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BRIEF REPORT

Brief Report: Methods for Acquiring Structural MRI Data in Very Young Children with Autism Without the Use of Sedation

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Abstract We describe a protocol with which we achieved a 93% success rate in acquiring high quality MRI scans without the use of sedation in 2.5–4.5 year old children with autism, developmental delays, and typical development. Our main strategy was to conduct MRIs during natural nocturnal sleep in the evenings after the child's normal bedtime. Alternatively, with some older and higher functioning children, the MRI was conducted while the child was awake and watching a video. Both strategies relied heavily on the creation of a child and family friendly MRI environment and the involvement of parents as collaborators in the project. Scanning very young children with autism, typical development, and developmental delays without the use of sedation or anesthesia was possible in the majority of cases.

Keywords MRI · Autism · Natural sleep · Sedation · Children · Toddlers

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Structural magnetic resonance imaging (MRI) has provided important information about the neuropathology of autism. Recent evidence suggests that there may be an altered trajectory of brain growth, with a period of precocious overgrowth in total cerebral volume that occurs in the first years of life (Aylward et al. 2002; Courchesne et al. 2001; Hazlett et al. 2005). However, there are relatively few studies that focus on children younger than six years of age (Carper et al. 2002; Courchesne et al. 2001; Hazlett et al. 2005; Sparks et al. 2002). It is critical to examine brain structure during early development, closer to the time of clinical diagnosis.

In part, the paucity of MRI studies in very young children is due to the methodological challenges of acquiring high quality MRI images. MRI is extremely sensitive to head motion, and the child must remain still for the duration of the MRI scan, typically ranging from 30 min to 1 h. Even slight movements of a few millimeters create motion artifact that can distort the image and confound all types of subsequent structural analyses. Another challenge is the loud acoustic noise created by the interaction of gradient currents with the main magnetic field during the MRI scan. Children with autism often have auditory sensitivities (Rogers and Ozonoff 2005; Tharpe et al. 2006). Thus, the thought of enduring scanner noise may increase anxiety and decrease willingness to participate for both parents and children.

To circumvent these methodological challenges, the use of moderate sedation or general anesthesia is often used in children with autism. Although these methods are generally considered safe (Ross et al. 2005), parents are often hesitant to expose their children to sedation, especially when it is not medically indicated. Taking sedation out of the MRI protocol is likely to increase the motivation of parents whose anxiety about sedation or anesthesia had precluded them from participating in a research study involving MRI. Alternatives to sedation are also essential for those institutions that do not have capabilities to support sedation or anesthesia.

The strategy of acquiring MRI scans during natural sleep has been used in typically developing children in studies of normal brain development (Almli et al. 2007; Evans 2006; Giedd et al. 1999) as well as in studies that use typically developing children as comparison groups (Carper et al. 2002; Hazlett et al. 2005; Sparks et al. 2002). We examined the possibility of acquiring MRI scans during natural sleep in 2.5–4.5 year old children with autism, developmental delays, and typical development. We developed a protocol for acquiring scans during natural sleep with special attention to the sensitivities and needs of children with autism and their families. We tested our protocol in children with autism as well as those with developmental delays and typical development since these groups represent the most widely used control populations for research on autism. Ultimately our goal was to develop methods to scan children of different developmental levels and with varying behavioral presentations. Although our protocol was developed with attention to the special needs of children and families with autism, our hope is that this protocol could be used in populations of children with other developmental disabilities as well.

Methods

Participants

All participants in this study were recruited through the UC Davis M.I.N.D. Institute and received MRIs as part of a large-scale multidisciplinary study, the Autism Phenome Project (APP). Forty-five participants completed the MRI familiarization protocol outlined below: 25 with autism (AU), 16 typically developing (TD), and 4 developmentally delayed (DD). Children with autism and children with developmental delays were diagnosed prior to their enrollment in the study. Diagnostic confirmation included assessments for autism by a licensed clinical psychologist who specializes in the diagnosis of children with autism (CZ). The tools used included the Autism Diagnostic Observation Schedule-Generic (ADOS-G) (DiLavore et al. 1995; Lord et al. 2000) and the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al. 1994). Developmental level was obtained using the Mullen Scales of Early Development (Mullen 1995). For children who were found to be functioning at an overall developmental level of 24 months, the Stanford Binet 5 Abbreviated Battery (Thorndike et al. 1986) was administered to obtain an IQ score. Diagnoses within the developmental delay group included Down's Syndrome, Angelmen's Syndrome, and generalized global delays. To ensure that these children did not also have autism, the Social Communication Questionnaire (Berument et al. 1999) was administered to the parent(s). None of the children in the developmental delay group obtained scores above the marginal level (i.e., a score of 15 or above). Subject demographics are provided in Table 1. Exclusionary criteria for the study were limited to those with physical contraindication to MRI.

MRI Protocol

All scans were acquired at the UC Davis Imaging Research Center on a 3T Siemens Trio whole-body MRI system (Siemens Medical Solutions, Erlangen, Germany) using an 8-channel head coil. The Trio has a short bore (2 m length) as well as a fast gradient system that provides high-speed imaging. The imaging protocol included several pulse sequences, acquired in the following prioritized order: Sagittal T1 localizer (TR 20 ms; TE 5 ms; FOV 28 cm; 10 mm thick; scan time 9.2 s), 3D T1-weighted MPRAGE (TR 2,170 ms; TE 4.82 ms; FOV 24 cm; 192 slices—1.0 mm thick; scan time 8:06), 60-direction DTI (TR 5000 ms, TE 104 ms, FOV 22, 23 slices—5 mm thick;

Table 1 Participant characteristics

	Autism ($n = 25$)	TD ($n = 16$)	DD ($n = 4$)
Gender (M:F)	23:3	12:3	4:0
Chronological age (months)	43.0 (7)	45.3 (7)	43.7 (4)
	32–59	35–57	39–47
Developmental level[a]	67.8 (24)	107.9 (13)	57.6 (22)
	27–134	89–135	29–78
ADOS	14.6 (4)	–	–
	7–21		
ADI-R domain scores	17.9 (4)	–	–
Social communication	8–23	–	–
	11.6 (5)		
Repetitive behavior	5–21	–	–
	5.5 (2)		
	2–8		

Note: Data are expressed as mean (standard deviation) and range

[a] Based on Mullen Scale of Early Learning and, if applicable, Stanford Binet 5

scan time 5:30), 3D T2-weighted (TR 3,000 ms, TE 354 ms, FOV 256, 160 slices—1.0 mm thick; scan time 7:05). The total time to complete the imaging protocol outlined above was about 30 min.

MRI Familiarization Protocol

Overview

Preparation of both the parents and child began approximately 2 weeks prior to the date of the scheduled MRI scanning session with materials developed specifically for the population of this study. Figure 1 provides an overview of the MRI familiarization process.

Upon enrollment into the study, parents were first given a handout regarding the purpose of the study, information about MRI techniques and safety issues, and a general plan for the MRI visits. In addition, the child received a photo storybook containing pictures of the MRI researchers, the entry way to the UC Davis Imaging Research Center, and the mock and 3T MRI scanners. The storybook writing was adapted for very young children containing simple language, factual information and short sentences and read much like a Social Story (i.e., therapeutic method of communicating factual information to children with autism) (Gray and Garand 1993). Next, an MRI researcher discussed the general MRI procedures with the parents and developed an individualized strategy for the child, taking into account the child's typical bedtime routines and habits. A subsequent visit to the Imaging Research Center for a mock or practice MRI session served to familiarize the parent and child with the MRI environment. During this visit, the parents were also given an MRI habituation kit to practice with at home. This included earplugs, headphones and a CD of the exact MRI gradient sounds that were used during the scanning session. On the night of the actual MRI scan, the 3T MRI suite was disguised as a child-friendly nighttime environment. Details about devising a sleep strategy, the mock MRI session, and the actual MRI session are provided below. A general overview of the MRI procedures is also available (http://www.ucdmc.ucdavis.edu/mindinstitute/research/app/video.html#).

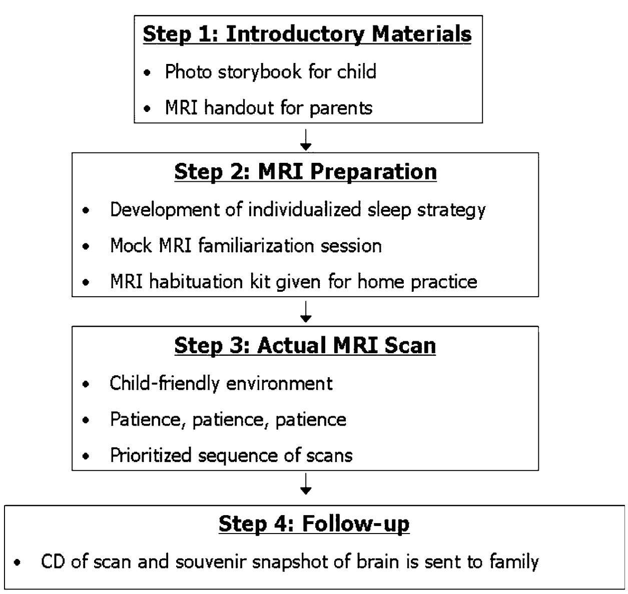

Fig. 1 Overview of MRI familiarization process

Devising a Sleep Strategy

During the initial discussion with the parents, an individualized strategy was devised taking into account details regarding the child's bedtime and sleep habits. Specific questions are outlined in Table 2. Typically, the MRI scan was scheduled to begin around the child's normal bedtime or slightly later and the parent was encouraged to keep their child awake and active during the day. If the child could fall asleep in the car and stay asleep while being transferred to a bed, the parent was encouraged to drive until the child was deeply asleep before arriving at the Imaging Research Center. However, if the child tended to wake up when being transferred from the car to a bed, then the parent was encouraged to keep their child awake during the drive to the appointment.

At the Imaging Research Center, efforts were made to recreate the child's bedtime routine and sleeping environment. For example, if the child was accustomed to watching a movie before going to bed, a toddler bed was set up just outside of the MRI suite and the child watched his or her favorite movie on a portable DVD player. Similarly, the lighting conditions in the MRI suite were matched to the child's preference of either sleeping with a nightlight or in the dark, and music or white noise could also be played in the background if desired. Parents were encouraged to bring security objects such as blankets, pillows, or stuffed animals (pre-screened by researchers for MRI compatibility) that helped the child feel comfortable. If desired, parents could also lay down with their child to help them feel secure and fall asleep. If the child typically slept on his or her side or stomach, the parent was encouraged to begin practicing having the child sleep on his or her back at home. If desired, a weighted blanket was used on the night of the scan to help keep the child on his or her back.

If the parent reported that their child woke up easily to noise, the parent was encouraged to practice at home with the habituation kit (earplugs, headphones and CD of MRI noises—see details below). If practice with the habituation kit failed, then alternatives to acquiring the scan during

Table 2 Questions used to devise individualized sleep strategy

1. Does your child have a regular bedtime and bedtime routine? If so, please describe.
2. Is your child a heavy sleeper? For example, can you vacuum or watch television in the next room after your child is in bed?
3. Does your child fall asleep in the car? If so, will he/she stay asleep while being transferred from the car to a bed?
4. Is your child accustomed to co-sleeping with a parent?
5. Does your child have any security objects that help him/her sleep? If so, screen these items for MRI-compatibility (no metal).
6. Does your child nap? If so, how does he/she react if the nap is skipped?
7. Will your child sleep on his/her back?
8. How does your child do when sleeping away from home?
9. Does your child have any head or sensory sensitivities?
10. Describe your child's bedroom environment. (e.g. lighting conditions, music or white noise in background)

natural sleep were discussed. The alternatives included either attempting to acquire the scan while the child was awake and watching a video or using sedation or anesthesia.

Mock MRI Visit

Unlike the actual MRI scan, the mock MRI visit was conducted during the day while the child was awake. The semi-structured play session was designed to achieve two goals. One was to give the child the opportunity to become acquainted with the same MRI researchers that were to be present at the night time scan to alleviate the possibility of stranger anxiety on the night of the scan. The second was to familiarize the child with the appearance of an MRI scanner and to associate it with a positive experience so that the scanning environment would not induce anxiety at any point during the actually scanning session when the child was awake in the scanner room. The mock MRI scanner was decorated with a train theme (see Fig. 2), and the child was encouraged to 'ride' the MRI bed into the 'tunnel' or watch his or her parents or researchers ride into the 'tunnel'. The materials for decoration of the room as well as elements of the play session were developed in consultation with a clinical psychologist who specializes in working with very young children with autism (SR). The MRI researchers that interacted with the children received instruction from the clinical psychologist (CZ) on play and interaction style with children with autism as well as how to manage any behavioral challenges in the room while providing information to the parent(s).

During the mock MRI visit, parents were asked to bring in their child's pajamas and any toys or security objects that helped the child fall asleep so that an MRI researcher could screen the items for MRI compatibility and safety. Parents also filled out an MRI screening form for themselves and their child. Parents then received the habituation kit with the CD of MRI gradient sounds, soft foam earplugs (Hearos SuperSoft NRR 32db or Mack's SafeSound Jr. NRR 29), and child size headphones (Howard Leight

Fig. 2 Setup for mock MRI session. The simulated MRI scanner is setup with a train theme with stuffed animals and child-friendly stairs

Folding Earmuffs) to practice with at home in the days preceding the MRI scan. Parents were given specific verbal and written instructions on how to practice with the habituation kit. The instructions suggested that the parents practice placing earplugs and headphones on their child after she/he had fallen asleep at night, but to stop if the child woke up. The parents were instructed either to try again when their child had fallen back into a deep sleep or wait until the following night. Once the parent was successful in placing earplugs and headphones on their sleeping child, they were encouraged to play the CD of MRI sounds at progressively louder volumes to habituate their sleeping child to the noises. Parents were encouraged not to use earplugs and headphones during the day while the child was awake, especially if the child had head and/or sound sensitivities, to avoid creating anxiety over the sound attenuating materials.

Natural Sleep MRI Visit

The MRI suite was set up to maximize the comfort level of the parents and child. Figure 3 depicts before and after setups for the MRI suite. Importantly, all of the modifications to the MRI suite were removable and could be set up in approximately 15 min. The external surroundings and MRI bore were disguised with child-friendly fabric, attached to the walls and the scanner using hidden Velcro strips, and screens were set up to block off computers from sight in the control room. MRI-compatible bedroom furniture and toys were set up around the MRI scanner. The MRI bed was widened by placing an MRI-compatible gurney with guardrails (Biodex MRI Stretcher) on each side of the bed. Extra padding (2 inch visco-elastic memory foam topper) was placed on the MRI bed and gurneys for comfort. The enlarged bed allowed the parents to lie down with their child to help them to fall asleep if desired. Once the child was asleep, the gurneys were rolled out of the way prior to commencing the scan. Various child-friendly bedding, including a weighted blanket, was available for the child to use.

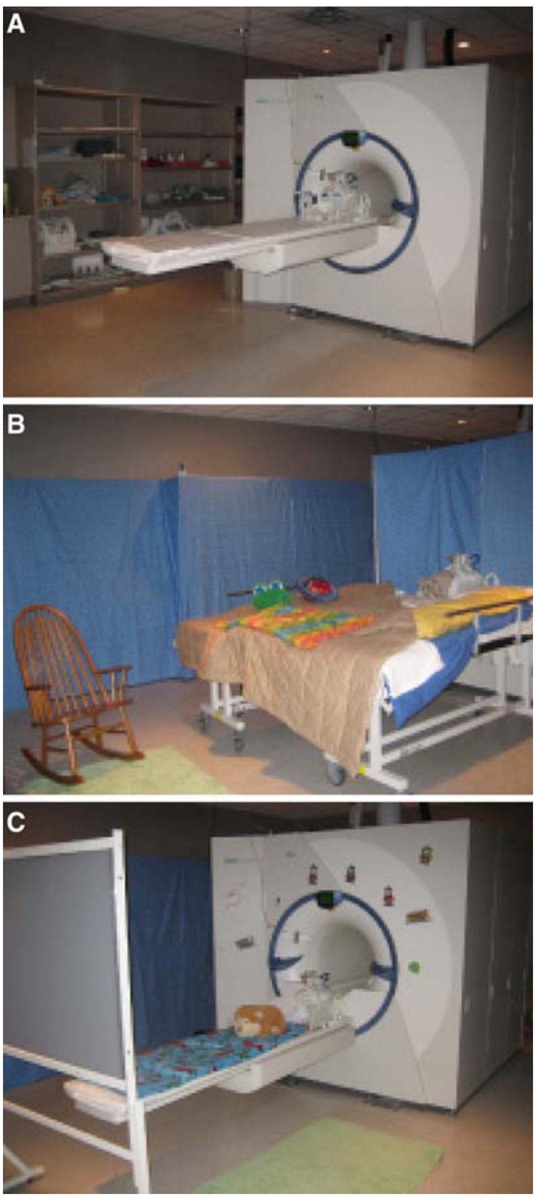

Fig. 3 (**a**) 3T MRI suite before set up. (**b**) Pediatric-friendly 3T MRI suite setup for nighttime sleep scanning. All items are MRI compatible and easily removable. Setup time between 2A and 2B is approximately 15 min. (**c**) Setup for scanning child while awake and watching a video

On the night of the scan, an MRI researcher met the family outside the Imaging Research Center and removed any metal objects (e.g. keys, cell phones, coins, belts) from the parent and child prior to entering the building. Lighting within the building corridors was dimmed. If the child was already asleep, the MRI researcher escorted the parent into the MRI suite and helped the parent situate their child onto the MRI bed. If the child arrived awake, their individual bedtime routine was recreated as closely as possible. Parents often stayed with their child until their child fell asleep. Importantly, contact between the child and the MRI researchers was limited in order to reduce the child's anxiety and increase the likelihood of the child falling asleep.

Once the child had fallen asleep, he/she was given an additional 15–20 min to fall into a deep sleep before proceeding. The first step was for the parent and/or MRI researcher to place the sound attenuating devices on the child. These included the same soft foam earplugs that were given with the habituation kit (Hearos SuperSoft NRR 32db or Mack's SafeSound Jr. NRR 29) and MRI-compatible headphones (Newmatic Sound Systems, NRR 25db) lined with two extra layers of sound attenuating foam (Polymer Technologies Inc, Polydamp Acoustical Foam). Once the earplugs and headphones were on, the child was given a chance to fall back into a deep sleep, usually an additional 10–15 min. Once back into a deep sleep, the child was positioned into a sound and vibration attenuating pillow or 'helmet' (made out of 1.5 inch visco-elastic memory foam). This helmet fit inside of the head coil and surrounded the head and headphones, thereby providing a further layer of sound attenuating material as well as head support. Several factors determined whether the child was sleeping deeply enough for the scan to commence. Generally, if a child was able to sleep through having the sound attenuating devices placed on his or her head and positioning into the head coil, scanning could safely commence. Patience was critical to successful scanning. If the child stirred or woke up at any time during placement of sound attenuating devices, the child was given ample time (at least 10–15 min) to fall back into a deep sleep before attempting placement again. Once scanning commenced, an MRI researcher and the parent (both fitted with ear protection) stayed with the child during the MRI scan, and the scan was stopped immediately if the child woke up during the scan. If the child did not fall asleep within 1.5–2 h after arrival to the imaging center or woke up during the scan and could not return to sleep, the parents were encouraged to schedule a second visit to attempt the scan again.

Awake/Video MRI Visit

If the scan was conducted while the child was awake and viewing a video, the scan was scheduled at a time most convenient for the parent and child. A separate photo storybook was sent to the child to help prepare them for the video MRI visit. The parents were asked to provide a movie or suggest the title of a movie to play for the child during the scan. Upon arrival at the Imaging Research Center, MRI researchers who had previously interacted with the child during the mock MRI visit played with the child in a waiting area until the child felt comfortable. The number of adults interacting directly with the child was minimized. The MRI suite was set up in a similar manner to the night time MRI visit, except that the extra gurneys were not used and the MRI bore was not covered up. Instead, the MRI bore was decorated with train-themed removable stickers (see Fig. 3c).

The video was projected onto a screen at the foot of the MRI bed and the child viewed the video via a mirror inside the head coil. Sound was played through a high quality digital (i.e. non pneumatic) audio and communication system through which researchers and/or a parent could also communicate with the child. Extra foam was used to surround the child's head in order to minimize head movement during the scan. An MRI researcher and, if desired, a parent, remained with the child during the scan. The scan was stopped immediately if the child became distressed or could not tolerate the scan.

Follow-Up

Upon enrollment into the study, parents were informed that scans were not routinely evaluated by a radiologist for any clinical abnormalities. Scans were only referred to a radiologist for clinical evaluation if a gross abnormality was observed by any of the MRI researchers. In these cases, the study pediatrician conveyed the information to the family and efforts were made to provide the scan to the child's primary care physician and/or neurologist. All parents were given a printout picture of their child's MRI as well as CD containing images of their child to keep for their records. The CD contained three MPEG files of the T1-weighted scan, one each in the axial, sagittal, and coronal views. Each MPEG file depicted a 'movie' of the child's MRI, scrolling through all of the slices in each of the three orientations. In addition, raw DICOM files for the T1- and T2-weighted images were included on the CD. Instructions for viewing the CD as well as an informational handout with an overview of basic neuroanatomy and findings related to autism were included with the CD.

Longitudinal Scans

At this point in time, 12 children from the sample described above have become eligible for a 1-year longitudinal scan. Parents were contacted approximately one month prior to the target date (1 year after their first scan) by an MRI researcher that they had worked with previously to discuss whether they were willing to return for a second MRI. If parents consented, the researcher discussed with the parent whether the same strategy that was used for the child in the previous year (either awake with video or nocturnal sleep) would be the best approach for the second MRI and devised a strategy for the longitudinal MRI scan. A practice kit of earplugs, headphones, and the CD of MRI sounds was sent to the parents to familiarize their child again.

MRI Survey

To solicit feedback from parents who had participated in the MRI familiarization protocol, we designed a short anonymous online survey for parents to complete. Parents were asked to identify the diagnostic category of their child as well as whether the MRI was successful (defined as at least one 'picture' complete, even if their child woke up at some point during the scan).

Parents of children with autism were asked to rate how important it was to have the option of not using sedation or anesthesia to complete the MRI scan as well as whether they would have participated in the study if sedation or anesthesia were the only option. The rating scale had four options: 'Very Important,' 'Important,' 'Somewhat Important,' and 'Not Important.' TD and DD children did not have the option of using sedation or anesthesia; all TD and DD children carried out their scans during natural sleep or awake and watching a video.

With the same four point rating scale, parents were also asked to rate the importance of each of the preparatory steps: Introductory MRI handout, Photo storybook for child, Discussion(s) with MRI researcher, Mock MRI visit, Practice kit (earplugs, headphones, and CD), Child-friendly environment of MRI scanner, and Flexibility in scheduling.

Finally, parents were asked to rate their satisfaction with the follow up materials (CD of MRI scan, informational handouts) and their overall experience with the MRI process. Ratings were made on a four point scale of 'Very Satisfied,' 'Satisfied,' 'Somewhat Satisfied,' and 'Not Satisfied.' Open-ended space for additional comments or suggestions was also provided.

Results

A scanning session was deemed successful if, at a minimum, the MPRAGE T1-weighted sequence (the first and highest priority sequence) was completed. Our success rate for acquiring scans without the use of sedation was 93%: only 3 children (1 AU and 2 TD) out of the 45 attempted were unable to complete the scanning procedures during either natural sleep or with video. Table 3 provides details on the number of children by diagnostic group who underwent scanning asleep vs. awake and watching a video. Of the 42 successful scans, 38 (90%) completed both the T1-weighted and DTI sequences, and 28 (67%) completed all three sequences (T1-weighted, DTI, and T2-weighted). Thirty-four (81%) were successful on the first attempt, and the remaining children required a second (or in one case, third) attempt. In three cases requiring a second attempt, the child's first attempt was during natural sleep and the second attempt was while the child was awake and watching a video. The children who underwent scanning awake with a video were slightly older (mean = 52.6 months, sd 5.6) than children who underwent scanning during natural sleep (mean = 42.9 months, sd 6.7). The average length of an MRI scanning session, beginning with setup prior to arrival of the family to cleanup after the family left the Imaging Research Center was approximately 2.5 h. Importantly, scanning was successful in children with a wide range of autism severity and functioning (ADOS range: 7–21; DQ range: 27–135).

Figure 4 depicts the typical quality of the acquired scans. All scans were evaluated for level of motion artifact and image quality using the University of Iowa Mental Health Clinical Research Center rating scale (http://www.psychiatry.uiowa.edu/mhcrc/IPLpages/qa_main.htm). The rating scale ranges from 0 to 4, with a score of 4 indicating

Table 3 Scanning success rates

	Autism	TD	DD	Total
#Attempted	25	16	4	45
#Successful	24	14	4	42
#Natural sleep	23	11	4	38
#Video	1	3	0	4

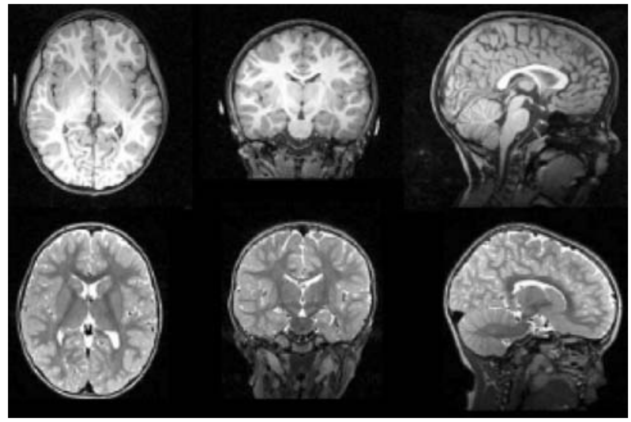

Fig. 4 Examples of image quality for T1 and T2 weighted scans in 3 year olds with autism

no motion artifact and excellent image quality. All MRIs acquired during natural sleep were given a rating of 4, indicating that children did not move during sleep. MRIs acquired while the child was awake and watching a video had limited motion artifact, but were still of good image quality (rating of 3).

For one of the failures (AU; age 3.5), parents reported the child to be a light sleeper, so the scan was attempted with him awake watching a video. The child was unable to hold still for the duration of the scan, so scanning was halted. For the other two failures, (TD; age 2.9 and 4.0 years), the child was unable to fall asleep on the night of the scan. However, for one of these children, the MRI familiarization process had not been completed due to family circumstances. The mock MRI visit was carried out on the same day as the night time scan, and the family had no chance to practice with the habituation kit. For the other child, a second attempt was planned with video, however the family withdrew from the study prior to completing the second attempt.

Longitudinal Scanning

Twelve children in the study have become eligible for a 1-year longitudinal scan. Of these, two have moved out of the area and were unable to complete the longitudinal visit. The remaining 10 have returned for another MRI scan. Scanning was successful for 9 out of 10 of the longitudinal scans (6 [5AU, 1TD] sleep; 3 [1AU, 2TD] awake with video). One child (AU) could not attain a deep enough level of sleep at the scanner. All of the nine successful scans were acquired on the first attempt. This is in contrast to the previous year when 5 (4AU, 1TD) out of the 9 had to come in for multiple attempts. In addition, during the first MRI scan, 3 out of the 9 children woke up and were unable to complete all of the scanning sequences, but all 3 stayed asleep for acquisition of all sequences during the 1-year longitudinal scan. Anecdotally, parents indicated that preparation for the longitudinal scan was very easy, and they were less anxious about the whole procedure. All indicated that they would be willing to come in for additional longitudinal scans.

Feedback from MRI Survey

Responses to the survey designed to solicit feedback from families who had participated in the study were collected over a 2-week period. We received responses from 27 (60%) families who had participated (15 AU, 10 TD, 2DD). Regarding the importance of having the option of conducting the scan without using sedation, 80% of parents of children with autism (12/15) rated it as 'Very Important,' 13% (2/15) rated it as 'Important,' and the remaining 7% (1/15) rated it as 'Somewhat Important.' Parents were asked a follow-up question of whether they would have participated in the study if sedation were the only option. Nine parents answered this question, and of these, seven responded that they would not have participated in the study if sedation were the only option. One parent responded with a yes, but indicated that she would have been much more concerned about the study had she needed to use sedation for her child.

Table 4 summarizes how parents rated the importance of each of the preparatory steps. In general most of the preparatory steps were rated as either 'Very Important' or 'Important,' suggesting that all of the steps are worthwhile to carry out. Flexibility in scheduling, child-friendliness of MRI room, and discussion(s) with the MRI researcher received the most ratings of 'Very Important.' The photo storybook and the mock MRI visit were the only two components to receive any ratings of 'Not Important,' however, parents of typically developing children tended to rate these components with more importance (more than 90% of TD parents rated each of these components as either 'Very Important' or 'Important').

Two of the families for which the MRIs were not successful responded to our survey. One (parent of TD child) indicated that "The night MRI was difficult. My child just wouldn't stay asleep. I ended up being very tired the next day." The other family (parent of AU child) indicated that "Everyone was very accommodating with the MRI process. I was disappointed that we were not able to complete this part of the project." These families rated their overall satisfaction with the project as 'Somewhat Satisfied' and 'Satisfied.'

Regarding satisfaction with the follow-up materials of the CD of the child's MRI scan along with the informational handouts, feedback was generally positive. Seventy-seven percent (21/27) were 'Very Satisfied,' 15% (4/27) were 'Satisfied,' and two parents gave a rating of 'Somewhat Satisfied.' Finally, feedback about the overall MRI experience was very positive. Eighty-five percent of families indicated that they were 'Very Satisfied,' 12% were 'Satisfied,' and one parent gave a rating of 'Somewhat Satisfied.' All of the open-ended comments were positive, one example being "The team was great in providing useful information for preparing for the MRI visit. Everyone was very helpful and made us feel very comfortable with the procedure. It was a very positive experience for our family."

Discussion

Acquiring high resolution MRIs in very young children with autism and repeating MRIs at later points in development to follow brain growth trajectories longitudinally will be critical in understanding the timing and nature of precocious overgrowth that has been reported in autism.

Table 4 Survey feedback on importance preparatory steps for MRI

	Very important (%)	Important (%)	Somewhat important (%)	Not important (%)
Informational MRI handout	**54**	42	4	0
Photo storybook for child	35	**46**	12	8
Discussion(s) with MRI researcher to develop individualized strategy	**73**	27	0	0
Mock MRI visit	**39**	**39**	11	11
Practice earplugs, headphones, and CD	**54**	35	11	0
Flexibility in scheduling (able to schedule scans around child's bedtime and on any weeknight)	**92**	8	0	0
Child-friendly environment in MRI room (extra beds, blankets, pillows, wall coverings)	**88**	8	4	0

Ratings with the highest number of responses are bolded

This study shows that acquiring high quality structural MRI scans without the use of sedation or anesthesia is quite tractable in very young children, and preliminary data suggests that longitudinal scanning is also highly successful. Although the use of sedation is safe in children with autism (Ross et al. 2005), having the option of acquiring MRIs without sedation or anesthesia may encourage more parents and children to participate in research studies and may make longitudinal MRI studies more feasible. Indeed, feedback from parents who participated in this study indicated that a significant portion of them would not have enrolled in the study if sedation had been the only option for completing the MRI.

We were able to complete scanning without the use of any sedation in children with a wide range of autism severity and levels of functioning. Although sleep disturbances in autism are widely reported by parents (Filipek 2005), most parents in our study indicated that if present, sleep disturbances occurred later in the night and that the first cycle of deep sleep was often successful. For children with bedtime resistance and/or prolonged sleep latency, we commenced scanning at a later hour and encouraged parents to allow their child to fall asleep in the car before arriving to the MRI scan. However, we recognize that this strategy will not work for all children with autism, particularly for those who wake easily to noise or when moved.

Although scanning during natural sleep was our primary method for acquiring MRIs, we did offer parents of children with autism the option of using general anesthesia if they thought that scanning during natural sleep would not be successful, and approximately 15% of parents did opt directly for anesthesia. These were parents who indicated that their children were very light sleepers who awoke easily to noise. Thus, if a study were conducted with no option for sedation or anesthesia, there would most likely be some selection bias in the children that are sampled. Another potential limitation to scanning without sedation or anesthesia is the amount of time and research staff required to prepare families and children for the MRI procedure. In addition, mock MRI machines are not available in all research settings, and conducting scans during night time hours is not always feasible.

Still, acquiring MRI scans in very young children is a critical step towards understanding the neuropathology of autism. This study suggests that scanning young children, including those with autism, other developmental disorders, and typical development, without using sedation or anesthesia can be successful in the vast majority of cases. The implications of developing completely non-invasive methods for scanning 2–4 year old children are likely farther reaching than what can be applied to autism. This protocol could certainly be used in children with a variety of neurodevelopmental disorders as well as in studies of typically developing children.

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