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High success rates of sedation-free brain MRI scanning in young children using simple subject preparation protocols with and without a commercial mock scanner—the Diabetes Research in Children Network (DirecNet) experience

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Abstract

Background—The ability to lie still in an MRI scanner is essential for obtaining usable image data. To reduce motion, young children are often sedated, adding significant cost and risk.

Objective—We assessed the feasibility of using a simple and affordable behavioral desensitization program to yield high-quality brain MRI scans in sedation-free children.

Materials and methods—222 children (4–9.9 years), 147 with type 1 diabetes and 75 age-matched non-diabetic controls, participated in a multi-site study focused on effects of type 1 diabetes on the developing brain. T1-weighted and diffusion-weighted imaging (DWI) MRI scans were performed. All children underwent behavioral training and practice MRI sessions using either a commercial MRI simulator or an inexpensive mock scanner consisting of a toy tunnel, vibrating mat, and video player to simulate the sounds and feel of the MRI scanner.

Results—205 children (92.3%), mean age 7 ± 1.7 years had high-quality T1-W scans and 174 (78.4%) had high-quality diffusion-weighted scans after the first scan session. With a second scan session, success rates were 100% and 92.5% for T1- and diffusion-weighted scans, respectively. Success rates did not differ between children with type 1 diabetes and children without diabetes, or between centers using a commercial MRI scan simulator and those using the inexpensive mock scanner.

Conclusion—Behavioral training can lead to a high success rate for obtaining high-quality T1- and diffusion-weighted brain images from a young population without sedation.

Keywords

MRI; Diffusion-weighted imaging; Sedation-free; Sedation; Mock scanner; Behavioral preparation; Children; Diabetes

Introduction

Young children are often sedated for MRI scans to reduce anxiety and to ensure acquisition of interpretable images without motion artifacts. However, sedation adds significant cost and risk of adverse reaction to medications used for anesthesia or sedation. Further, recent studies have raised concern regarding adverse effects of anesthesia in developing brains [1, 2]. Specifically, evidence from studies in rodents and non-human primates suggests that anesthesia exposure during brain development might trigger apoptotic neuro-degeneration [3, 4]. Effects of anesthesia on developing human brains are still under investigation. Some preliminary studies have shown an association between early exposure to anesthesia and learning disabilities or behavioral disturbances [5, 6], whereas others have not [7]. Given these concerns, it is desirable to develop interventions that would allow sedation-free imaging studies whenever possible. Previous studies have reported success rates of non-sedated MRI scans in different clinical populations of young children, using either scanning during natural sleep, a play MRI model, or a commercial mock scanner [8–11]. However, there are no reports of the success rates of non-sedated MRI scans in a large sample of

young children following a comprehensive, simple and cheap behavioral preparation and training program. In this report we describe our behavioral preparation program employed in a large multicenter study of young children with type 1 diabetes and age-matched non-diabetic controls undergoing brain MRI to assess the effects of type 1 diabetes on the developing brain, and report the success rates of obtaining high-quality brain MR images from this sample.

Materials and methods

Recruitment and exclusion criteria

Study participants between 4.0 years and <10.0 years of age were recruited at five clinical centers in the Diabetes Research in Children Network study group (Nemours Children's Clinic in Jacksonville, FL; Stanford University; University of Iowa; Washington University in St. Louis; and Yale University) from August 2010 to March 2012. For both the type 1 diabetes participants and the non-diabetic controls, exclusions included: preterm birth (prior to 34 weeks' gestation), low birth weight (less than 2,000 g), intellectual or learning disability, prior inpatient psychiatric treatment or any neurological disease unrelated to diabetes.

Informed written consent was obtained from the parent or legal guardian of all participants, and assent was obtained as required by local institutional review boards. The studies were reviewed and approved by the five centers' institutional review boards and an NIH designated Data Safety Monitoring Board. All participants were screened for MRI contraindications (e.g., metal implants, orthodontic appliances or claustrophobia).

Cognitive testing

Children were given four subtests (block design, similarities, vocabulary, matrix reasoning) from the Wechsler Preschool and Primary Scale of Intelligence III (WPPSI III) [12] or the Wechsler Adult Intelligence Scale [13], depending on their age. Full Scale IQ could not be calculated from these subtests for the WPPSI III, so we averaged the scaled scores from the subtests to provide an estimate of overall intelligence compared to a normative population (mean 10, SD 3).

Child preparation

All centers received detailed manuals on MRI scan preparation as well as an on-site training session. Behavioral preparation of the participants for the brain MRI scans included the following:

1. In-home behavioral exposure to scanner sounds and environment using (a) a video describing the MRI environment and procedure, (b) recordings of MRI sounds played to the child at home and (c) a brochure describing a game designed to encourage the child to practice staying still like a statue ("The Statue Game"). The brochure was written in child-friendly language and included a sticker chart and star stickers. Parents were asked to practice with their child until he or she was able to lie still for 10 min-intervals (the length of the longest single scan sequence in our study). The children earned a sticker for every time-increment they were able to lie still. Resources for preparing children for their brain MRI scan can be found on the Center for Interdisciplinary Brain Sciences Research (CIBSR) website: <http://cibsr.stanford.edu/participating/HomePreparation.html> and <http://cibsr.stanford.edu/participating/Games.html>.
2. Practice at the clinical center with a mock-MRI session. Children underwent practice sessions (30–60 min) in an MRI simulator. If the child moved his or her

head, staff provided behavioral feedback by interrupting the movie and using gentle verbal reminders to keep still. Different simulators were used at different sites, using either a commercial MRI simulator (a plastic shell that resembles an MRI scan with a moving table that simulates the MRI experience) or an inexpensive mock scanner consisting of a toy tunnel, a hat box and foam padding (simulating the head-coil), a vibrating massage mat (to simulate scanner movement during the diffusion-weighted scan), and a portable small video player (iPod Touch®; Apple Co., Cupertino, CA) to simulate the sounds and feel of the MRI scanner (Fig. 1). An iPod Touch connector was used to connect the video player to the play tunnel through small slits cut into the tunnel wall. The video player was controlled by remote control (e.g., movie was stopped for a few seconds if the child was observed to move his or her head). The cost of the inexpensive mock scanner is approximately \$80, plus the cost of the video player.

3. Researchers were trained to use child-friendly interactions to promote the child's comfort and motivation during the MRI scan.
 - a. Research staff used child-friendly language. For example, the MRI was described as a "large camera," the head coil was introduced as the "mirror holder" (the mirror is necessary to watch the movie) [14].
 - b. The children were shown pictures of brain scans in which the child moved and scans without motion to demonstrate the importance of keeping still.
 - c. The children were offered incentives for their participation at the scan center, including a small prize after the mock scanner and another small prize of their choice for completing the MRI scan. They also received a picture of their brain.
 - d. The children were offered a blanket prior to the scan. The blanket was wrapped tightly around the child and provided comforting warmth while also restricting movements, serving as a reminder to keep limbs still.
 - e. Four of the scan sites had the capability to play a movie during the real MRI.

Image acquisition

Sagittal T1-weighted images of the brain were acquired using a magnetization-prepared rapid gradient echo (MP-RAGE) pulse sequence with scan duration of 4:54 min. A diffusion-weighted image was acquired with duration of 4:59 min. By default, two MP-RAGE and two diffusion-weighted acquisitions were obtained for all participants to increase the probability that at least one scan would be collected with minimal head motion; this is similar to recommendations by the Alzheimer's Disease Neuroimaging Initiative [15]. Scan operators were instructed to review the image quality of the scans and add T1-W or diffusion-weighted scans if necessary, up to a 50-min scan session. A typical scan time was 25 min.

All scanning sites used a Siemens 3-T Tim Trio MRI scanner (Siemens Healthcare, Erlangen, Germany) with a 12-channel head coil along with standard Siemens product sequences to minimize multisite effects. A single scanning protocol was prepared and distributed to all sites. All sites used secure communication protocols to transmit image data to the Image Coordinating Center (at the Center for Interdisciplinary Brain Sciences Research at Stanford University) for the analyses. All participant data were transferred to the Image Coordinating Center within 48 h of scan acquisition; there the images were reviewed for quality. T1-W and diffusion-weighted image data were evaluated separately for

acceptability. T1-W images were first assessed by visual inspection to exclude scanner or motion-related artifacts. Images were then processed using the Freesurfer 5.1 image analysis suite at <http://surfer.nmr.mgh.harvard.edu/>, a semi-automated image processing pipeline, to obtain initial estimates of the cortical surfaces of the brain (i.e., gray matter–white matter boundary). It is important to note that the quality of these cortical surface estimates is dependent on the presence of sufficiently high signal and contrast in the images and minimal motion-related artifacts. Images were deemed unacceptable if cortical surface estimates were poor. Diffusion-weighted images were inspected for artifacts using DTIstudio (www.mristudio.org). Diffusion-weighted scans were rated as usable if a visual review revealed no artifacts or if artifacts were small and did not affect surrounding images (in which case, the images with artifacts were removed from further calculations). Individual sites were notified if a child needed to be called back for a second scanning session. A second MRI session was performed on a separate day if image quality of the T1-W or diffusion-weighted scans was deemed unacceptable after the first attempt. If needed, training was repeated before the second scan.

Results

Results are shown in Tables 1, 2 and 3. One hundred fifty children with type 1 diabetes and 76 non-diabetic control children participated in this study. Four children (3 with type 1 diabetes and 1 non-diabetic control) were unable to successfully complete the mock MRI training session and were therefore not included in the study.

A total of 147 children with type 1 diabetes and 75 non-diabetic controls (98% of all participants) between the ages of 4 years and <10 years (120 boys, 102 girls) attempted a brain MRI scan and were included in this analysis. It is important to note that our definition of a usable scan was one that could be used for high-resolution anatomical studies. These criteria are generally more stringent than those required for clinical scans because radiologists can interpret brain images for ruling out significant pathology even when images have mild-to-moderate artifacts. Despite these stringent criteria, 92.3% of the total cohort had usable T1-W scans and 78.4% had usable diffusion-weighted scans after the first attempt. Furthermore, of the 43 children who returned for a second MRI, 100% had usable T1-W scans and 76.2% had usable diffusion-weighted scans. Children who failed the diffusion-weighted scan were predominantly boys (one girl). There were no differences in age, average scaled score of IQ subtests ($P=0.2$) or parent-rated anxiety ($P=0.6$) and hyperactivity scores ($P=0.6$) between children who successfully completed a diffusion-weighted scan and those who did not (Table 3). Six children, three with type 1 diabetes and three controls, needed a second scan but did not return for a second scan. There was no significant difference between scan success rates for children with type 1 diabetes and controls (Table 1) (Fig. 2). Two centers used the inexpensive mock scanner for child preparation. One center (45 children) did not have video capability during the real MRI scan (an important contributor to scan success) and thus it is not possible to use its results to compare among mock scanners. The other center (45 children) had video capabilities and had similar success rates to those observed using a commercial mock scanner. Specifically, there was 100% success for T1-weighted scans using both mock scanners and 93.3% success rate for diffusion-weighted scans using the inexpensive mock scanner compared with 94.7% success rate for centers using the commercial mock scanner ($P=0.72$). At the center that used the inexpensive mock scanner without video capabilities the success rates were 91.2% for diffusion-weighted scans and 100% for T1-W scans.

Discussion

In this report we demonstrate that brief behavioral training can lead to a high rate of success for obtaining excellent-quality brain MR images without sedation from very young children. This study presents data from children with type 1 diabetes and non-diabetic controls; however there was no significant difference in scan usability between the two groups, suggesting these positive results are applicable to other situations requiring MRI scanning in typically developing children of comparable age.

For the cohort of children who were able to stay still in the mock scanners after behavioral preparation, the success rate for T1-W images on first attempt was very high at 92.3% (including 84.6% success in children age 4- to <5 years), and that rose to 100% after a second attempt. These success rates after the first attempt are likely to be even higher in a clinical setting because the scans in this study were used for high-resolution analyses and thus the threshold criteria for usability were higher than the criteria needed for clinical scans.

The scanner environment can be intimidating for young children because the MRI scanner is an unfamiliar, loud and large machine, which they may be required to enter without a parent. Previous studies have demonstrated that behavioral techniques can help prepare and desensitize children for their MRI experience [8, 9, 11, 14], resulting in increased usability of MRI scan data for clinical or research purposes. These strategies include at-home preparations similar to those used in our study, use of commercial mock scanners, creation of a child-friendly environment (e.g., MRI-safe decorations and soft toys), and scanning during natural sleep. However a comprehensive program of simple, inexpensive behavioral strategies has not been tested in a large sample of children. The behavioral desensitization techniques used in this study are simple and affordable (e.g., with the use of the inexpensive mock scanner), and can be used in many settings acquiring MRI scans in children. It is also important to note that only four children (1.8%) were not able to stay still in the mock scanner and thus were excluded from the primary study. Children who find it more challenging to be still for the period of time needed to complete an MRI scan might benefit from additional training sessions or might be candidates for an MRI under sedation based on clinical urgency and preferences of the families.

Interestingly, the success rates for high-quality scans using a commercial mock scanner and a cheap play tunnel simulating the MRI environment were not significantly different. This finding suggests that the practice of lying down in an enclosed structure may be adequate in most cases to provide the desensitization and practice needed for a successful MRI scan, when combined with in-home preparation, calming interaction during the scan and image-quality control during the scan session. Our mock MRI is affordable and can be stored when not in use. It also can be sent home for further practice if needed. Thus, centers with limited funds can use the methods we describe without the financial and space requirements of a commercial mock scanner.

We had expected greater difficulty in scanning the non-diabetic age-matched cohort than our cohort with type 1 diabetes because the first group is less familiar with medical interventions, hospitals and clinics. However, both sets of children had comparable success obtaining MRI scans without sedation when using the preparation procedures. Recently, sedation-free brain and liver MRIs were obtained successfully in a group of 71 children with sickle cell disease between 5 years and <13 years old, 33 of whom had preparation and support procedures [8]. Collectively, these data suggest that this type of behavioral preparation is applicable to a variety of chronic conditions in childhood.

Conclusion

Using sedation during elective MRI scans involves significant expense, risk of adverse response to sedation medications, and possible long-term cognitive and behavioral effects in young children. Behavioral desensitization, along with practice MRI sessions using a commercial mock scanner or a cheap mock-scanner made of readily available materials, is a viable alternative to the use of sedation for young children who need to undergo a routine MRI scan.

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Fig. 1.
MRI practice session. A 7-year-old boy practices in an inexpensive mock scanner made from a toy tunnel

Fig. 2.
Flow chart of scan usability by diagnosis. *DWI* diffusion-weighted imaging scan, *T1* T1-Wimaging scan

Table 1

Successful scan percentages for first and second attempts in children with diabetes and controls

	Type 1 diabetes	Controls	Fisher exact test	Total
Total children	147	75	N/A	222
Usable 1 st scan (T1-W)	136 (92.5%)	69 (92.0%)	$P=1.0$	205 (92.3%)
Usable 1 st scan (DWI)	114 (77.5%)	60 (80.0%)	$P=0.73$	174 (78.4%)
Usable T1-W after 2 scans [*]	144 [*] (100%)	72 [*] (100%)	$P=1.0$	216 [*] (100%)
Usable DWI after 2 scans [*]	134 [*] (93.7%)	66 [*] (91.7%)	$P=0.58$	200 [*] (92.6%)

^{*} Three children with type 1 diabetes and three control children did not return for a repeat scan and were excluded from the post-second-scan statistics *DWI* diffusion-weighted imaging scan, *T1-W* T1-weighted imaging scan

Table 2

Success rates of first and second attempts by age range

Age range (years)	Total children	Success rate 1 st attempt (T1-W)	Success rate 2 nd attempt (T1-W)
4–4.9	39	84.6%	100%
5–5.9	32	87.5%	100%
6–6.9	39	92.3%	100%
7–7.9	62	95.2%	100%
8–8.9	12	91.7%	100%
9–9.9	38	100%	100%
Total	222	92.3%	100%

Table 3

Demographic, cognitive and behavioral information of participants who had successful scans after the second scan, and those who had a failed diffusion-weighted scan after two attempts (all participants had a successful T1-W scan after two attempts)

	Children with usable T1-W and DWI scans after 2 attempts	Children with unusable DWI scans after 2 attempts	<i>t</i> -test
Age	7+1.7	6.5+1.7	$t=0.9, P=0.4$
Averaged scaled score of IQ subtests	11.7+2	12.6+2	$t=-1.4, P=0.2$
Parent-rated anxiety score *	51+10.4	49+11.3	$t=0.5, P=0.6$
Parent-rated hyperactivity score *	49.3	51.4	$t=-0.5, P=0.6$

* Parent Rating Scale (PRS), DWI diffusion-weighted imaging scan, T1-WT1-weighted imaging scan