attention, and poor visuospatial processing common areas of impairment.[3] These manifest in a variety of ways, including attention deficit-hyperactivity disorder (ADHD),[4] psychosocial maladjustment,[5] and academic failure caused by specific learning disabilities.[6]

Reading difficulties, including impairments in single-word reading and comprehension, are well documented in the NF1 literature[3,7-12] and are the most frequently reported concern of parents and teachers, reflecting a deep functional impact.[13] Although the factors contributing to reading difficulty in NF1 are not well understood, several studies have reported weaknesses in phonological awareness, also a significant predictor of reading ability in the general population.[14] Thus, deficits in identifying and manipulating units of oral language likely contribute to reading difficulty in NF1. Impairments in linking letters/letter groups to their corresponding sounds (phonological decoding or grapheme-to-phoneme correspondences) have also been identified, with up to 67% of children with the condition exhibiting impaired nonword reading.[12] Furthermore, the highly prevalent visuospatial deficits in children with NF1 also additionally contribute to the high frequency of reading impairments.[7] With an increased risk of internalizing and externalizing disorders such as ADHD and depression in children with reading difficulty,[15,16] it is critical to evaluate the efficacy of theory-driven reading interventions in this at-risk group with a unique cognitive phenotype.

ADHD	Attention deficit-hyperactivity disorder
CC2	Castles and Coltheart 2
FISIQ	Full-scale IQ
NF1	Neurofibromatosis type 1
SES	Socioeconomic status
t1	Time point 1
t2	Time point 2
t3	Time point 3
t4	Time point 4
WISC-IV	Wechsler Intelligence Scale for Children 4th Edition, Australian Adaptation

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Supported by Children Tumor Foundation Young Investigator Award (2011-01-009 [to J.P.]). The authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2016.06.037

To date, one study has examined the efficacy of remedial training in children with NF1 and reading difficulty.[17] In that randomized trial, patients with NF1 received 15 hours of direct individual instruction on phonological awareness and sound-symbol correspondences via either a kinesthetic-based teaching approach (n = 8) or a visual-based method (n = 9). Reading outcomes improved in both conditions and established that mainstream methods of remedial reading instruction are likely to be appropriate for treating reading difficulty in children with NF1.

Here we examined the efficacy of a low-cost, home-based, phonics-training program in improving reading and reading-related abilities of children with NF1. On the basis of evidence that systematic instruction in phonics is effective in improving the literacy skills of children with reading difficulty from the general population[18] and preliminary evidence that mainstream reading instruction also may be effective in treating reading difficulty in children with NF1, we hypothesized that formal instruction in letter-to-sound correspondences would improve the reading of words that require phonological decoding (ie, grapheme-to-phoneme correspondences). Secondary aims were to determine whether the intervention resulted in gains across a broader range of literacy skills that were more distal to the intervention, including reading comprehension.

Methods

Participants were recruited from the Neurogenetics Clinic at The Children's Hospital at Westmead, Sydney, Australia (Australian New Zealand Clinical Trials Registry: ACTRN12611000779976). The majority of participants were screened after presentation for routine evaluation of their neuropsychologic functioning, which is part of the standard-of-care services offered to children with NF1 through our clinic. Participants were screened with the following criteria: (1) clinical diagnosis of NF1;[19] (2) age 7-12 years; (3) impaired nonword reading (≥1.5 SD below mean) on the Castles and Coltheart 2 (CC2) reading test;[20] (4) IQ ≥80; and (5) possession of a home computer with Internet access. Exclusion criteria were: (1) documented evidence of symptomatic intracranial pathology; (2) insufficient English to complete assessments; or (3) inadequate vision/hearing. No participant received any other intervention for reading difficulties during the study. Approval for the study was granted by the Sydney Children's Hospital Network (HREC/11/CHW/28) and University of Sydney (15371) Human Research Ethics Committees. Written informed consent was obtained from all participants' parents.

This was a prospective, single-site, double-baseline intervention trial during a 24-week period. Participants were assessed at 4 separate time points (**Figure 1**; available at www.jpeds.com). Outcome measures and additional neurocognitive tasks (see the section "Mediating Measures") were administered at the initial baseline assessment, lasting approximately 150 minutes (time point 1; t1). All outcome measures were repeated across 3 time points (time points 2-4), each assessment lasting approximately 90 minutes. Time point 2 (t2) was a double-baseline assessment after 8 weeks of no treatment. This enabled us to assess for the impact of test-retest effects and normal developmental growth. Participants then completed the intervention for 8 weeks, after which outcome measures were readministered at a post-treatment assessment (time point 3; t3). Maintenance effects were evaluated after a further 8 weeks of no treatment (time point 4; t4). At each time point, participants were assessed individually in a quiet clinical setting by a psychologist. Short rest breaks were provided as needed. The only incentive offered to participants was a certificate provided by the study team.

Outcomes

Our primary outcome was nonword reading accuracy on the CC2 reading test, a measure of phonological decoding.[20] This measure consisted of 40 nonwords (nonsense words that could be read using common letter-to-sound rules; eg, gop) intermingled in a set order with 40 regular and 40 irregular words. Words were presented on an individual card, one at a time. One point was awarded for each correctly read nonword and a stopping rule of 5 consecutive errors was used. Secondary outcomes included regular word reading (words that follow letter-to-sound rules; eg, pump) and irregular word reading (words that cannot be read using letter-to-sound rules; eg, yacht) from the CC2 reading test.[20] Other secondary outcome measures included the Test of Word Reading Efficiency,[21] which assesses phonemic decoding and sight word fluency, and the Repetition of Nonsense Words from the Developmental Neuropsychological Assessment, 2nd edition,[22] which measures phonological encoding and decoding. The Test of Everyday Reading Comprehension[23] was administered to assess understanding of passages on everyday items (eg, shopping list), and spelling abilities were assessed via the Spelling subtest from the Wechsler Individual Achievement Test, 2nd edition.[24] All of these measures were administered and scored in accordance with test manuals.

Several experimental measures also were included. Letter knowledge was assessed by presenting participants with 14 single letters printed in either upper or lower case and asking them to write the same letter in upper case if it was presented in lower case and vice versa. Children's letter-sound knowledge was assessed by presenting 51 individual letters or letter combinations printed on flashcards and asking them to identify the sounds they made. Correct responses were awarded 1 point, and there was no discontinue rule. For the Blending task, children were presented verbally with a nonword segmented into phonemic parts (eg, v-ar) and they were asked to put the parts together to make a complete, made-up word. There were 28 items; correct identifications were awarded 1 point and the test was discontinued after 5 consecutive errors.

Mediating Measures

Mediating measures were administered at t1 only. Intelligence was assessed with either the Wechsler Abbreviated Scale of Intelligence (n = 8)[25] or the Wechsler Intelligence Scale for Children 4th Edition, Australian Adaptation (WISC-IV; n = 22)[26]; the latter was used if IQ had been clinically