Journal of Visualized Experiments

Studying Brain Function in Children Using Magnetoencephalography

--Manuscript Draft--

Article Type:	Invited Methods Article - JoVE Produced Video
Manuscript Number:	JoVE58909R2
Full Title:	Studying Brain Function in Children Using Magnetoencephalography
Keywords:	Brain development; Brain function; Children; Cognitive neuroscience; Head movement; Magnetoencephalography; Mock scanner; Neuroimaging
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Additional Information:	
Question	**Response**
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Please indicate the **city, state/province, and country** where this article will be **filmed**. Please do not use abbreviations.	Sydney, NSW, Australia

Cover Letter

August 6, 2018

Dear Editor,

We wish to submit the revised manuscript entitled "**A research protocol for studying brain function in children using magnetoencephalography**" to *JOVE.*

We confirm that this work is original and has not been submitted elsewhere for publication. A preprint of this manuscript, however, will be uploaded to bioRxiv, if allowed by JOVE before acceptance.

We have included our response to the editor and reviewers' comments in the rebuttal letter, and have revised the manuscript accordingly.

As you have confirmed the receipt of our payment of the publication fee, we hope this article to be "in-press" by the end of Dec 2018.

Thank you very much for your consideration.

Yours sincerely,

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TITLE:

Studying Brain Function in Children Using Magnetoencephalography

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KEYWORDS:
brain development, brain function, children, cognitive neuroscience, head movement, magnetoencephalography, mock scanner, neuroimaging

SUMMARY:
This article introduces a child-friendly research protocol designed to improve data quality by reducing head movement during pediatric magnetoencephalography (MEG). We familiarize families with the MEG environment, train children to remain still using an MEG simulator, and correct for residual head movement artefacts using a real-time head movement detection system.

ABSTRACT:
Magnetoencephalography (MEG) is a non-invasive neuroimaging technique which directly measures magnetic fields produced by the electrical activity of the human brain. MEG is quiet and less likely to induce claustrophobia compared with magnetic resonance imaging (MRI). It is therefore a promising tool for investigating brain function in young children. However, analysis of MEG data from pediatric populations is often complicated by head movement artefacts which arise as a consequence of the requirement for a spatially-fixed sensor array that is not affixed to

the child's head. Minimizing head movements during MEG sessions can be particularly challenging as young children are often unable to remain still during experimental tasks. The protocol presented here aims to reduce head movement artefacts during pediatric MEG scanning. Prior to visiting the MEG laboratory, families are provided with resources that explain the MEG system and the experimental procedures in simple, accessible language. An MEG familiarization session is conducted during which children are acquainted with both the researchers and the MEG procedures. They are then trained to keep their head still whilst lying inside an MEG simulator. To help children feel at ease in the novel MEG environment, all of the procedures are explained through the narrative of a space mission. To minimize head movement due to restlessness, children are trained and assessed using fun and engaging experimental paradigms. In addition, children's residual head movement artefacts are compensated for during the data acquisition session using a real-time head movement tracking system. Implementing these child-friendly procedures is important for improving data quality, minimizing participant attrition rates in longitudinal studies, and ensuring that families have a positive research experience.

INTRODUCTION:

Magnetoencephalography (MEG) is a non-invasive functional neuroimaging technique which measures magnetic fields produced by the electrical activity of the human brain[1,2]. MEG offers excellent temporal resolution and superior spatial resolution compared with electroencephalography (EEG) due to the lack of signal smearing from the biological tissues between the brain sources and the sensors. In addition, MEG does not involve exposure to loud noises, radiation or magnetic fields. Set-up time is rapid and participants can be accompanied by a parent or caregiver throughout testing. Taken together, these features make MEG a promising tool for investigating the development of typical and atypical brain function in young children[2].

To measure brain responses using MEG, research participants must insert their heads into a helmet housing a fixed array of superconducting sensors. It is crucial that the participants keeps their heads still throughout the MEG recording, as changes in the head position relative to the sensors both degrade the neuromagnetic signal distribution and impede accurate source estimation. Inaccurate source estimation inevitably leads to inaccurate statistical inferences in source power, functional connectivity and network analyses[3].

Minimizing head movement can be particularly challenging during pediatric MEG assessment for a number of reasons. First, assessing young children in an adult MEG system is problematic as children's heads are much smaller than those of adults, and the increased space between the helmet and the child's scalp allows for unconstrained head movement. Second, the novel MEG environment – a large machine locked inside a windowless magnetically shielded room – can be intimidating for young children, and head movement may be a consequence of anxiousness. Third, without training, children may not fully understand or comply with the requirement to remain still for the duration of the experiment. Finally, children who have a limited capacity to tolerate boredom may find that some MEG experiments take too long or are tedious, resulting in restlessness and head movement artefacts.

To tackle the long-standing challenge of head movement in pediatric MEG research, this article presents recent hardware and methodological advances that are implemented in the child-friendly MEG protocol used at the KIT-Macquarie Brain Research Laboratory (Macquarie University, Sydney, Australia). As outlined in a previous paper from this laboratory[4], the problems involved in the use of a loose-fitting adult-sized helmet dewar have been addressed by installing a world-first, whole-head pediatric MEG system with a bespoke helmet dewar to better fit the heads of young children between approximately three-to-six years of age. This hardware adaptation improves the signal-to-noise ratio, as the sensors are physically closer, on average, to the child's scalp[5,6]. More recently, the KIT-Macquarie Brain Research Laboratory has developed several new and novel procedures to overcome the aforementioned antecedents of head movement and hence to improve data quality.

All of the procedures in this protocol are explained through a narrative in which the child participant actively engages in an "astronaut space mission". This narrative ensures that the child's MEG research experience is not only less intimidating, but also exciting. Implementing these procedures into a child-friendly MEG protocol is important for improving data quality, minimizing participant attrition rates in longitudinal studies, and ensuring that families have a positive experience in their research participation.

PROTOCOL

This research protocol has been approved by the Macquarie University Human Research Ethics Committee.

1. MEG familiarization resources

1.1. Provide families with resources to learn about MEG prior to visiting the MEG laboratory, such as a child-friendly scientific article[7] explaining MEG and the MSR, a story-board detailing the steps involved in completing the MEG experiment (e.g., **Supplementary Figure 1** and an MEG information sheet for parents or caregivers (e.g., **Supplementary Figure 2**).

2. MEG familiarization session

NOTE: The familiarization session typically runs for 30 min, including an introduction to the MSR (5 minutes), a practice digitization (5 minutes), and MEG simulator training, including practice on the experimental task (20 minutes). Conduct the familiarization session between one-to-seven days prior to data acquisition.

2.1. MSR introduction

2.1.1. Take the child on a tour of the MSR ("spaceship") which is decorated in space-related wall art to reinforce the space mission theme.

2.1.2. Ask the child to practice lying back with their head in the helmet dewar.

2.1.3. Tell the child to lie as still as possible so that the spaceship stays on course and can reach its final destination.

2.2. Digitization:

2.2.1. Seat the child on a high chair and fit them with a polyester swimming cap ("astronaut helmet") containing five marker coils. Adapt loose-fitting caps by folding up the sides. NOTE: The coils send data to a continuous motion tracking unit.

2.2.2. Place a transmitter and three receivers around the child's neck.

2.2.3. Ask the child to demonstrate their best 'statue' pose and offer frequent positive reinforcement when they stay still.

NOTE: This serves to minimize head movement during digitization that may compromise the accuracy of the subsequent co-registration with the MEG sensors[8].

2.2.4. Use a pen digitizer (see **Table of Materials**) to record the position of three fiducial points (the nasion and left and right pre-auricular points) and the five marker coils, as well as the shape of the surface of the head. NOTE: This data is used to later determine the position of the child's head in relation to the MEG sensors.

2.2.5. Remove the cap, transmitter and three receivers from the child's neck.

2.3. MEG simulator:

2.3.1. Take the child to the room housing the MEG simulator (see **Table of Materials** and steps 9 and 10 in **Supplementary Figure 1**), a full-size replica of an MEG system. The MEG simulator is decorated with space-themed stickers and is equipped with a mock helmet dewar, a bed, a button box and, for visual displays, a screen situated above the mock dewar

2.3.2. Briefly describe the MEG scanning procedures (i.e., lying still and participating in the practice experimental task) through the narrative of a practice space mission.

2.3.3. Fit the child with an 'astronaut helmet' – a polyester swimming cap which has a motion detector attached at the front (see **Table of Materials**).

2.3.4. Invite the child to lie in the simulator and watch a video of their choosing. If the child appears nervous, first demonstrate the experimental procedures with a toy.

NOTE: Whenever the child's head movement exceeds a pre-determined threshold (e.g., 5 mm), the motion tracking system (see **Table of Materials**) will automatically pause the video and wait for the experimenter to manually restart the video and restore the movement baseline.

2.3.5. When the child completes this part of the simulator training, provide the child with training on the experimental task using a separate set of unique stimuli.

2.3.6. At the end of the task training, offer the child an astronaut training certificate.

3. MEG data acquisition session

NOTE: The data acquisition session typically runs for approximately 30 min, including digitization (5 minutes), setting up the participant inside the MSR (5 minutes) and data acquisition (approximately 20 minutes, depending on the length of the experimental paradigm).

3.1. Preliminary procedures

3.1.1. Conduct a 30-to-60 second empty room recording approximately 15 minutes before the child arrives to identify any significant external noise that is detected by the MEG system[8].

3.1.2. When the child arrives, confirm that they are not wearing any magnetic material on their clothes or carrying any in their body, as magnetic materials can distort the MEG signal (see **Figure 1B** for an example of signal noise due to metal on the participant).

NOTE: If the parent or caregiver wishes to accompany their child inside the MSR, the removal of magnetic materials applies to them too.

3.2. Digitization

3.2.1. Check whether the child needs to go to the toilet before commencing digitization, as once the digitization step is completed, the cap cannot be removed until the MEG acquisition session has finished.

3.2.2. Repeat the digitization procedure outlined in the "MEG familiarization session" section above.

NOTE: If the cap moves more than 5 mm over the course of the experiment, perform a second digitization at the end of the experiment

3.3. MSR set-up

3.3.1. Take the child to the MSR ("the spaceship").

NOTE: Two researchers are required for this procedure – one to accompany the child inside the MSR as the “assistant researcher” (along with the parent or caregiver, if desired) and one to run MEG data acquisition outside the MSR as the “main researcher”. The MSR set-up typically takes 5 minutes.

3.3.2. Set up equipment inside the MSR (assistant researcher)

3.3.2.1. Ask the child to place their head into the helmet dewar.

3.3.2.2. Check that the child’s head is centrally aligned such that the crown of the head is as close as possible to the back of the helmet dewar without touching.

3.3.2.3. Ensure that the child is comfortable, relaxed, and remains as still as possible during MEG recording.

3.3.2.4. During the set-up, keep the child entertained by playing a video of their choosing on a screen above the dewar.

3.3.3. Set up equipment outside the MSR (main researcher)

3.3.3.1. Conduct a pre-experiment/baseline marker coil measurement to record the initial head position with respect to the helmet dewar.

3.3.3.2. Conduct a co-registration between the child’s head and the sensor array using both the initial marker coil measurement and the digitization head shape data.

NOTE: These preparatory measurements enable visual inspection of head position inside the dewar to ensure that the child’s head is correctly positioned. If these conditions are not met, re-position the child and conduct another co-registration before starting data acquisition.

3.4. Data acquisition

3.4.1. Once satisfied with the head position with respect to the helmet dewar, start the MEG recording and the experimental task.

3.4.2. Record ongoing head movements with a pediatric MEG software system called Real-Time Head Movement (ReTHM)[9].

3.5. Ending the experiment

3.5.1. When the experimental task is finished, turn off ReTHM and end the MEG recording. Conduct a post-experiment marker coil measurement to measure the final head position with respect to the helmet dewar.

NOTE: This measurement provides a simple visual inspection of overall head movements during the experiment.

3.5.2. Offer the child a gift bag ("astronaut kit") for their participation and remunerate the family for their time and travel costs.

REPRESENTATIVE RESULTS

Common Magnetoencephalography signals

Common MEG signals are displayed in **Figure 1**, including a normal MEG signal (**Figure 1A**), as well as MEG signal noise due to metal on the participant (**Figure 1B**), in which case unlock the sensors, open the MSR door and ask the participant to remove any metal from their body, then take the metal object out of the MSR and perform an auto-tune before repeating the procedures outlined in section 3.5; interference from an electronic device (**Figure 1C**, most often from a mobile phone), in which case turn off any electronic devices or move them away from the MSR; a clenched jaw (**Figure 1D**), in which case remind the participant to relax their jaw for the duration of the MEG recording; alpha waves (**Figure 1E**; these are defined by eight to 12 continuous waves in a 1-second interval), in which case check that the participant is not asleep (it is fine to continue if they are awake); and trapped magnetic flux (**Figure 1F**); in which case unlock the sensors and turn on the coil heaters on for 5 minutes. If the flux persists after a subsequent auto-tuning, mark affected channel for removal from subsequent data analysis.

Head movement during data acquisition

Pediatric MEG data before and after ReTHM correction is displayed in **Figure 2**. Data was collected from a three-year-old boy who passively listened to auditory tones for 15 minutes. Data was de-noised[10], band-pass filtered[11] (1-15 Hz), baseline-corrected and averaged. Root-mean-square (RMS) magnetic waveforms (in the right column) were computed from all sensors. Averaged in-scanner head movements were 44.3 mm. As demonstrated, ReTHM compensated for motion-related artefacts, resulting in more focal isofield contour maps (at the peak of the RMS waveforms; A), less distorted RMS magnetic waveforms (B), and more meaningful source reconstruction (C) in the bilateral auditory lobes.

FIGURE LEGENDS:

Figure 1. Examples of common MEG signals. **(A)** A normal MEG signal. (**B**–**F**) MEG signal noise due to **(B)** metal on the participant (specifically, noise caused by a small metal buckle on a singlet strap), **(C)** interference from an electronic device, **(D)** a clenched jaw, **(E)** alpha waves, and **(F)** trapped magnetic flux. For panels C, E, and F, the time scale on the x-axis is in 10-second intervals, and amplitude scale on the y-axis is 32768 A/D.

Figure 2. Pediatric MEG data before and after Real-Time Head Movement (ReTHM) correction. Data was collected from a three-year-old boy who passively listened to auditory tones for 15 minutes. Averaged in-scanner head movements were 44.3 mm. (A) More focused isofield contour maps (at the peak of the RMS waveforms; (B) less distorted RMS magnetic waveforms, and (C)

more meaningful source reconstruction in the bilateral auditory lobes are revealed after ReTHM correction.

Supplementary Figure 1. A story board outlining 10 simple steps for completing the "astronaut training" (i.e., the MEG experiment). This is sent to families prior to visiting the MEG laboratory in order to guide children's expectations for the acquisition session, as well as to build excitement in anticipation of the "astronaut training". On data acquisition day, the children follow the story as the experiment progresses and collect stamps after completing each step. Photographs reproduced with informed written parental consent.

Supplementary Figure 2. An MEG information sheet for parents or caregivers explaining the MEG, the MSR, what to expect on data acquisition day and what to wear. Photograph reproduced with informed written parental consent.

DISCUSSION

In recent years, MEG has been established as a valuable non-invasive neuroimaging technique for investigating the neural mechanisms underpinning brain development[1]. However, in-scanner head movements pose a notorious barrier to obtaining good quality MEG data, particularly when assessing pediatric populations. To overcome this problem, this article presented a pediatric MEG research protocol which builds upon procedures outlined in a previous paper from the KIT-Macquarie Brain Research Laboratory [4].

The critical procedures include (1) providing children with MEG familiarization resources from which they can learn about the MEG experiment prior to visiting the lab, which include a child-friendly research article[7] explaining the MEG system and the magnetically shielded room (MSR), a story-board outlining 10 simple steps for completing the MEG experiment (**Supplementary Figure 1**), and an MEG information sheet for parents and caregivers (**Supplementary Figure 2**); (2) Preceding the MEG acquisition session with a familiarization session, wherein children are acquainted with MEG procedures and are trained to keep their heads still whilst lying inside an MEG simulator; (3) using passive or "gamified" experimental paradigms to minimize head movement due to boredom and restlessness; and (4) tracking ongoing head movements during online data acquisition using a Real-Time Head Movement (ReTHM) system[9]. Data obtained from ReTHM can be used to conduct offline correction of head movement artefacts when pre-processing the MEG data.

The acquisition of high-quality MEG data critically depends upon the child feeling at ease in the novel MEG environment. To foster this sense of ease, researchers are encouraged to devote time to familiarizing children and their families with the MEG environment and procedures prior to commencing data acquisition. This can be achieved through offering children and their parents MEG resources which explain the MEG procedures in simple, accessible language. Furthermore, families can be invited to visit the MEG laboratory before the data acquisition session to meet the researchers and practice the MEG testing procedures. Through training on the MEG simulator, children implicitly learn the importance of keeping their heads still whilst lying in the

MEG. While the MEG familiarization requires both the researchers and the families to devote additional time to the data collection process, the advantages of improving MEG data quality, as well as minimizing the time and cost of conducting subsequent MEG data acquisition sessions, arguably outweighs this downside. Furthermore, performance and compliance during the familiarization session can be used to indicate whether the child is or is not suitable to invite back for an actual MEG data acquisition session.

To minimize in-scanner head movement due to restlessness, it is preferable to use a passive experimental paradigm which does not require instructions, overt attention or active participation. For example, a reliable evoked response can be obtained with an auditory oddball paradigm[12], whereby the participant passively listens to a sequence of auditory tones whilst entertained by a silent video. For studies requiring an overt response, the researcher should aim to embed the experimental task in an engaging game-style paradigm[11]. This improves cooperation and minimizes restlessness during the task. In visual experiments, the use of an MEG-compatible eye-tracker entails little additional set-up time but is necessary in ensuring that children have fixated on the position of the visual stimulus[13].

Any residual head movement artefacts can be corrected for using real-time head motion tracking. For example, data obtained from ReTHM can be stored in the MEG recording file and used to compensate for head movement during data acquisition in such a way that head-to-sensor localization can be restored to the pre-movement level to allow for an optimal source reconstruction which is essential for subsequent source level data analyses[14].

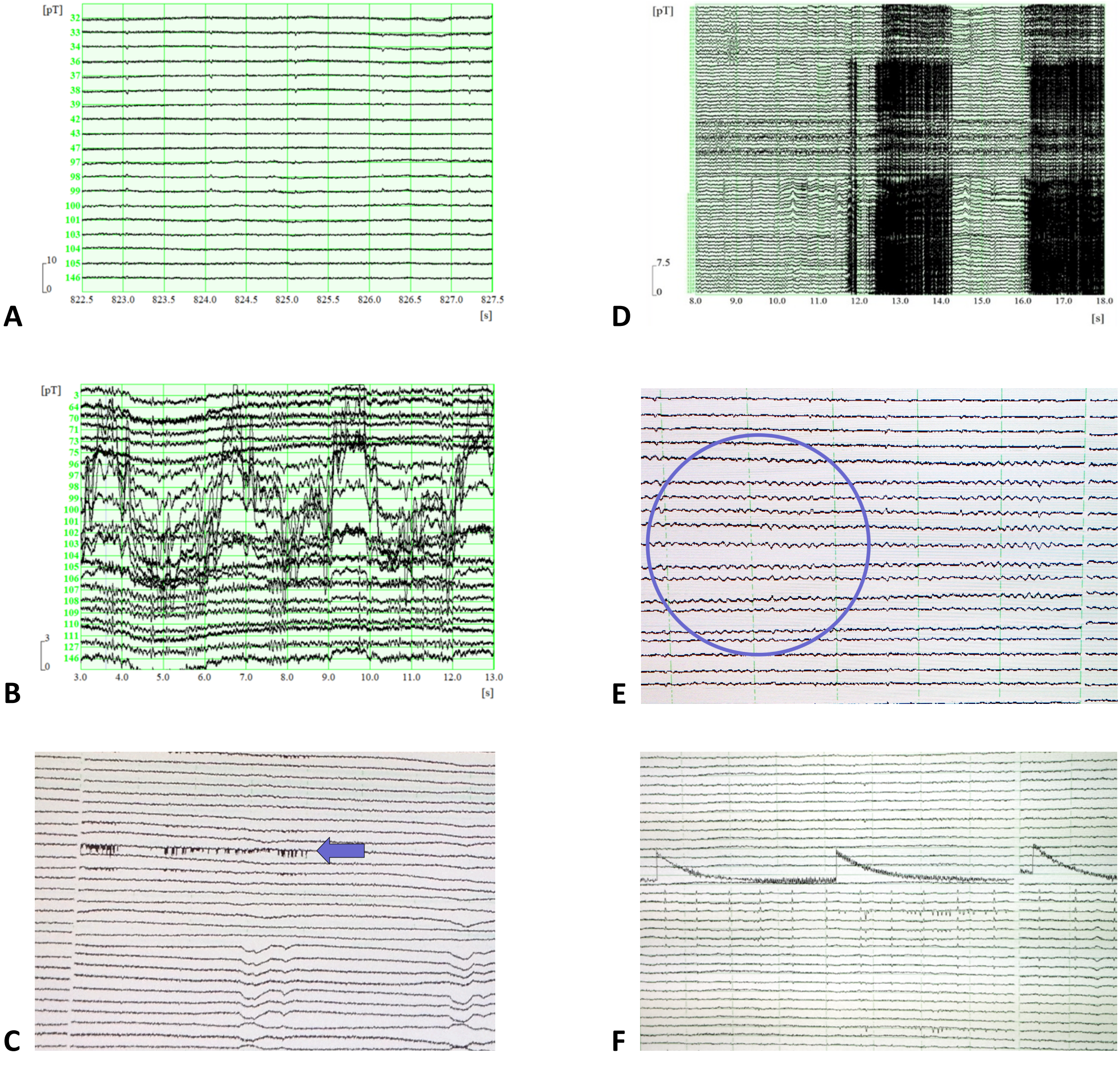
The implementation of this protocol seeks to improve the quality of pediatric MEG data, minimize participant attrition rates in longitudinal studies, and ensure that families have an enjoyable experience of MEG research participation, with the overarching goal of improving our understanding of early brain development in both typical and atypical populations.

ACKNOWLEDGMENTS
This work was supported by the Australian Research Council grants CE110001021, DP170103148 and DP170102407. Wei He was supported by a Macquarie University Research Fellowship (MQRF, IRIS Project: 9201501199). Hannah Rapaport was supported by the Australian Government's Research Training Program (RTP) and the Macquarie University Research Excellence Scholarship (MQRES). Robert A Seymour was supported by PhD scholarships from Aston University, Birmingham, UK and Macquarie University, Sydney, Australia. Paul F. Sowman was supported by the National Health and Medical Research Council (1003760) and the Australian Research Council (DE130100868). The authors acknowledge the collaboration with the Kanazawa Institute of Technology and the Yokogawa Electric Corporation in establishing the KIT-Macquarie Brain Research Laboratory.

DISCLOSURES
The authors have nothing to disclose.

REFERENCES:

1. Baillet, S. Magnetoencephalography for brain electrophysiology and imaging. *Nature Neuroscience.* **20,** 327–339 (2017).
2. Gaetz, W. *et al.* Magnetoencephalography for clinical pediatrics: Recent advances in hardware, hethods, and clinical applications. *Journal of Pediatric Epilepsy.* **04,** 139–155 (2015).
3. Stolk, A., Todorovic, A., Schoffelen, J.-M., Oostenveld, R. Online and offline tools for head movement compensation in MEG. *Neuroimage.* **68,** 39–48 (2013).
4. Tesan, G., Johnson, B. W., Reid, M., Thornton, R., Crain, S. Measurement Of Neuromagnetic brain function in pre-school children with custom sized MEG. *Journal of Visualized Experiments.* **36,** 2923–2934 (2010).
5. Johnson, B. W., Crain, S., Thornton, R., Tesan, G., Reid, M. Measurement of brain function in pre-school children using a custom sized whole-head MEG sensor array. *Clinical Neurophysiology.* **121,** 340–9 (2010).
6. He, W., Brock, J., Johnson, B. W. Face-sensitive brain responses measured from a four-year-old child with a custom-sized child MEG system. *Journal of Neuroscience Methods.* **222,** 213–217 (2014).
7. Brock, J., Sowman, P. Meg for kids: listening to your brain with super-cool SQUIDs. *Frontiers for Young Minds.* **2,** 10–13 (2014).
8. Gross, J. *et al.* Good practice for conducting and reporting MEG research. *Neuroimage.* **65,** 349–363 (2013).
9. Oyama, D. *et al.* Real-Time coil position monitoring system for biomagnetic measurements. *Physics Procedia.* **36,** 280–285 (2012).
10. de Cheveigné, A., Simon, J. Z. Denoising based on spatial filtering. *Journal of Neuroscience Methods.* **171,** 331–339 (2008).
11. Cheyne, D., Jobst, C., Tesan, G., Crain, S., Johnson, B. Movement-related neuromagnetic fields in preschool age children. *Human Brain Mapping.* **35,** 4858–4875 (2014).
12. Näätänen, R., Pakarinen, S., Rinne, T., Takegata, R. The mismatch negativity (MMN): towards the optimal paradigm. *Clinical Neurophysiology.* **115,** 140–4 (2004).
13. He, W., Brock, J., Johnson, B. W. Face processing in the brains of pre-school aged children measured with MEG. *Neuroimage.* **106,** 317–327 (2015).
14. Wehner, D. T., Hämäläinen, M. S., Mody, M., Ahlfors, S. P. Head movements of children in MEG: quantification, effects on source estimation, and compensation. *Neuroimage.* **40,** 541–550 (2008).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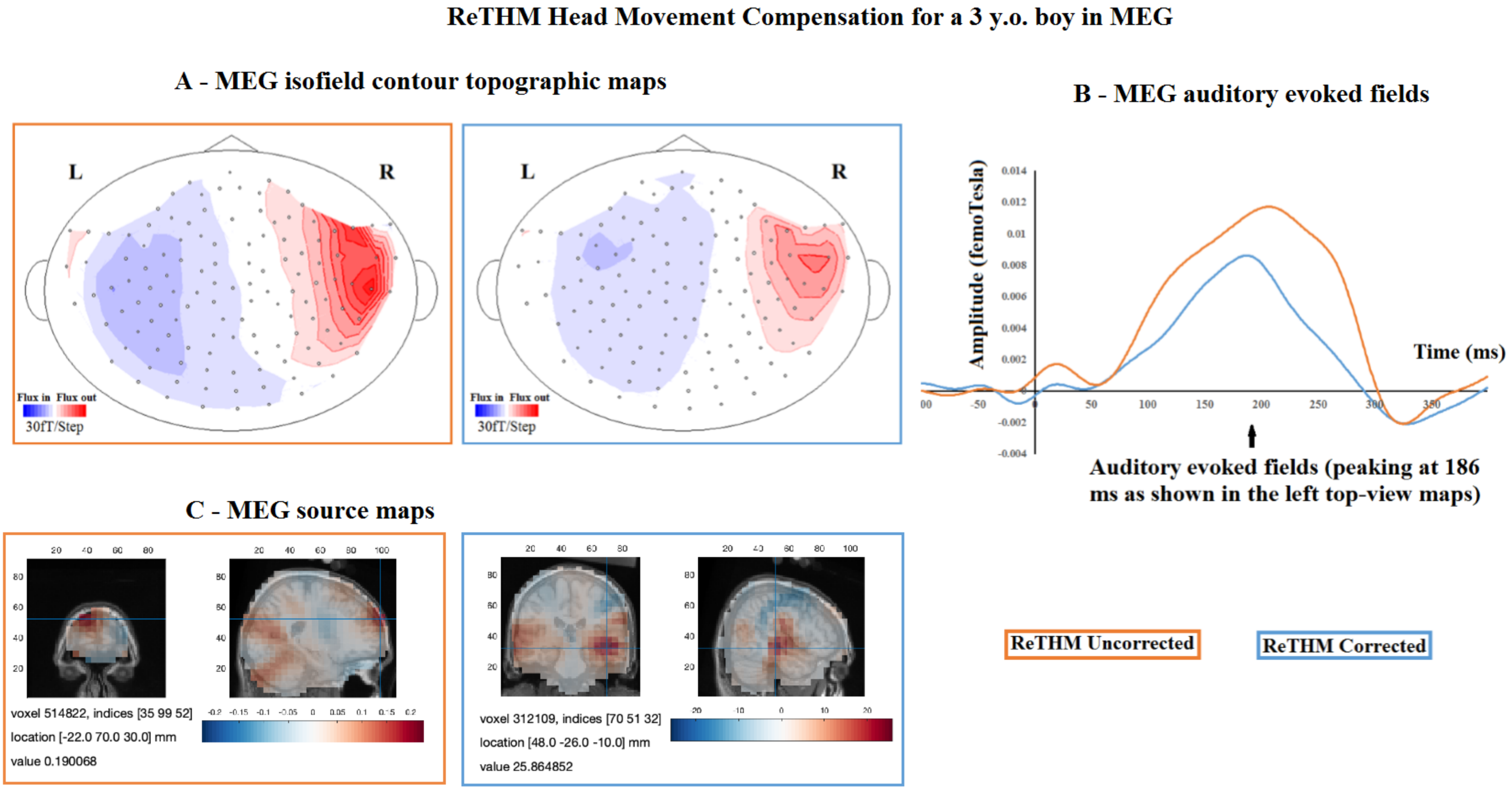
ReTHM Head Movement Compensation for a 3 y.o. boy in MEG
A - MEG isofield contour topographic maps
L
R
Flux in Flux out
30fT/Step
L
R
Flux in Flux out
30fT/Step
B - MEG auditory evoked fields
Amplitude (femoTesla)
0.014
0.012
0.01
0.008
0.006
0.004
0.002
-0.002
-0.004
Time (ms)
-50
0
50
100
150
200
250
300
350
Auditory evoked fields (peaking at 186 ms as shown in the left top-view maps)
C - MEG source maps
voxel 514822, indices [35 99 52]
location [-22.0 70.0 30.0] mm
value 0.190068
-0.2 -0.15 -0.1 -0.05 0 0.05 0.1 0.15 0.2
voxel 312109, indices [70 51 32]
location [48.0 -26.0 -10.0] mm
value 25.864852
-20 -10 0 10 20
ReTHM Uncorrected
ReTHM Corrected

Name of Material/ Equipment	Company	Catalog Number
5 marker Coil set	Kanazawa Institute of Technology (KIT) and Yokogawa Electric Corporation, Japan	PQ11MKA
Fastrak Digitizer – 3D	Polhemus Cochester, VT, USA	1A0383-001
Magnetoencephalography (MEG)	Kanazawa Institute of Technology (KIT) and Yokogawa Electric Corporation, Japan	PQ1160C
MEG simulator	Fino, NSW, Australia	
MoTrack system	Psychological Software Tools, PA, USA	MTK-09314-1307
Polyester caps	Speedo	N/A

Comments/Description

Pen digitizer

Motion tracking system
product code: SPE11733.435

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Title of Article: A research protocol for studying brain function in children using magnetoencephalography

Author(s): Hannah Rapaport, Robert A. Seymour, Paul F. Sowman, Nick Benikos, Elisabeth Stylianou, Blake W. Johnson, Stephen Crain, Wei He

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Signature: Date: August 6 2018

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Rebuttal Document

ARTICLE TITLE:
A research protocol for studying brain function in children using magnetoencephalography

AUTHORS AND AFFILIATIONS:
Hannah Rapaport[1,2], Robert A. Seymour[1,2,3], Paul F. Sowman[1,2], Nick Benikos[1,2], Elisabeth Stylianou [1,2], Blake W. Johnson[1,2], Stephen Crain[1,4], Wei He[1,2]

4th December 2018

Editorial comments:

1. One of the authors has a UK affiliation; please have them sign the UK ALA (attached) and include it with your revised submission; in particular if they receive funding from a UK agency.
This author (Robert A. Seymour) has signed the UK ALA, which is attached with our revised submission.

2. Figure 1F: Please explain the 2 halves of the image shown in this panel.
We have updated Figure 1 such that panel F now only has a single image of the normal screen view.

3. Figure 2: The legend for this is still somewhat unclear-please explicitly state what each part of the figure is.
We have explained explicitly in the legend of the figure 2 about what each part of the figure is.

4. Have you received informed consent regarding the photos of children in Supplemental Figures 1 and 2? Please indicate if so.
A photo consent form, covering both Supplemental Figures 1 and 2, is attached.

Note: As we could not track down the consent form for the photo in Supplemental Figure 2 (an old photo of a little girl), we have replaced the photo with one that is covered by the attached consent form. A new version of the Supplemental Figure 2 is attached.

7th September 2018

Editorial comments:
Changes to be made by the Author(s):

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.
We have proof-read and corrected the manuscript for spelling and grammar issues.

2. Please print and sign the attached Author License Agreement - UK. Please then scan and upload the signed ALA with the manuscript files to your Editorial Manager account.
The ALA is attached.

3. Figures 1 and 2: Please move them to supplemental files.
Moved to supplementary files and changed in text.

4. Figure 3: Please use screenshots instead of taking images of the computer screen.
We have tried our best to improve the quality of this figure. Please find our detailed response to the same comment raised by Reviewer #1 below.

5. Please adjust numbers following author names to indicate different affiliations. Numbering follows the order of authors. First author gets 1, next author with different affiliation gets 2, etc., following from first to last.
The numbers are in the correct order now.

6. Please revise the protocol text to avoid the use of any personal pronouns (e.g., "we", "you", "our" etc.).
All personal pronouns have been removed from the protocol text.

7. Please revise the protocol to contain only action items that direct the reader to do something (e.g., “Do this,” “Ensure that,” etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as “could be,” “should be,” and “would be” throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a “Note.” Please include all safety procedures and use of hoods, etc. However, notes should be used sparingly and actions should be described in the imperative tense wherever possible.
The protocol now only contains action items. Any text that could not be written in the imperative tense has been added as a “Note”. Notes have been used sparingly. Phrases, such as “could be,” “should be,” and “would be”, have been removed.

8. The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.
All discussion items that were previously in the Protocol section have been moved to the Discussion section.

9. The Protocol should be made up almost entirely of discrete steps without large paragraphs of text between sections. Please simplify the Protocol so that individual steps contain only 2-3 actions per step and a maximum of 4 sentences per step. Use sub-steps as necessary.
The protocol items have been simplified to 2-3 actions per step, with a maximum of 4 sentences per step.

10. Please include single-line spaces between all paragraphs, headings, steps, etc.
Single-line spaces have been added.

11. After you have made all the recommended changes to your protocol (listed above), please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.
Highlighting has been completed.

12. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one action that is written in imperative tense.
Full sentences have been highlighted. All highlighted parts include actions.

13. Please include all relevant details that are required to perform the step in the highlighting. For example: If step 2.5 is highlighted for filming and the details of how to perform the step are given in steps 2.5.1 and 2.5.2, then the sub-steps where the details are provided must be highlighted.
All relevant details are highlighted.

14. JoVE articles are focused on the methods and the protocol, thus the discussion should be similarly focused. Please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:
a) Critical steps within the protocol
We have emphasised the critical steps within the protocol (i.e., familiarisation resources and session, and movement detection/correction system).

b) Any modifications and troubleshooting of the technique
This is addressed in the Representative Results section ("1. Common Magnetoencephalography signals"), which details several causes of signal interference and advises on how to resolve the interference.

c) Any limitations of the technique
We mention the main downside of this protocol in the Discussion, namely the additional time that researchers and families would need to devote to the experiment with the inclusion of the MEG familiarisation session.

d) The significance with respect to existing methods
We mention the significance in the final paragraph – namely that our protocol will hopefully improve paediatric MEG data quality, which will improve our understanding of early brain development.

e) Any future applications of the technique.
We suggest, in the final paragraph, that implementing these protocols will improve the quality of future paediatric MEG data.

15. References: Please do not abbreviate journal titles.
Abbreviations have been removed and journal titles are written in full.

Reviewers' comments:

Reviewer #1:
Manuscript Summary:
The manuscript presents a research protocol to perform MEG recordings on pediatric population while reducing head movement artefacts. The head movement minimization is carried out by training the children to stay still during the recording (thanks to a MEG familiarization session prior to the recording session), as well as by using a real-time head movement tracking system to correcting for residual artefacts. The manuscript is very well written and easy to read.

Major Concerns:
The quality of Figure 3 **[now labelled Figure 1]** must be improved. This figure is meant to show differences in the MEG signals when affected by specific noise sources, however the quality of all the panels is very low:
- some writings are cut or out of focus;
- signals appear sideways in some panels (A and C);
- the amplitude scale and the time scale are not always reported;
- in panel F is not clear what two different windows are showing.
This figure is now labelled Figure 1 in the manuscript. We have deleted the text that was out of focus. We have tried our best to improve the quality of this figure by replacing panels A, B, and D with screenshots as suggested. Regarding panels C and F – unfortunately we do not have this data saved, and recreating these interference signals would be harmful to the MEG system. We also believe the two window view in panel F facilitates a better overview of this particular type of noise, i.e., where all channels are collapsed on the left side and where a single channel is affected on the left side. The amplitude scale in panels A, B, and D are all in place now, whereas the amplitude scale in other panels is in A/D unit and is now reported in the title of the figure.

Previous works describing the importance and the clinical use of MEG in pediatric population should be properly cited, such as Gaetz et al. (2015) and Papadelis et al. (2013).
We have cited these key references in the Introduction section.

It would be also interesting to see the difference in the source reconstruction results, before and after the compensation for movement-related artefacts.
We have now added the source localisation results in the revised Figure 2. Please note for simplicity we removed the motor response data since the movement-related confounds were not clear.

The discussion should be expanded, by including a discussion on which are the most critical steps in the protocol and which are the limitations.

We have expanded the discussion and included an emphasis on the critical steps within the protocol (namely, the familiarisation resources and session, and movement detection/correction system).

Reviewer #2:
Manuscript Summary:
The manuscript describes their protocol for successfully collecting MEG data from young children. It is well-described and likely useful for the field. The manuscript is well-written and the figures provide useful information that will help others follow a similar protocol. The methods used are consistent with other labs and are expected to be useful for individuals new to pediatric MEG.

Major Concerns:
no major concerns

Minor Concerns:
no minor concerns.

Supplemental Figure 1

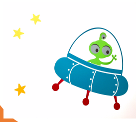
ccd ARC CENTRE OF EXCELLENCE IN COGNITION AND ITS DISORDERS

Neuronauts brain science club

MACQUARIE University

1

Hi ______________ (name) !
Welcome to Neuronauts Brain Science Club!
Read the 10 steps to find out about your **astronaut training**.



2

Here is the **space station** where you will do your **astronaut training**.
Take the lift to **level 3**!

3

Wait here to meet your **astronaut friends**.

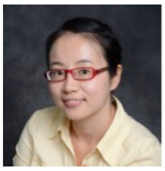
4

Here are your **astronaut friends**. You will meet some of them when you arrive.


Hannah


Paul


Liz


Wei


Nick


Liz


Robert

5

The astronauts will give you a **tour** of the **space station**.

6

The astronauts will put an **astronaut cap** on your head.

7

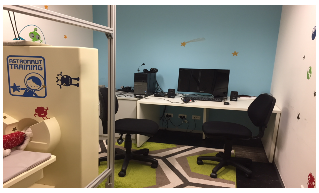
You will lie down in the **rocket ship** and watch a video. You will hear some **sounds** 𝄞 coming from the **rocket ship**.

8

You will do some word **games** and **puzzles**.

9

You will listen to some **sounds** 𝄞 through headphones.



10

Well done! You finished your astronaut training! You will receive a special **astronaut kit** to take home!

See you next time!

Australian Government Australian Research Council · MACQUARIE University · THE UNIVERSITY OF WESTERN AUSTRALIA · THE UNIVERSITY OF SYDNEY · UNSW SYDNEY · une University of New England

e: hannah.rapaport@hdr.mq.edu.au

MACQUARIE University

ccd ARC CENTRE OF EXCELLENCE IN COGNITION AND ITS DISORDERS

Pre-schooler MEG study Information Sheet

Thank you for your interest in the study! Here's how to prepare for your MEG experiment.

The MEG

The MEG is completely silent. Many participants comment on how relaxing it is! The MEG is completely safe and non-invasive; it passively records magnetic fields. The room is shielded to block out all magnetic fields except for those emitted by the brain.

During the experiment, your child will lie on a bed inside the MSR room with their head resting in the plastic helmet.

The MSR

The MEG recorder is housed inside a magnetically shielded room (MSR). No metal can be taken inside the MSR and you will be asked to remove metal items from yourself and your child such as keys, belt buckles, jewellery and mobile phones. Please alert the experimenter ahead of time if you or your child has any of the following as it may exclude you sitting in the MSR with your child during the experiment:

- Dental crowns, bridges, or implants
- Braces or permanent dental wires
- Non-removable retainers or dentures
- Cardiac Pacemaker/pacing wires or artificial heart valves
- Hearing aids, cochlear/ear implant, ocular/eye implant
- Other surgical implants (e.g. screws, plates, rods, shunts)
- Hip replacement, artificial joint or artificial limb
- IUD
- Non-removable jewellery (e.g. rings, body piercings)
- Other metal permanently attached to your body

Please also let the experimenter know if you have:

- Claustrophobia or are unable to be in the MSR for the length of the experiment

Participant information is kept strictly confidential.

What to Expect

- When you arrive, the experimenter will show you and your child around the lab and ask you to sign a consent form. Participation is always voluntary.
- Your child will wear a stretchy cap containing a few electrodes. We will use a digitising pen to create a digital 3D representation of the shape of your head.
- Your child will be asked to lie very still inside the MSR for the length of the experiment, while watching a silent movie of their choice.
- You can also sit with your child in the MSR.
- After the MEG recording, your child will wear some headphones to check their hearing, and play some short games.

What to Wear

Just prior to the scan we will ask you to remove all metal items. Please note you will not be able to wear the following in the MEG:

- Glasses (you may wear contact lenses). Just prior to entering the MEG we can provide you with MEG compatible glasses.
- Underwire bras or bras with metal clasps (you may wear a cloth-only bra; we have a gown should you wish to use it)
- Jewellery
- Clothing with large metal buttons or zippers (standard zippers on jeans are OK)
- Clothing with sequins, glitter, or metallic thread
- Makeup containing metal (e.g. mascara, metallic eyeshadow, glitter nail polish)

Where to Find Us

We are located at:
Level 3, The Australian Hearing Hub
16 University Avenue
Macquarie University
North Ryde NSW 2109

Parking is available in the basement of our building. We are also easily accessible by public transport. The closest train station is Macquarie University station. Bus routes also go through campus and drop off on University Avenue.