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Behavioral-play familiarization for non-sedated magnetic resonance imaging in young children with mild traumatic brain injury

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Behavioral-play familiarization for non-sedated magnetic resonance imaging in young children with mild traumatic brain injury

Abstract

Background: Mild traumatic brain injury (mTBI) sustained in early childhood affects the brain at a peak developmental period and may disrupt sensitive stages of skill acquisition, thereby compromising child functioning. However, due to the challenges of collecting non-sedated neuroimaging data in young children the consequences of mTBI on young children's brains have not been systematically studied. In typically developing preschool children (TDC, 3-5 years), brief a behavioral-play familiarization provides an effective alternative to sedation for acquiring awake magnetic resonance imaging (MRI) in a time- and resource-efficient manner. To date, no study has applied such an approach for acquiring non-sedated MRI in preschool children with mTBI who may present with additional MRI acquisition challenges such as agitation or anxiety.

Objective: The present study aimed to compare the effectiveness of a brief behavioral-play familiarization for acquiring non-sedated MRI for research purposes between young children with and without mTBI, and to identify factors associated with successful MRI acquisition.

Materials and methods: Preschool children with mTBI (n=13) and TDC (n=24) underwent a 15-minute behavioral-play MRI familiarization followed by a 35-minute non-sedated MRI protocol. Success rate was compared between groups, MRI quality was assessed quantitatively, and factors predicting success were documented.

Results: Among the 37 participants, 15 TDC (63%) and 10 mTBI (77%) reached the MRI acquisition success criteria (i.e., completing the two first sequences). The success rate was not significantly different between groups ($p=.48$; 95% CI [-0.36 14.08]; Cramer's $V=.15$). The images acquired were of high-quality in 100% (for both groups) of the structural images,

and 60% (for both groups) of the diffusion images. Factors associated with success included older child age ($B=0.73$, $p=.007$, $\exp(B)=3.11$, 95% CI [1.36 7.08]) and fewer parental concerns ($B=-1.56$, $p=.02$, $\exp(B)=0.21$, 95% CI [0.05 0.82]) about the MRI procedure.

Conclusion: Using brief behavioral-play familiarization allows acquisition of high-quality non-sedated MRI in young children with mTBI with success rates comparable to those of non-injured peers.

Keywords: magnetic resonance imaging, sedation, familiarization, early childhood, concussion, brain injury

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Introduction

Traumatic brain injury (TBI) is highly prevalent in children younger than six years old [1, 2], in whom, even mild insult to the brain, such as concussion or mild TBI (mTBI) - characterized by transient neurological symptoms such as headache, alteration of consciousness, amnesia, or nausea following a violent blow or jolt to the head or body [3] -, has the potential to disturb brain structure or function and affect cognitive, emotional, behavioral, and social functioning [4]. Due to the challenges of collecting neuroimaging data in children five years and younger, toddlers and preschoolers are typically excluded from research efforts to document brain changes after TBI [5].

Magnetic resonance imaging (MRI) is highly sensitive to motion which induces blurring and ghosting in the images, thus requiring children to stay still in the scanner for prolonged acquisition periods. In clinical settings, computed tomography (CT) is commonly used for children with TBI for detection of skull fractures and subarachnoid hemorrhage. It can be performed quickly with less need for immobilization than MRI; however, it is a source of ionizing radiation and has low sensitivity to subtle brain lesions following mTBI [6, 7]. Alternatively, MRI protocols are sometimes prescribed for clinical purposes, but sedation is generally used in young children to facilitate high-quality and efficient image acquisition. Though necessary in some cases and settings, sedation can be associated with risk of adverse side effects such as seizures and apnea, or mild cognitive or brain disruption (i.e., neurotoxicity and neurodegenerative changes) [8, 9]. It is thus not an optimal procedure in young children in addition to being prohibited ethically for research purposes.

Subtle brain lesions or changes following mTBI cannot be adequately visualized on CT or conventional MRI [6, 7]. In contrast, advanced MRI techniques (e.g., surface-based morphometry, susceptibility-weighted imaging [SWI], diffusion-weighted imaging [DWI]) are highly sensitive for detecting subtle changes in brain structure following pediatric mTBI in school-age children and adolescents. Using these techniques in children 6-17 years old, studies have documented the presence of brain lesions, reduced global and regional brain volumes and cortical thickness, as well as altered white matter microstructure months, even years, following mTBI [5, 10, 11]. However, putative brain alterations following early mTBI remain unexplored.

A recent study tested the feasibility of fast MRI (i.e., abbreviated, motion-tolerant sequences) without sedation in young children (<6 years old) with TBI of all severities [8]. The approach was successful for obtaining MRI data in six minutes without the need for anesthesia or sedation. However, the utility of the procedure was constrained due to the limited sensitivity of fast MRI to detect subtle brain insult, which is more typical of milder injuries, the detection of which is necessary for fully appreciating the consequences of mTBI on the developing brain. In addition, fast MRI sequences are not suited for quantitative MRI analysis.

Children younger than 5 years are the most difficult to scan without sedation [12, 13]. While they are gradually more able to cooperate over this period, reduced daytime sleep complicates scanning during natural sleep, an approach often used successfully in neonates and infants. In typically developing children (TDC) of this age, a brief behavioral familiarization (i.e., introduction of the MRI procedure to the child by play) provides an effective alternative to sedation for acquiring awake MRI in a time- and resource-efficient manner [12, 13]. This procedure is associated with success rates of at least 63% in children younger than six years [14–16], against 54% when melatonin is used to induce sleep in

children under five years [17]. In clinic, using preparation procedures and distraction (e.g., video) during MRI acquisition in children younger than 7 years significantly reduces the frequency of sedation by 34.6% [18]. However, no study to date has applied a behavioral-play approach for acquiring MRI in the context of early mTBI research.

TBI-related symptoms and consequences may make it harder for children to lay still in the scanner, and the MRI environment may induce heightened stress and anxiety. For example, mTBI sustained in early childhood has been associated with increased internalizing and externalizing behavior problems [19, 20], as well as anxiety symptoms occurring in the context of post concussive symptoms [21]. The present study aimed to compare the effectiveness of a behavioral-play familiarization for acquiring non-sedated research MRI between preschool children (3-5 years) with mTBI and their typically developing peers, and to identify factors associated with successful acquisition.

Materials and Methods

The current data were collected as part of a pilot study (DOLFIN Project) prior to a longitudinal cohortstudy (KOALA) on the impact of early mTBI on child development) [22]. The studies were approved by the local human research ethics committee and conducted in agreement with the Helsinki declaration. All families provided written informed consent for participation.

Participants

Children with mTBI were recruited at two pediatric emergency departments (CHU Sainte-Justine and Montreal Children's Hospital, Montreal, Canada). TDC were recruited from the general population via pamphlets distributed in local daycares and early childhood care centers.

Inclusion criteria for all children were as follows: (a) aged 36 to 71 months old at recruitment; (b) sufficient mastery of English or French to complete questionnaires (parents)

or to understand the MRI familiarization (child); and (c) no MRI contraindications. The following exclusion criteria were applied to all participants: (a) any diagnosed congenital, neurological (other than the mTBI associated with inclusion in this study), developmental, psychiatric, or metabolic disorder; (b) less than 36 weeks of gestation; and (c) prior TBI (other than the mTBI associated with inclusion in this study) serious enough to warrant a visit to the ED of any hospital. The following additional exclusion criteria were applied to mTBI group: (a) hypoxia, hypotension, or shock during or following the injury; (b) administration of sedative medication; (c) surgical intervention following the injury; (d) non-accidental/intentional injury. Diagnostic criteria for the mTBI group were: (a) ED presentation within 48 hours post-injury to one of the two recruitment sites, (b) documented, non-intentional, traumatic event (e.g. hit, fall, motor vehicle accident) resulting in a non-penetrating injury, (c) age-appropriate Glasgow coma scale (GCS) score between 13 and 15, and (d) one or more of the following signs or symptoms: palpable skull fracture; headache(s); altered mental status (including agitation, somnolence, slow response, repetitive questioning, confusion); excessive irritability (more than usual) or ‘not acting normally’ (according to parents); loss of consciousness (any).

Non-sedated neuroimaging protocol

One to three months post-injury (or post-recruitment for the control group; minimum time interval = 15 days), children participated in a 15-minute familiarization adapted from Thieba et al. [14] and immediately underwent a non-sedated MRI protocol.

MRI familiarization. Parents were provided with detailed information on MRI procedures via a pamphlet which included answers to the most frequently asked questions by children regarding the MRI. Parents and children were also provided two samples of MRI sounds prior to their appointment. The familiarization was provided just before the MRI acquisition by a trained research assistant using customized material as follows: (a) ask the child to

choose a TV show/movie to watch during the image acquisition; (b) introduce the child to a puppet (also the main character of the cartoon story) and to a toy MRI; (c) read the puppet's cartoon story which incorporates the MRI procedures step-by-step. While reading the book, invite the child to interact with the puppet and the toy MRI. At the moments indicated in the story, introduce the child to the hospital gown worn during MRI acquisition and to the MRI sounds using headphones similar to the ones used in the MRI; (d) once the story completed, show pictures of children positioned in the MRI scanner and ask the child if they have any questions or concerns. Following this preparation, children were invited to wear the hospital gown. The pediatric MRI technician then welcomed them and made the child comfortable in the MRI. As per usual hospital procedures, the MRI technician showed the equipment to the child and explained what it was used for. During the acquisition, children were allowed to bring the puppet, a plush toy (if MRI-compatible) or a blanket with them. When present in the MRI room, the parent was provided earplugs and could either stay near their child touching their legs during the acquisition or stay seated near the door.

Non-sedated MRI acquisition. MRI data were acquired on a 3T scanner (Discovery MR750, GE Healthcare Systems, Milwaukee, WI) using a 32 Channel matrix head while children watched a movie. MRI sequences included a BRAVO T1-weighted anatomic MRI (T1-w), quantitative susceptibility mapping (QSM), 30 directions DWI, SWI, T2-weighted anatomic MRI (not for 4 participants) and resting-state functional MRI (rs-fMRI; not for 1 participant) for a total duration of 35 minutes (see [omitted for review] for complete sequence parameters). The rs-fMRI sequence occurred while the participants continued to watch the movie, as in previous work [23].

Measures

Sociodemographic. Child sex assigned at birth (i.e., male or female), handedness, ethnicity, birth characteristics, developmental and medical history, as well as parental education, income and family characteristics were documented.

MRI acquisition success and full completion. MRI acquisition was considered successful when the child entered the scanner and completed the two first sequences (T1-w and QSM) corresponding to approximately 15 minutes of MRI acquisition, was set a priori as the MRI acquisition success criterion for two reasons. First, it aligns with the length of previous protocols in neuroimaging studies on typically developing young children [14, 15, 24, 25]. Second, the QSM sequence is of particular interest in the context of mTBI. Susceptibility imaging, included in QSM, is sensitive for detecting and quantifying microbleeds following mTBI [26, 27], and possibly more effective than diffusion imaging in the sub-acute phase of mTBI. Indeed, diffusion imaging shows lower sensitivity to detect subtle brain changes in the acute phase (i.e., in the days post-injury) than in the chronic phase (i.e., after 6 months post-injury) of mTBI [28].

The MRI acquisition was considered fully completed when all the sequences from the MRI protocol were completed.

MRI data quality assessment.

Visual quality check. A team member with 10 years expertise in pediatric neuroimaging (FD) visually inspected each image for motion artefacts (e.g., ringing, blurring) and image quality, and were rated as ‘usable’ versus ‘unusable’.

Quantitative quality check. In addition to the visual inspection, structural, DWI and rs-fMRI sequence quality was estimated quantitatively as follow:

- 1) Structural MRI quality was estimated quantitatively using the CAT-12 toolbox (version: CAT12.6-rc1 [r1429]) part of SPM12 (version: 7487) based on noise, inhomogeneities and image resolution [29].

- 2) DWI quantitative quality check was performed based on the outlier report provided by the Eddy tool [30, 31] part of FSL (version: 5.0.11) [32]. The images were rated on a six-point Likert scale as follows: 0=*unusable*, > 6 volumes (out of 35) with > 10 slices (out of 54) of signal dropout detected; 1=*poor*, 1-5 volumes with > 10 slices of signal dropout detected; 2=*fair*, > 1 volume with [5-10] slices of signal dropout detected; 3=*good*, [15-20] slices of signal dropout detected in total; 4=*very good*, [11-15] slices of signal dropout detected in total; 5=*excellent*, [1-10] slices of signal dropout detected in total.
- 3) Rs-fMRI images were visually inspected for motion artefacts and image quality and were first rated as usable versus unusable (by FD). Then, rs-fMRI image quality was quantitatively assessed using the FSL (version: 5.0.11) motion outliers tool [33] to detect outlier volumes based on root mean square intensity difference to the reference volume. The threshold was defined as the 75th percentile + 1.5 times the InterQuartile Range.

Parent, child, and research MRI qualitative reports. The *Parent MRI Report* is an in-house 6-item parent-report questionnaire designed to document parent knowledge about the MRI before participating in the study, their opinion about the usefulness of the information provided, their child's level of concern about the MRI, and their projection concerning the likelihood that their child will successfully complete the MRI protocol. The questionnaire was given to parents before the familiarization, upon arriving in the MRI waiting room. Parents were asked to assess these aspects using a 5-point Likert scale (1=Not at all, 5=Very much) before the MRI acquisition while the research assistant set up the material for the familiarization.

The *Child MRI Report* is an in-house 8-item questionnaire designed to document the child's overall enjoyment and experience of the familiarization and MRI acquisition. It was

administered by the research assistant to the participant after the MRI. The items include general questions about the procedure (e.g., Did you like the book?) as well as technical aspects of the MRI experience (e.g., Did you see the video well?). Answers were provided either by yes/no format or a 5-point smiley face Likert scale.

On their *Research Team MRI Report*, the research assistant and the MRI technician respectively assess the child's and parent's level of concern regarding the MRI acquisition and predict the likelihood of the child completing all MRI sequences.

Statistical analysis

Analyses were run in SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

MRI acquisition success and full completion. Group differences in the rate of success and full completion of the MRI protocol were tested using Fisher's exact test.

Child experience. Children's answers to the *Child MRI* questionnaire were compared between the mTBI and TDC groups using Fisher's exact test (categorical data) and t-test (continuous data).

MRI acquisition success prediction. The role of the following variables on the MRI acquisition success rate (coded as 0=fail, 1=success) was tested using univariate logistic regressions: likelihood of completeness predicted by the research assistant, the MRI technician, and the parent (*Do you think the child will get to the end of the MRI protocol? ; I think my child will be able to complete the MRI.*). These predictors were selected to examine whether parent, research staff and MRI technologist observations could provide insights into whether the child is ready to complete the MRI. In addition, variables known to influence child MRI performance [14, 34] were also chosen as predictors of success including: parent and child concern about the MRI (*Are you worried about the MRI? ; Is your child worried about the MRI?*), child age and sex, as well as parental education, and parental knowledge of

MRI. Considering the sample size and the absence of significant differences between mTBI and TDC in terms of MRI success rate (see results), full MRI protocol completeness, or child experience, the prediction analyses were conducted on the entire sample.

Results

Participants

Thirty-seven children (mean age at MRI = 58.30 ± 11.86 months; 18 females) with mTBI (N=13; mean age at MRI = 56.85 ± 12.83 months; 6 females) and without mTBI (N=24; mean age at MRI = 59.08 ± 11.50 months; 12 females) were included in the study. There were no significant group differences in terms of age at MRI ($p = .60$; 95% CI [-6.59 11.07]) or sex ($p = .82$; 95% CI [-0.27 0.342]). Most mTBI patients underwent MRI one-month post-injury except two who were scanned three months post-injury (mean delay since injury = 43.38 ± 25.15 days; Range = 25 – 102 days). One typically developing child had previously undergone an MRI.

MRI acquisition success and full completion

Of the 37 children who completed the familiarization, 5 TDC and 2 mTBI refused to undergo MRI scanning. In addition, 1 TDC asked to stop the MRI protocol during the first sequence. Fifteen TDC (63%, mean age at MRI = 62.3 ± 9.8 months) and 10 mTBI (77%, mean age at MRI = 62.2 ± 8.9 months) completed the two first sequences, thereby reaching the MRI acquisition success criterion (Figure 1, Table1). There was no significant difference in the rate of MRI acquisition success between TDC and mTBI ($p=.48$; 95% CI [-0.36 14.08]; Cramer's $V=.15$). Within the mTBI group, there was no significant association between time post-injury and MRI acquisition success rate ($p=.33$; 95% CI [-0.31 0.73]).

Thirteen TDC (54%, mean age at MRI = 61.7 ± 10.5 months) and 5 mTBI (38%, mean age at MRI = 66.6 ± 5.5 months) completed the full MRI protocol, staying between 30 and 41 minutes in the scanner (Figure 1, Table 1). There was no significant difference in the

rate of children who fully completed the MRI protocol between TDC and mTBI ($p=.49$; 95% CI [0.10 2.53]; Cramer's $V=.15$). Within the mTBI group, there was no significant association between time post-injury and the rate of children who fully completed the MRI protocol ($p=.69$; 95% CI [-0.63 0.46]).

Among the 5 mTBI and 2 TDC who met the MRI acquisition success criterion, but who did not complete the full MRI protocol, none explicitly asked to end the acquisition because of fear or discomfort. All children asked to stop the acquisition because they were getting restless or bored or simply stated that they did not want to continue. Note that for three of these participants, technical issues involving the audio-visual equipment or the MRI console occurred before or during the MRI acquisition that prolonged the duration of the exam.

Mean MRI duration was 24.22 ± 14.76 minutes (range = 0-41 minutes). There was no significant group difference in the overall MRI duration between mTBI ($M = 25.54 \pm 14.00$) and TDC ($M = 23.50 \pm 15.40$; $p = .70$; 95% CI [-12.29 8.22]).

MRI data quality

The images acquired were of high quality: 92% (TDC) and 92% (mTBI) of total images acquired were rated as 'usable' after visual inspection (Table 2). Usable image rates ranged from 75% (T2-w sequence, TDC) to 100% (T1-w and rs-fMRI, both groups). Image quality remained stable throughout the entire protocol.

Structural MRI. T1-w images were acquired in 18 TDC (75%) and 11 mTBI (85%; Table 1). The images were of high quality, as reflected by visual inspection (Table 2) and quantitative quality (Table 3) rates: 100% of the images were rated as "usable" based on visual inspection, and as "good to excellent" using a quantitative indicator of quality (CAT12 percentage rating points, range=80–92%).

Diffusion-weighted imaging. DWI was acquired on 15 TDC (62%) and 10 mTBI (77%; Table 1). The images were of high quality (Table 2), as reflected by visual inspection and quantitative quality rates: 93% (TDC) and 100% (mTBI) of the images were rated as ‘usable’ after visual inspection. In both groups, the images were of high quality with 60% of the images rated as ‘good to excellent’ quality based on the outlier report provided by the Eddy tool.

Rs-fMRI. Rs-fMRI was acquired on 12 TDC (50%) and six mTBI (43%; Table 1). Rs-fMRI data for two participants were lost due to a technical problem during data transfer. All the images (100%) were rated as ‘usable’ after visual inspection (Table 2). The images were of high quality with fewer than 13% (TDC) and 10% (mTBI) of volumes revealing excessive motion artifacts (outliers). Removing these volumes would provide at least 13 minutes of resting-state data without motion artifacts.

Child experience

All children were attentive and compliant during the MRI familiarization and 36 (97%) reported that they enjoyed the procedure. The only child that did not like it explained afterwards that he did not enjoy stories in general and that it was not something specific about the MRI familiarization. Among the 19 TDC and the 11 mTBI who agreed to proceed with the MRI acquisition, 13 (68%) TDC and 9 (82%) mTBI liked the experience ‘a lot’ or ‘very much’, and 11 (58%) TDC and 8 (73%) mTBI indicated that they would be willing to do an MRI again (Table 3). No significant differences were found between the two groups (Table 3).

Success prediction. MRI success was significantly predicted by the research assistant (logistic regression coefficient (B)=1.39, $p=.005$, odds ratio ($\exp(B)$)=4.02, 95% CI [1.51 10.67]) and the MRI technician (B=0.74, $p=.02$, $\exp(B)$ =2.10, 95% CI [1.12 3.94]), but not by the parent (B=0.59, $p=.10$, $\exp(B)$ =1.81, 95% CI [0.90 3.64]). Parental concern

significantly decreased the chance of success, with 0.21 times less chance of success per point of concern ($B=-1.56$, $p=.02$, $\exp(B)=0.21$, 95% CI [0.05 0.82]), but this was not the case for child concern about the MRI procedure ($B=-0.35$, $p=.34$, $\exp(B)=0.70$, 95% CI [0.35 1.44]). Older children were more likely to succeed the MRI protocol, with 3.11 times more chance of success per year of age ($B=0.73$, $p=.007$, $\exp(B)=3.11$, 95% CI [1.36 7.08]). Child sex was not associated with MRI success ($B=-0.58$, $p=.42$, $\exp(B)=0.56$, 95% CI [0.14 2.26]). Parental education and knowledge about the MRI were not significantly associated with MRI success (education: $B=0.02$, $p=.96$, $\exp(B)=1.02$, 95% CI [0.55 1.89]; knowledge: $B=0.14$, $p=.63$, $\exp(B)=1.15$, 95% CI [0.65 2.05]).

Discussion

The present study aimed to evaluate the effectiveness of a brief behavioral-play familiarization for acquiring non-sedated MRI in young children with mTBI, as well as to evaluate factors associated with non-sedated MRI acquisition success. Almost all children (97%) reported that they enjoyed the behavioral-play familiarization and most were willing to do an MRI again. In addition, the 15-minute behavioral-play familiarization developed for this study allowed us to acquire high-quality MRI with excellent success rates without the need for sedation. The majority of children (77% and 63% of 3-to-5-year-old children with and without mTBI) completed at least the two first sequences corresponding to about 15 minutes of acquisition (success threshold). About half of the children (38% mTBI and 54% TDC) stayed in the scanner between 30 and 41 minutes and completed the full MRI protocol. Success and full completeness rates were similar between children with and without mTBI, suggesting that factors associated with mTBI do not impact the success of the acquisition. This success rate (i.e., 63-77%) is consistent with that previously reported in TDC of the same age using a similar procedure for acquiring non-sedated awake MRI (ranging from 63 to 88%) [14–16], or during natural sleep in children aged 0-to-4 years (ranging from 66 to

96%) [35]. It was substantially higher than that obtained by using melatonin during MRI acquisition in children under five years (54%) [17].

Beyond the excellent acquisition success rate, this familiarization facilitated the acquisition of high quality structural and functional brain images with low motion artifacts. More than 70% of the T1-w images were rated as ‘excellent’ according to quantitative quality criteria, 60% of the diffusion images rated as ‘good to excellent’ quality based on the outlier report and excessive motion artifacts were reported in fewer than 13% of rs-fMRI volumes. Less than 4% (1/29 structural MRI, 1/25 DWI and 0/18 rs-fMRI) of acquired images were rated as unusable.

Interestingly, parent concern about the MRI was negatively associated with MRI success, but their knowledge about the MRI and level of education were not. Information about the MRI were communicated to the parent via a pamphlet and by phone during the recruitment and appointment scheduling, and again in person before the MRI protocol. Although the study team was attentive to parents’ questions and concerns, it is possible that this result reflects an intrinsic anxiety or stress trait of the parent, rather than a state specific to the MRI. Further investigations are needed to better understand whether intrinsic parent factors (e.g., anxiety, stress level) or mental state are associated with child MRI success.

Child age, but not sex, was associated with MRI success. Older children were more likely to succeed the MRI protocol. Age-specific familiarization steps or adaptations in the procedure may be needed. As the MRI acquisition was conducted on a clinical scanner with restricted and specific timeslots for research MRI, it was not always possible to adapt the MRI appointment to the child's rhythm and daily routine (e.g., naps, snack times). Also, young children are likely to be more sensitive to any issues that extend the time they have to wait for the MRI and technical delays may wear out their patience.

Research assistants and MRI technicians accurately predicted the success of the MRI acquisition. It might be expected that the parent, who knows the child best, would be the one better able to predict how their child will react. However, the MRI protocol is an unfamiliar situation for both the parent and the child, compared to an MRI technician or research assistant who accompany large numbers of children in the scanner and therefore might be able to quickly and accurately see signs that the child will succeed or not. Further investigation is needed to understand which child and parent comments or behaviors suggested to the team that the child would or would not succeed. This knowledge could eventually be shared with the parent during the familiarization to decrease their own concern.

Finally, time post-injury was not associated with success or full protocol completion. Since almost all children underwent MRI scanning after the acute post-injury period (around one month), symptoms directly resulting from the mTBI may have already subsided and not affected MRI success or quality. In future studies, the procedure should be applied in the acute phase post-injury to investigate whether acute post-concussive symptoms [36] affect children's ability to undergo MRI scanning.

The following limitations need to be considered in interpreting the study results. First, given the study design and objectives, we cannot draw conclusions regarding the utility of the familiarization procedure compared to standard MRI acquisition with no behavioral preparation. Previous work has addressed this question in other groups of children [12–16], and future studies could document the efficacy of the familiarization compared to other forms of preparation in mTBI specifically. Second, our sample size was modest and larger studies are needed to further investigate the full range of mTBI-related factors that could impact MRI success and quality, such as post-concussive symptoms, time since injury, behavior problems, or parental concerns and anxiety. Future studies should document in more detail both qualitative signs of stress or anxiety as well as quantitative rates of perceived stress or

anxiety. Based on the acquisition of good quality MRI images such as presented here, future work in larger samples should aim to investigate brain structure and functional outcomes following early mTBI.

In conclusion, the present findings indicate that a brief behavioral-play familiarization allows acquisition of high-quality, non-sedated MRI in young children with mTBI with success rates comparable to those of non-injured peers. Such familiarization does not require a mock scanner (often expensive and unwieldy), nor highly specialized training or background knowledge. It is therefore easily applicable to different environments in both research and clinical settings and could possibly be extended to other pediatric clinical populations to acquire non-sedated MRI.

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Data Availability

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly; therefore, supporting data are not available.

Declarations

Conflicts of interest None.

References

1. Thurman DJ (2016) The epidemiology of traumatic brain injury in children and youths: A review of research since 1990. *J Child Neurol* 31:20–27
2. Koepsell TD, Rivara FP, Vavilala MS, et al (2011) Incidence and descriptive epidemiologic features of traumatic brain injury in King County, Washington. *Pediatrics* 128:946–954. <https://doi.org/10.1542/peds.2010-2259>
3. Zemek RL, Farion KJ, Sampson M, McGahern C (2013) Prognosticators of persistent symptoms following pediatric concussion: a systematic review. *JAMA Pediatr* 167:259–65. <https://doi.org/10.1001/2013.jamapediatrics.216>
4. Séguin M, Gagner C, Türk C, et al (in press) What about the little ones? Systematic review of cognitive and behavioral outcomes following early TBI. *Neuropsychol Rev*
5. King DJ, Ellis KR, Seri S, Wood AG (2019) A systematic review of cross-sectional differences and longitudinal changes to the morphometry of the brain following paediatric traumatic brain injury. *Neuroimage Clin* 23:101844. <https://doi.org/10.1016/j.nicl.2019.101844>
6. Beauchamp MH, Ditchfield M, Babl FE, et al (2011) Detecting traumatic brain lesions in children: CT versus MRI versus susceptibility weighted imaging (SWI). *J Neurotrauma* 28:915–927. <https://doi.org/10.1089/neu.2010.1712>
7. Shenton ME, Hamoda HM, Schneiderman JS, et al (2012) A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain Imaging Behav* 6:137–192. <https://doi.org/10.1007/s11682-012-9156-5>
8. Lindberg DM, Stence N V., Grubenhoff JA, et al (2019) Feasibility and accuracy of fast MRI versus CT for traumatic brain injury in young children. *Pediatrics* 144:. <https://doi.org/10.1542/peds.2019-0419>
9. Andropoulos DB (2018) Effect of Anesthesia on the Developing Brain: Infant and Fetus. *Fetal Diagn Ther* 43:1–11. <https://doi.org/10.1159/000475928>
10. Lindsey HM, Wilde EA, Caeyenberghs K, Dennis EL (2019) Longitudinal Neuroimaging in Pediatric Traumatic Brain Injury: Current State and Consideration of Factors That Influence Recovery. *Front Neurol* 10
11. Dennis EL, Babikian T, Giza CC, et al (2017) Diffusion MRI in pediatric brain injury. *Child's Nervous System* 33:1683–1692. <https://doi.org/10.1007/s00381-017-3522-y>
12. Barkovich MJ, Xu D, Desikan RS, et al (2018) Pediatric neuro MRI: tricks to minimize sedation. *Pediatr Radiol* 48:50–55
13. Copeland A, Silver E, Korja R, et al (2021) Infant and Child MRI: A Review of Scanning Procedures. *Front Neurosci* 15:632
14. Thieba C, Frayne A, Walton M, et al (2018) Factors Associated With Successful MRI Scanning in Unsedated Young Children. *Front Pediatr* 6:146. <https://doi.org/10.3389/fped.2018.00146>
15. Vannest J, Rajagopal A, Cicchino ND, et al (2014) Factors determining success of awake and asleep magnetic resonance imaging scans in nonsedated children. *Neuropediatrics* 45:370–377. <https://doi.org/10.1055/s-0034-1387816>
16. De Bie HMA, Boersma M, Wattjes MP, et al (2010) Preparing children with a mock scanner training protocol results in high quality structural and functional MRI scans. *Eur J Pediatr* 169:1079–1085. <https://doi.org/10.1007/s00431-010-1181-z>
17. Johnson K, Page A, Williams H, et al (2002) The use of melatonin as an alternative to sedation in uncooperative children undergoing an MRI examination. *Clin Radiol* 57:502–6. <https://doi.org/10.1053/crad.2001.0923>
18. Khan JJ, Donnelly LF, Koch BL, et al (2007) A program to decrease the need for pediatric sedation for CT and MRI

19. Gagner C, Landry-Roy C, Bernier A, et al (2017) Behavioral consequences of mild traumatic brain injury in preschoolers. *Psychol Med* 1–9. <https://doi.org/10.1017/S0033291717003221>
20. Li L, Liu J (2013) The effect of pediatric traumatic brain injury on behavioral outcomes: a systematic review. *Dev Med Child Neurol* 55:37. <https://doi.org/10.1111/J.1469-8749.2012.04414.X>
21. Dupont D, Beaudoin C, Désiré N, et al (2021) Report of early childhood traumatic injury observations & symptoms: Preliminary validation of an observational measure of postconcussive symptoms. *Journal of Head Trauma Rehabilitation*. <https://doi.org/10.1097/HTR.0000000000000691>
22. Beauchamp MH, Dégeilh F, Yeates K, et al (2020) Kids' Outcomes and Long-term Abilities (KOALA): Protocol for a prospective, longitudinal cohort study of mild traumatic brain injury in children 6 months to 6 years of age. *BMJ Open*. <https://doi.org/10.1136/bmjopen-2020-040603>
23. Long X, Kar P, Gibbard B, et al (2019) The brain's functional connectome in young children with prenatal alcohol exposure. *Neuroimage Clin* 24:102082. <https://doi.org/10.1016/j.nicl.2019.102082>
24. Dean DC, O'Muirheartaigh J, Dirks H, et al (2014) Modeling healthy male white matter and myelin development: 3 through 60 months of age. *Neuroimage* 84:742. <https://doi.org/10.1016/J.NEUROIMAGE.2013.09.058>
25. Dai X, Hadjipantelis P, Wang JL, et al (2019) Longitudinal associations between white matter maturation and cognitive development across early childhood. *Hum Brain Mapp* 40:4130. <https://doi.org/10.1002/HBM.24690>
26. Levin HS, Diaz-Arrastia RR (2015) Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *Lancet Neurol* 14:506–517. [https://doi.org/10.1016/S1474-4422\(15\)00002-2](https://doi.org/10.1016/S1474-4422(15)00002-2)
27. Liu J, Kou Z, Tian Y (2014) Diffuse axonal injury after traumatic cerebral microbleeds: an evaluation of imaging techniques. *Neural Regen Res* 9:1222–30. <https://doi.org/10.4103/1673-5374.135330>
28. Studerus-Germann AM, Gautschi OP, Bontempi P, et al (2018) Central nervous system microbleeds in the acute phase are associated with structural integrity by DTI one year after mild traumatic brain injury: A longitudinal study. *Neurol Neurochir Pol* 52:710–719. <https://doi.org/10.1016/J.PJNNS.2018.08.011>
29. Whitfield-Gabrieli S, Nieto-Castanon A (2012) Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connect* 2:125–41. <https://doi.org/10.1089/brain.2012.0073>
30. Andersson JLR, Sotiropoulos SN (2016) An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *Neuroimage* 125:1063–1078. <https://doi.org/10.1016/j.neuroimage.2015.10.019>
31. Andersson JLR, Graham MS, Zsoldos E, Sotiropoulos SN (2016) Incorporating outlier detection and replacement into a non-parametric framework for movement and distortion correction of diffusion MR images. *Neuroimage* 141:556–572. <https://doi.org/10.1016/j.neuroimage.2016.06.058>
32. Smith SM, Jenkinson M, Woolrich MW, et al (2004) Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23:S208–S219. <https://doi.org/10.1016/j.neuroimage.2004.07.051>
33. Jenkinson M, Beckmann CF, Behrens TEJ, et al (2012) FSL. *Neuroimage* 62:782–90. <https://doi.org/10.1016/j.neuroimage.2011.09.015>
34. Johnson CA, Garnett EO, Chow HM, et al (2021) Developmental Factors That Predict Head Movement During Resting-State Functional Magnetic Resonance Imaging in 3–

- 7-Year-Old Stuttering and Non-stuttering Children. *Front Neurosci* 15:1488.
<https://doi.org/10.3389/FNINS.2021.753010/BIBTEX>
35. Almlı CR, Rivkin MJ, McKinstry RC (2007) The NIH MRI study of normal brain development (Objective-2): Newborns, infants, toddlers, and preschoolers. *Neuroimage* 35:308–325. <https://doi.org/10.1016/j.neuroimage.2006.08.058>
 36. Dupont D, Beaudoin C, Désiré N, et al (2022) Report of Early Childhood Traumatic Injury Observations & Symptoms: Preliminary Validation of an Observational Measure of Postconcussive Symptoms. *J Head Trauma Rehabil* 37:E102–E112. <https://doi.org/10.1097/HTR.0000000000000691>

Figure 1. Percentage of children completing each MRI sequence. Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; mTBI: mild traumatic brain injury; QSM, quantitative susceptibility mapping; SWI, susceptibility-weighted imaging; T1-w, T1-weighted anatomic MRI; T2-w, T2-weighted anatomic MRI.

Table 1: Number and percentage of children completing each MRI sequence.

	mTBI	TDC	Total
Familiarization – n (%)	13 (100)	24 (100)	37 (100)
No MRI – n (%)	2 (15)	5 (21)	7 (19)
T1-w – n (%)	11 (85)	18 (75)	29 (78)
QSM – n (%) Success	10 (77)	15 (63)	25 (68)
DWI – n (%)	10 (77)	15 (63)	25 (68)
SWI – n (%)	6 (46)	14 (58)	20 (54)
T2-w – n (%)	7 (54)	12 (60)*	19 (57)*
Rs-fMRI – n (%)	6 (46)	12 (52)**	18 (50)**
Full MRI protocol – n (%)	5 (38)	13 (54)	18 (49)

Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; mTBI: mild traumatic brain injury; QSM, quantitative susceptibility mapping; SWI, susceptibility-weighted imaging; T1-w, T1-weighted anatomic MRI; T2-w, T2-weighted anatomic MRI. * Not included in the protocol of the 4 first participants. ** Not included in the protocol of the first participant.

Table 2: Number and percentage of images rated “usable” based on visual inspection of each MRI sequence

	mTBI	TDC	Total
T1-w – usable/collected (%)	11/11 (100)	18/18 (100)	29/29 (100)
QSM – usable/collected (%)	9/10 (90)	14/15 (93)	23/25 (92)
DWI – usable/collected (%)	10/10 (100)	14/15 (93)	24/25 (96)
SWI – usable/collected (%)	5/6 (83)	12/14 (86)	17/20 (85)
T2-w – usable/collected (%)	6/7 (86)	9/12 (75)	15/19 (79)
Rs-fMRI – usable/collected (%)	6/6 (100)	12/12 (100)	18/18 (100)
Total – usable/collected (%)	47/50 (94)	79/86 (92)	126/136 (93)

Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; mTBI: mild traumatic brain injury; QSM, quantitative susceptibility mapping; SWI, susceptibility-weighted imaging; T1-w, T1-weighted anatomic MRI; T2-w, T2-weighted anatomic MRI.

Table 3: MRI quantitative quality control.

	mTBI	TDC
T1-w		
unacceptable/failed [0-49.99] - n (%)	0 (0)	0 (0)
critical [50-59.99] - n (%)	0 (0)	0 (0)
sufficient [60-60.99] - n (%)	0 (0)	0 (0)
satisfactory [70-79.99] - n (%)	0 (0)	0 (0)
Good [80-89.99] - n (%)	4 (36)	2 (11)
Excellent [90-100] - n (%)	7 (64)	16 (89)
DWI		
Unusable [0] - n (%)	0 (0)	1 (7)
Poor [1] - n (%)	2 (20)	1 (7)
Fair [2] - n (%)	2 (20)	4 (26)
Good [3] - n (%)	0 (0)	1 (7)
Very good [4] - n (%)	4 (40)	2 (13)
Excellent [5] - n (%)	2 (20)	6 (40)
Rs-fMRI		
Mean [range] percent of volume with artefact	6.18 [1-10]	5.83 [1-13]
Framewise displacement - Mean (SD; IQR)	0.07 (0.39; 0.18)	-0.003 (0.84; 0.66)

Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; mTBI: mild traumatic brain injury; QSM, quantitative susceptibility mapping; SWI, susceptibility-weighted imaging; T1-w, T1-weighted anatomic MRI; T2-w, T2-weighted anatomic MRI.

Table 4 : Child experience - Comparisons between mild traumatic brain injury (mTBI) and typically developing children (TDC) groups

	mTBI	TDC	<i>p</i>-value (effect size)
Children who completed the familiarization- N (%)	13 (100)	24 (100)	
<i>Liked the familiarization</i>			.35 (95% IC=[-0.94 0.34])
Not at all - N (%)	1 (8)	0 (0)	
A little - N (%)	0 (0)	0 (0)	
Between a little and a lot - N (%)	0 (0)	1 (4)	
A lot - N (%)	4 (31)	7 (29)	
Very much - N (%)	6 (46)	13 (54)	
Children who proceeded to the MRI acquisition - N (%)	11 (85)	19 (79)	
<i>Liked the MRI</i>			.20 (95% IC=[-0.40 1.82])
Not at all - N (%)	0 (0)	4 (21)	
A little - N (%)	0 (0)	0 (0)	
Between a little and a lot - N (%)	1 (9)	2 (11)	
A lot - N (%)	3 (27)	3 (16)	
Very much - N (%)	6 (55)	10 (53)	
<i>Willing to do it again?</i>			.42 (Cramer's $V=.19$)
Yes - N (%)	8 (73)	11 (58)	
No - N (%)	2 (18)	7 (37)	

Online Supplementary Material

Parent MRI Report

Please fill out the questionnaire below in order to give us your opinion about the different steps of our study. Please use the scale (1 to 5) to answer the following questions.

Not at all 1	A little 2	Between a little and a lot 3	A lot 4	Very much 5
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1. What was your knowledge about the MRI before participating in the study?
1 2 3 4 5
2. Did you find the brochure about the MRI useful?
1 2 3 4 5
3. Did you talk about the MRI with your child before today?
1 2 3 4 5
4. Are you worried about the MRI?
1 2 3 4 5
5. Is your child worried about the MRI?
1 2 3 4 5
6. I think my child will be able to complete the MRI:
1 2 3 4 5

Child MRI Report

Not at all 1	A little 2	Between a little and a lot 3	A lot 4	Very much 5
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1. Did you like going in the machine?
1 2 3 4 5
2. Was it noisy?
1 2 3 4 5
3. Would you like to do it again?
No Yes
4. Did you want it to end?
1 2 3 4 5
5. Did you like the video? (Video chosen: _____)
1 2 3 4 5
6. Did you see the video well?
No Yes
7. Did you hear the video well?
No Yes
8. Did you like the book?
1 2 3 4 5

Research Team MRI Report

Not at all 1	A little 2	Between a little and a lot 3	A lot 4	Very much 5
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Research assistant:

1. I find the child receptive to the familiarization.
1 2 3 4 5
2. Do you think the child will get to the end of the MRI protocol?
1 2 3 4 5
3. Do you feel the child is worried about the MRI?
1 2 3 4 5
4. Do you feel find the parent is worried about the MRI?
1 2 3 4 5

MRI technician:

1. Do you think the child will get to the end of the MRI protocol?
1 2 3 4 5
2. Do you feel the child is worried about the MRI?
1 2 3 4 5
3. Do you feel the parent is worried about the MRI?
1 2 3 4 5