A Home-Based Approach to Auditory Brainstem Response Measurement: Proof-of-Concept and Practical Guidelines

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ABSTRACT

Broad-scale neuroscientific investigations of diverse human populations are difficult to implement. This is because the primary neuroimaging methods (magnetic resonance imaging, electroencephalography [EEG]) historically have not been portable, and participants may be unable or unwilling to travel to test sites. Miniaturization of EEG technologies has now opened the door to neuroscientific fieldwork, allowing for easier access to under-represented populations. Recent efforts to conduct auditory neuroscience outside a laboratory setting are reviewed and then an in-home technique for recording auditory brainstem responses (ABRs) and frequency-following responses (FFRs) in a home setting is introduced. As a proof of concept, we have conducted two in-home electrophysiological studies: one in 27 children aged 6 to 16 years (13 with autism spectrum disorder) and another in 12 young adults aged 18 to 27 years, using portable electrophysiological equipment to record ABRs and FFRs to click and speech stimuli, spanning rural and urban and multiple homes and testers. We validate our fieldwork approach by presenting waveforms and data on latencies and signal-to-noise ratio. Our findings demonstrate the feasibility and utility of home-based ABR/FFR techniques, paving the course for larger fieldwork investigations of populations that are difficult to test or recruit. We conclude this tutorial with practical tips and guidelines for

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recording ABRs and FFRs in the field and discuss possible clinical and research applications of this approach.

KEYWORDS: auditory brainstem response, frequency-following response, fieldwork, autism spectrum disorder

It has been nearly a hundred years since the advent of electrobiological measurements of brain function.[1] These electrobiological techniques are now commonly used in medical and research settings in numerous fields.[2] The electrical activity of the nervous system activity can be detected noninvasively at the scalp by small metal electrodes, making such techniques suitable for children and adults, as well as neurotypical and clinical populations.[2] Such neuroelectric measures are currently used to index a variety of sensory and cognitive processes including memory, attention, language, and the fidelity and stability of sensory neural processing.[3–7] Unlike behavioral tests that generally must be adapted according to the age and physical ability of the participant, many neuroelectric tests have the advantage that the same procedures can be implemented across the lifespan,[8] and are often easier to implement in individuals with diverse language and motor output, short attention spans, and who are generally hard to test.[9,10]

Historically, neuroelectric testing has required large, heavy, specialized equipment that was prone to electrical interference. This limited neuroelectric testing to laboratory settings where environmental conditions are easier to control, which in turn put restrictions on the populations that could participate in neuroscientific research. Participants who might have difficulties traveling to a research laboratory—due to geographic distance, the cost and time involved in coming to the laboratory, or medical/behavioral issues—have been less likely to participate in research, contributing to potential sampling bias and limiting the scientific questions that could be addressed. The past decade, however, has seen a trend to miniaturize electronics for consumer markets as well as research and clinical markets. Neurophysiological equipment is now smaller and even more portable,[11,12] allowing research teams to reach even highly remote populations[13] and opening the possibility for neuroelectric activity to be recorded in naturalistic settings.[14,15]

Across the various subdisciplines of human neuroscience research, portable neurophysiological technology is becoming more popular, with uses spanning psychiatric research,[16] cognitive performance-enhancing research,[17] and hearing and language research.[14,18–20] Here, we focus on the current trend within hearing and language research to use portable equipment to index early, low-voltage sound-evoked neural activity generated by brainstem sources. This new brand of auditory neuroscience, including the home-based approach to recording auditory brainstem responses (ABRs) that we have introduced, has the potential to propel many research and clinical questions, yet has largely fallen under the radar.

AUDITORY BRAINSTEM RESPONSES AND FREQUENCY-FOLLOWING RESPONSES

There are two broad classes of auditory evoked potentials (AEPs) generated from brainstem sources: (1) early-latency transient responses to the onset of sound, which are conventionally referred to as *ABRs* and (2) phase-locked, oscillatory responses to the frequency-bearing, periodic aspects of sound (e.g., tones, vowels), which are conventionally referred to as *frequency-following responses (FFRs*; but which go by other names as well, including speech ABR, complex ABR, envelope-following responses, steady-state evoked potentials). When complex acoustic stimulation such as speech (e.g., a speech syllable, "da") is used, onset and phase-locked responses can be recorded to the same stimulus. Whether it is in a laboratory, clinical, or home setting, AEPs from brainstem sources are usually recorded as a one- or two-channel recording from scalp electrodes, requiring a simple electrode montage of three to four electrodes placed on the head. This, combined with the fact that

they can be recorded during sleep or while the participant watches a movie, makes them well suited to nonlaboratory environments.

First described in the 1970s, ABRs are now in routine use by hearing health care professionals (audiologists, neurootologists).[21,22] Because the neural generators of the ABR are well delineated,[23] ABRs can provide important diagnostic information about the biological source of hearing impairment or neurological disorder, and they currently have wide-scale implementation as an objective measure of congenital deafness in newborn hearing screenings.[24,25] Their use, however, is not limited to populations with elevated hearing thresholds. More subtle variations in peripheral and central auditory system function are also evident in ABRs recorded from populations with clinically normal cochlear hearing.[26–28] Currently, there is growing interest in using ABRs (as well as FFRs) to index age- and noise-related declines to inner ear and central auditory function before they are revealed using standard, behavioral metrics of hearing sensitivity.[29–31]

FFRs, compared with ABRs, are principally used in research settings, although there is a movement to adopt them in clinical settings.[32,33] FFRs reflect phase-locked activity across multiple regions of the subcortical and cortical auditory system, but for audiometric test frequencies and frequencies in the range of the human voice, the generators of the FFRs recorded from scalp electrodes are primarily (but not exclusively) subcortical in source.[34] FFRs have been used to study a diverse set of questions, including the neural correlates of pitch processing,[35] the neural architecture of categorical speech sound perception,[36] the neurobiological consequences of sports-related head trauma,[37–39] and experience-dependent plasticity of the auditory system.[40,41]

While magnetic resonance imaging (MRI)-based techniques are popular among neuroscientists, the loud and enclosed environment of the scanner can be stressful for children, especially for those with neurodevelopmental disorders like autism spectrum disorder (ASD). Even if the testing environment were not a concern for such particular populations, when participants are geographic dispersed, and testing is conducted at multiple imaging centers, comparing data across different imaging centers has its own confounds.[42] The cost to rent MRI time is also high, compared with electroencephalography (EEG)-based techniques which have a relatively low per use cost (<$5 compared with hundreds of dollars for a single MRI scan). The electrodes used for ABR/FFR testing can be applied in a few minutes with a small number of electrodes, each applied individually, unlike some EEG testing that requires a full cap or net. ABR/FFR testing generally requires less instrumentation than other EEG-based techniques and total test times can be minimized to less than 30 minutes. Another advantage is that ABRs/FFRs do not require the participant to follow a complex set of instructions, to be vigilant during testing, or attend to the sound stimulus. These features, together with the extant literature connecting ABRs to language development,[43–45] made ABRs a particularly attractive tool for working with children generally and, in our case, children with ASD specifically.

The increased popularity of ABRs and FFRs has brought with it new approaches to recording, including a growing movement to record auditory brainstem activity in nontraditional laboratory settings, such as schools, locker rooms, and home settings, using portable neuroelectric equipment. Here, we aim to highlight these efforts and to provide practical guidelines for implementing ABRs in nontraditional settings.

There are four specific goals of this article:

- To review recent studies of auditory brainstem function (via ABRs and FFRs) performed in the field using portable neurophysiological equipment.
- To illustrate, with two examples from our research collaborations, how such techniques can be implemented in a home setting. As a proof of concept for this novel approach, we present findings from two home-based studies: one in children (nearly half of the sample with ASD) and one in adults.
- To provide practical tips and guidelines, based on our experience, for making neurophysiological recordings of auditory function in nontraditional contexts.
- To outline how this portable technology might be more broadly adopted in research and clinical contexts.

RECENT DEVELOPMENTS TO USE PORTABLE NEUROELECTRIC EQUIPMENT IN NONTRADITIONAL TEST ENVIRONMENTS

This section provides a brief overview of three distinct lines of work that have utilized portable neuroelectric technology to record early-latency neural responses to sound as part of newborn hearing assessments, to measure auditory neural plasticity in underserved populations, and as a neurophysiological index of head trauma. Collectively these three lines of work, in combination with our work using home-based approaches to ABRs, demonstrate the potential to use mobile technology to reach populations that are underserved by science, and to benefit study enrollment and participant retention by making the test location more convenient, more familiar, and therefore more comfortable, for the participant. They also demonstrate how this technology can be woven into ongoing work and combined with other metrics of health and cognition.

Using Mobile Techniques to Extend Current Newborn Hearing Assessments

In the United States, and many other developed nations, newborn hearing screenings are currently part of standard hospital care. Hearing tests are included in multipronged screening protocols undertaken after birth to assess risk for various congenital disorders. ABRs are one of two physiologic tests of newborn hearing, with the most comprehensive battery combining ABRs with otoacoustic emissions (OAEs), a measure of inner ear function.[25] These screenings, which are critical to early detection of childhood hearing problems, are typically performed by a nurse or technician using a small handheld ABR or OAE screener in a room during sleep or quiet rest. The screeners are generally single-purpose devices that automatically analyze and interpret the data and, by design, do not permit much control over the test stimulus or recording parameters. Current test protocols are not sensitive to mild hearing loss,[25] delayed onset-hearing loss,[44] or more subtle deviations to central auditory processing including those critical to spoken language development.[32]

Recent research, therefore, seeks to expand the current implementation of newborn ABR screenings to capture a wider array of auditory-based communication disorders and to advance our understanding of how the central auditory system development is impacted by environmental stimulation in the pre- and postnatal environment. Current work in this area is seeking to improve early-childhood diagnosis of communication impairments by using more complex, real-world acoustic stimulation like speech, instead of the simple clicks and tones used by the screener devices, to record ABRs. As part of this new line of research, FFRs are being recorded bedside in the maternity hospital room using portable equipment within the first few days if not hours of birth, after the newborn has passed the hearing screening. For example, in Spain, investigators are using the Intelligent Hearing System, Smart EP, a laptop-based system to develop a normative database of speech sound processing to aid the early detection of language impairment.[33] In China, a team of U.S. and Chinese researchers is using the Neuroscan Synamp 2 system (a system that is no longer in production) to study developmental and experience-dependent changes to the central auditory system and to refine techniques for the automated detection and analysis of the neural response.[47–49] The long-term products of this work will likely be smaller, more automated speech-ABR systems like those currently used for newborn hearing screenings.

Using Mobile Techniques to Measure Auditory Neuroplasticity in Low-Income and Minority Populations

The inclusion of minorities and women is mandated by the National Institutes of Health–funded research (Revitalization Act of 1993) to create greater equity for those who benefit from research outcomes and to promote higher quality medical care across race, gender, and economic divides. Yet, researchers often face difficulties fulfilling these mandates because of challenges in accessing and retaining participants from historically underrepresented populations, such as populations with neural and motor disabilities, from low socioeconomic backgrounds, and minority communities.[50] The barriers include ineffective communication between scientists and potential research participants, as well as

uncertainty and lack of transparency about the research process.[51] For studies that involve multiple test sessions or longitudinal designs, the convenience of the test time and location can also factor strongly into patient recruitment and retention of research participants. The ability to bring the research instruments to the test population is one promising avenue for increasing participation from underserved groups; this has been shown to be productive when coupled with collaborations with community-based organizations with established connections to underrepresented populations. For example, Kraus and colleagues[18,20,52–54] have partnered with a community-based music education organization that serves primarily low-income children and adolescents in Los Angeles, California, to study the impact of musical training on biological measures of sound processing (via FFRs) and to confirm trends that emerged from laboratory studies of children from more affluent backgrounds. To date, this partnership has yielded multiple publications,[18,20,52–54] three of which include neuroelectric data.[18,20,54] As part of this partnership, a cohort of music students was followed up over multiple years, with baseline data obtained before their matriculation into any music classes. Speech ABR testing was administered using the Intelligent Hearing Systems (IHS), SmartEP system (Miami, FL), via the "cABR" software module, in a small room within one of the music schools. The findings that emerged from this fieldwork converged with previous work[55,56] by showing that active engagement in instrumental music practice is associated with improved communication in noise[52] and more robust (i.e., larger amplitude) neural responses to sound.[18,20,54] This series of findings provided some of the earliest proof of concept for recording ABRs outside of a laboratory or clinical setting, and in so doing, it laid the groundwork for the in-home ABR protocol our team has taken on, which we describe later.

Using Mobile FFR Techniques to Assess the Neurophysiological Markers of Concussion

Concussions are brain injuries that can affect memory, balance, speech, and hearing.[57] Millions of people suffer from concussions each year, as the result of blows to the head and neck, but they can be difficult to diagnose and recovery may extend over months to years.[57,58] The auditory system is especially vulnerable to head injury. Injury can arise at multiple structures, including a ruptured eardrum, disruptions to the delicate bones of the middle ear, damage to the sensory receptors within the inner ear, and/or ischemia (reduced blood flow) to the hearing-associated cranial nerve (8th nerve) or other subcortical and cortical structures within the central auditory system.[59,60] This damage to the hearing apparatus can go undetected, especially in cases when it produces an injury that cannot be observed with standard hearing or radiologic tests. Electrophysiological tests, including ABRs, have been used for nearly 30 years to study the effect of severe head trauma but in recent years, as the public concern about sports-related concussion[61] has grown, interest in this technique and related techniques like the FFR has resurged.[37–39,62] One great advantage of electrophysiological tests of early auditory function, unlike most tests of language and cognition, is that they can be administered repeatedly to the same individual without compromising the test outcomes.[63,64]

Recent work has taken advantage of this feature and the mobility of the FFR technique to perform on-site testing of children with sports-related concussions who were undergoing treatment at a specialized sports medicine clinic[37] (using the Bio-logic Navigator Pro AEP System). Another study, this one with a longitudinal design, recorded neural responses on college football players at Tulane University using the IHS Duet in a locker room within their training facility.[39] The convenient and already-familiar location of the research test site was critical to participant retention over the 8-month period of the study. These two studies had a common finding: they showed that the amplitude of the FFR is suppressed in athletes with a history of concussion, even once the athlete is no longer displaying overt behavioral symptoms of a concussion. Although this research is in its infancy, these findings highlight the potential diagnostic applications of the FFR. The mobility of the FFR and the potential for locker-room or sideline recordings make

it an appealing alternative to radiological forms of diagnosis, which, in addition to being less portable, carry a higher price tag.

HOME-BASED APPROACH TO ABRS

In the studies reviewed earlier, the test equipment was kept in a relatively stable location within an office building or a locker-room environment, or the testing was performed in a hospital where the environment had a known quality, allowing the tester to acclimate to the test environment and optimize the test conditions before each time a new participant was tested. The equipment was also either taken to a location that was regularly frequented by the participant population to make the testing schedule more convenient for the research participants (e.g., their music school) or it was moved to a facility where the participant was already receiving medical care (e.g., their sports-medicine clinic). This type of field testing, however, might not be effective under other cases, such as when the target population is geographically dispersed, does not have a common meeting point, or has a neurodevelopmental, social, or physical disability that complicates travel to research, educational, or community-based facilities. In such cases, in-home approaches offer an alternative.

We developed an in-home ABR technique as part of our ongoing investigations into hearing and language development in school-age children that we have since expanded into testing adults. The children who participated in the first cohort of our fieldwork were recruited via the Longitudinal Study of Early Language (LSEL[65]). The LSEL, which has been ongoing for more than two decades, has provided detailed accounts of language development in children with ASD and children who are neurotypical, using specialized language tasks that are sensitive to language comprehension and language output. A cornerstone of the LSEL has been the development and implementation of portable tests of language and language-related functions that can be implemented with children in a home setting.[66]

Our group's first in-home ABR-based publication utilizing the LSEL cohort investigated if the neural response stability (i.e., the correlation between two blocks of recordings) of the ABR could predict syntactic, lexical, and phonetic performance in neurotypical children and children with ASD.[67] The study, conducted in the home of each child, showed that neural stability was associated with stronger phonological and syntactic performance in both groups of school-aged children. Moreover, it was our first study that showed that ABRs could feasibly be collected in the home environment, outside of a controlled laboratory setting.

The children who agreed to participate in that study included both neurotypical children and children with ASD across a wide range of language and cognitive abilities, all of who resided in New England and surrounding states, across rural and urban areas. In addition to the data collected in children, we collected data in a set of neurotypical adults. This extension of the study not only allowed us to make home-versus-laboratory comparisons to ABR/FFR data in terms of the test–retest reliability of latency, response consistency, and signal-to-noise ratio (SNR), but also confirm that the in-home data collection was a feasible and practical experience on adults.[68]

We have been performing in-home ABRs for the past 6 years with children (neurotypical and children with ASD) and adults. As a proof of concept for our in-home protocol, we undertook analyses on data quality with these two datasets. Collectively, these analyses confirm the feasibility of collecting ABR/FFR data in the home in both children and adults. We present our methods and a discussion on our findings later.

METHODS

All procedures were approved by the Institutional Review Board at the University of Connecticut.

Children

Beginning in the summer of 2015, LSEL participants were contacted about the possibility of participating in neurophysiological testing in their homes. As part of their involvement in LSEL, the participants had already been visited

in their homes multiple times, and the ABR session occurred anywhere from less than 1 to 10 years after the most recent visit. The diagnostic status of the children had been confirmed at the beginning of the LSEL and was reconfirmed using the Autism Diagnostic Observation Schedule (ADOS) within a year of the ABR data collection.

ABR and FFRs were recorded in 27 children's homes (6–16 years, mean: 10.70 years; 23 males, 3 females). In this dataset, 13 had a diagnosis of ASD, a neurodevelopmental disorder in which children show deficits in social interaction, communication, and restricted and repetitive behaviors.[69] While language and communication deficits are no longer part of the diagnostic criteria for ASD, they are frequently observed and often the parents' first indication of developmental atypicality.

Prior to scheduling a home visit, a member of our research team engaged in an extensive conversation with the parent about the ABR procedures. The research team for each ABR visit consisted of two to three team members (typically one graduate student, one to two undergraduate students). Upon entering the home, a testing location within the home was selected. Most families allowed us to scout several possible locations in the home before making a final selection. The final selection took into consideration the need for a space with natural light (as the lights in the room were turned off), and the desire to find a location that was free from distractions, that had access to a power outlet, and that was comfortable for the child. The most popular test locations were the child's bedroom or the living room couch. Once the testing space had been selected, one team member reviewed the study procedures with the participant and family, and the other(s) prepared the equipment and space for the hearing screening and ABR testing. As much as possible, we attempted to work with the existing room layout, without making major modifications. However, if any furniture needed to be moved, this was done prior to the hearing screening, and only with the family's permission. Participants were also given the opportunity to see and interact with the test equipment and materials before any testing began. ABR testing occurred after the hearing screening. During ABR testing, children watched a subtitled video of their choice on a laptop or tablet computer, with the volume of the device set to be just-barely audible. This is common practice for longer testing sessions: the video serves both means to distract the participant and as a tool to induce a relaxed state to minimize motor-based artifacts during data collection.[70] Children and family members were also instructed to turn off cell phones to minimize interference. Prior to ABR testing, parents gave written consent and participants provided written assent.

Adults

In the fall of 2019, twelve young adults (20–27 years, mean: 24.84 years; 1 male, 11 females), all students at the University of Connecticut, participated in this study. These participants were not a part of the LSEL but were brought in to study the differences between ABRs and FFRs recorded in the laboratory versus in the home as a follow-up to the LSEL collaboration.[68] All were neurotypical and had normal hearing (a hearing screening that included an audiogram and distortion product OAE screener was conducted in the laboratory prior to the in-home testing day), and most had prior experience with sitting for an ABR. The research team consisted of two graduate students, neither of whom had been involved with data collection in the LSEL cohort.

Unlike the children in the LSEL, the adult participants were not tested in their own home, but rather, one specific home location was used for testing. We have previously referred to this setting as a "simulated" home environment.[68] ABRs were recorded in the living room of a single-family home that had an open floor plan design where the living room is contiguous with the kitchen and main entrance. A room with natural light was selected for testing, as all lights were turned off to minimize electrical noise, but no major modifications to the house were made, and appliances throughout the home remained plugged in. A fully muted, subtitled video of the participant's choice was played through a laptop placed on a table about three feet in front of the participant via WI-FI on a battery-powered computer. All in-home testing occurred on 1 day, with participants traveling to the

"simulated" home environment at a scheduled time throughout the day. Testing, including electrode application and removal, took approximately 20 to 30 minutes per adult participant.

Recording Parameters for Children and Adults

For ABR measurement in both the children and the adults, three Ag/AgCl plated electrodes were placed on the head using a vertical, ipsilateral montage: top of the head (Cz, noninverting electrode), the center of the forehead (ground electrode), and the right ear (inverting electrode). Care was taken to place the electrode leads out of the line of sight of the participant to minimize visual distraction. To achieve a low-impedance recording (<5 kOhm), electrode sites were cleaned with a gentle scrub and adhered using conductive paste. A foam ear insert (Etymotic ER-14) was then placed in the right ear to deliver the sound stimuli.

ABRs were recorded first to a click stimulus (100-microsecond square, rarefaction polarity, 31.3 Hz with two runs of 1,000 trials at 80 dB SPL in children and 70 dB nHL in adults) followed by a "da" speech stimulus (40 ms synthesized token, alternating polarity, 10.9 Hz with two runs of 3,000 trials at 80 dB SPL in both adults and children). The stimuli, recording settings, and analysis parameters followed published reports.[10,71] For each stimulus, the two runs were made in immediate succession, with a brief pause to give the participant a chance to move, if needed. The Navigator Pro AEP system (Natus Medical, Inc.), a portable laptop ERP system, controlled stimulus delivery and the collection of the evoked potential. For the click stimulus, the ABR was filtered online from 100 to 1,500 Hz, using an averaging window that extended from 0 to 10 ms. For the /da/ stimulus, FFRs were bandpass filtered online from 100 to 2,000 Hz, with a recording window that began 15 ms prior to the stimulus onset and extended to 58 ms post–stimulus onset. Trials exceeding ± 23.8 volt for either stimulus were treated as artifacts (e.g., muscle artifacts) and were automatically excluded from the average. For the Navigator Pro AEP system, ± 23.8 volt is the default limit. For the speech stimuli, the responses to the condensation and rarefaction stimuli were averaged to minimize potential contamination from the stimulus artifact.[70,71]

Statistical Analyses

We focus our proof-of-concept analyses on descriptive statistics for three indices, comparing them to published normative values: (1) absolute latencies (reported in ms) from recordings of the click (waves I, III, and V) and /da/ (waves V, A, D, E, F, and O) stimuli; (2) SNR for the /da/ response reported as a ratio; and (3) age-related changes to the ABR. Wave peak picking, necessary for latency analyses, was manually completed by three to four members of our research team, including an expert rater. The SNR is the quotient of the quadratic mean of the post-stimulus period (19.5–44.2 ms) divided by the quadratic mean of the pre-stimulus period (−16.2 to 0 ms) of the recording to the /da/ stimulus. (Because with a click-evoked ABR, the pre-stimulus period is very short—less than a millisecond—the SNR to a click is not a particularly useful measure and thus not included here.) The higher the SNR, the less noise in the recording, with SNRs of less than 1.5 considered "unfavorable."[70] All ABR/FFR data and statistical analyses were completed using custom routines implemented in MATLAB version 21b (MathWorks, Inc., Natick, MA).

RESULTS

Descriptive statistics for the absolute latencies of each wave (I, III, and V for the click ABR, and V, A, D, E, F, and O for the /da/ FFR) are presented in Table 1, separated by neurotypical children, children with ASD, and adults. Latency was selected to highlight because it is highly repeatable both in click ABRs[73–75] and FFRs,[63,64,76] and is a common metric of interest in the audiology clinic.

We have also chosen to highlight a metric that may be of particular interest given the in-home nature of the recording location: SNR. These descriptive statistics are presented in Table 2.

In presenting the data from our child and adult studies for proof-of-concept purposes, we provide the waveforms for our recordings in

Table 1 Descriptive statistics for ABR and FFR Latencies Collected in a Home Setting

		Click-ABR Wave			FFR to /da/					
		Neurotypical children (n = 14, 6–12 years old)								
		I	III	V	V	A	D	E	F	O
Milliseconds (ms)	M	1.60	3.76	5.34	6.50	7.40	22.20	30.69	39.18	47.60
	SD	0.10	0.33	0.17	0.24	0.26	0.27	0.44	0.36	0.99
	SEM	0.03	0.09	0.05	0.06	0.07	0.07	0.12	0.10	0.27
	Range	0.33	1.29	0.50	0.75	0.91	0.92	1.42	1.08	4.17
	Minimum	1.45	2.74	5.36	6.07	6.91	21.74	30.07	38.66	44.74
	Maximum	178	4.03	5.86	6.82	7.82	22.66	31.49	39.74	48.91
		Children with autism spectrum disorder (n = 13, 6–16 years old)								
		I	III	V	V	A	D	E	F	O
Milliseconds (ms)	M	1.63	3.88	5.75	6.53	7.57	22.52	30.98	39.70	47.73
	SD	0.11	0.13	0.16	0.22	0.37	0.58	0.52	1.08	1.23
	SEM	0.03	0.04	0.04	0.06	0.10	0.17	0.14	0.30	0.31
	Range	0.34	0.42	0.58	0.75	1.33	2.25	1.75	3.75	4.42
	Minimum	1.53	3.61	5.53	6.24	6.99	21.66	30.24	38.99	44.24
	Maximum	1.87	4.03	6.11	6.99	8.32	23.91	31.99	42.74	48.66
		Neurotypical adults (n = 12, 18–27 years old)								
		I	III	V	V	A	D	E	F	O
Milliseconds (ms)	M	1.74	3.88	5.72	6.39	7.33	22.37	30.51	39.08	47.98
	SD	0.11	0.14	0.20	0.25	0.41	0.52	0.38	0.33	0.20
	SEM	0.03	0.04	0.06	0.07	0.12	0.15	0.11	0.20	0.06
	Range	0.42	0.54	0.63	0.83	1.42	2.09	1.09	1.09	0.66
	Minimum	1.49	3.70	5.36	5.97	6.80	21.55	30.05	38.55	47.72
	Maximum	1.91	4.24	5.99	6.80	8.22	23.64	31.14	39.64	48.38

Abbreviations: ABR, auditory brainstem response; FFR, frequency-following response; M, mean; SD, standard deviation; SEM, standard error of mean.

children (neurotypical and children with ASD) and adults in two forms: individually plotted waveforms and grand averages for each group. Fig. 1 plots ABR and FFR waveforms for neurotypical children, Fig. 2 is a plot for children with ASD, Fig. 3 is a plot for neurotypical adults, and Fig. 4 plots the grand averages of the three groups.

Finally, we correlated age and wave V latency (Fig. 5). We highlight this relationship

Table 2 Descriptive Statistics for FFR Signal-to-Noise Ratio (Presented as a Ratio where Larger Numbers are More Favorable) Collected in a Home Setting

SNR for /da/ (ratio)			
	Neurotypical children (*n* = 14, 6–12 years old)	Children with autism spectrum disorder (*n* = 13, 6–16 years old)	Neurotypical adults (*n* = 12, 18–27 years old)
M	3.13	2.95	4.22
SD	1.55	1.64	1.06
SEM	0.41	0.45	0.31
Range	4.84	5.79	3.64
Minimum	1.25	1.25	2.17
Maximum	6.09	7.06	5.81

Abbreviations: FFR, frequency-following response; M, mean; SD, standard deviation; SEM, standard error of mean.

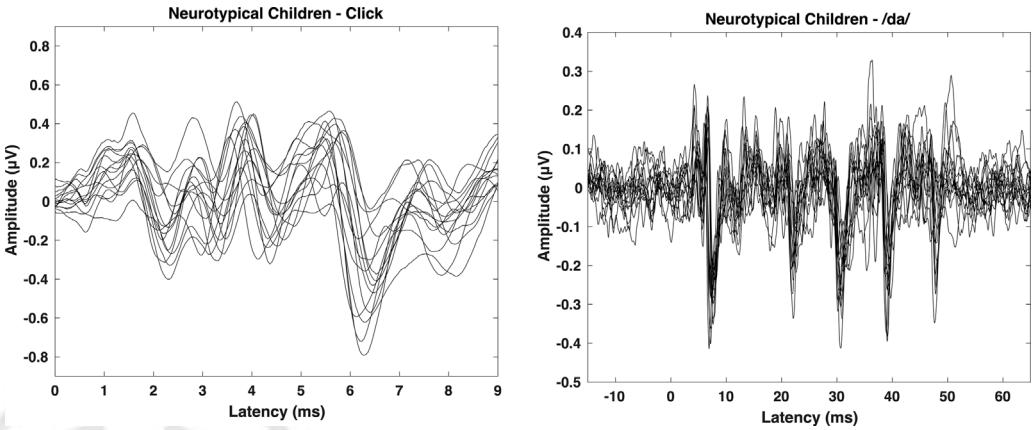

Figure 1 Individually plotted auditory brainstem response (left) and frequency-following response (right) waveforms for neurotypical children (n = 14).

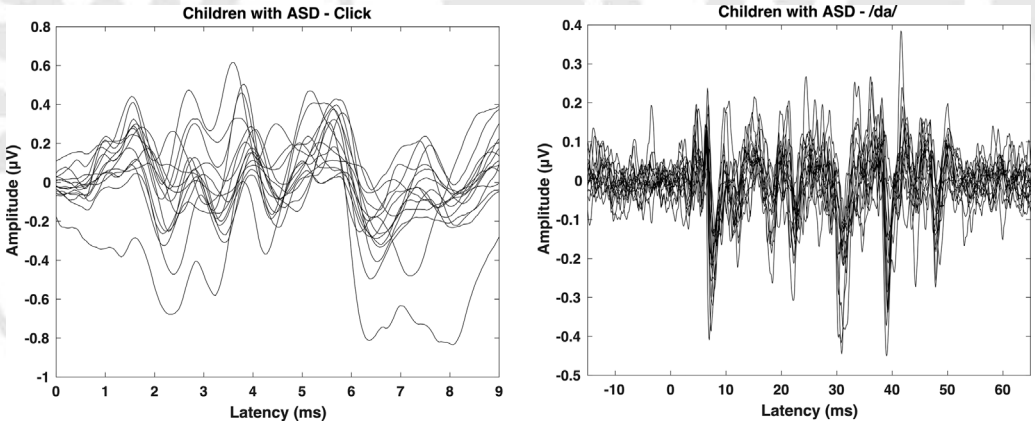

Figure 2 Individually plotted auditory brainstem response (left) and frequency-following response (right) waveforms for children with autism spectrum disorder (ASD; n = 13).

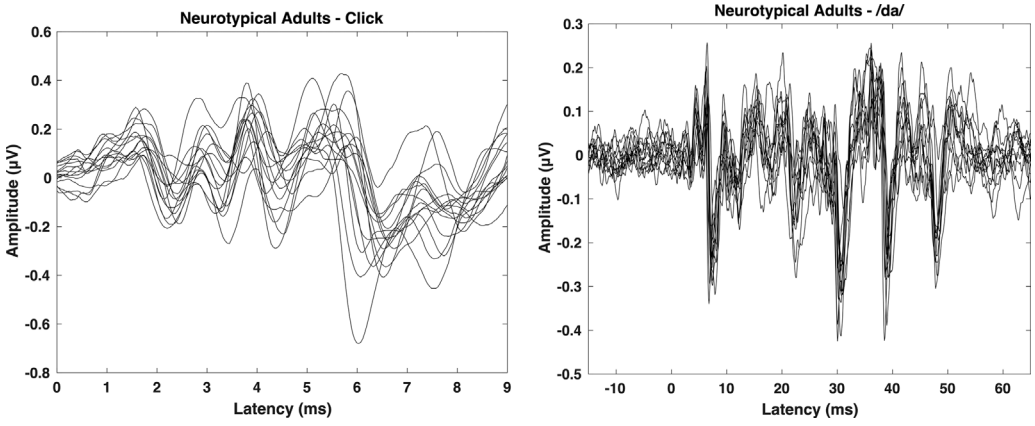

Figure 3 Individually plotted auditory brainstem response (left) and frequency-following response (right) waveforms for neurotypical adults (n = 12).

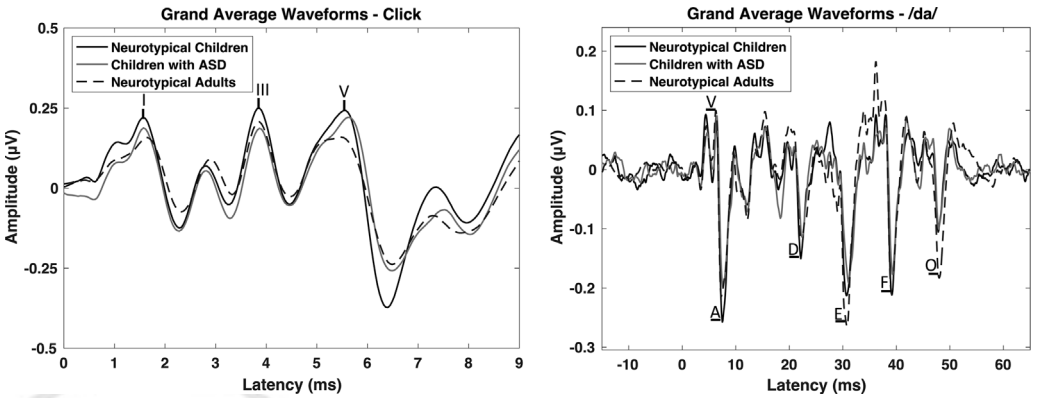

Figure 4 Grand average auditory brainstem response (left) and frequency-following response (right) waveforms for neurotypical children, children with autism spectrum disorder (ASD), and neurotypical adults.

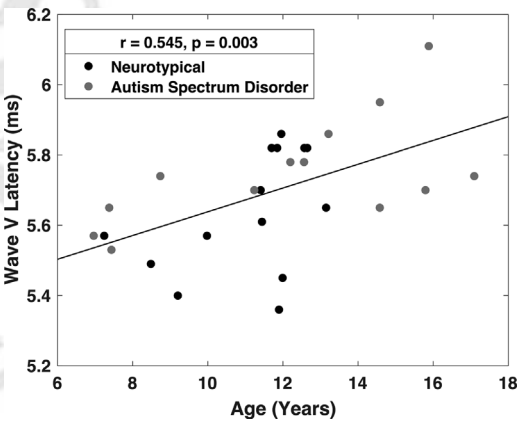

Figure 5 The correlation between age (years) and wave V latency (ms) shows a significant, positive correlation in our group of children (neurotypical and children with autism spectrum disorder). That is, younger age pairs with shorter latencies, and vice versa.

to show that our ABR data, even when collected outside of a laboratory setting, follow a known pattern where age and wave V latency correlate positively.[6] That is, younger children tend to have shorter wave V latencies, and older children longer.

DISCUSSION, SUMMARY, AND LIMITATIONS

We performed auditory neurophysiological testing on 27 children (13 with a diagnosis of ASD) in their homes and 12 neurotypical adults in a "simulated" home environment. Our results presented as a proof-of-concept for in-home ABR/FFR testing and to demonstrate the quality of the data we can collect in a remote, outside-the-laboratory setting. As shown in the descriptive statistics on ABR/FFR latency in Table 1, latencies, one of the most popular metrics of use in the audiology clinic known for its high levels of test–retest reliability, are on par with well-established normative values that have been collected in a controlled laboratory setting. For example, one seminal textbook on the ABR lists normative values for the click-evoked ABR as 1.6 ms for wave I, 3.7 ms for wave III, and 5.6 ms for wave V,[72] and other uses 1.5 ms for wave I, 3.5 ms for wave III, and 5.8 ms for wave V as their normative values.[23] Our measurements collected in the home fall well within this vicinity. Moreover, our peak latencies for our FFR data follow suit. A handful of studies[70,78,79] have provided normative values for FFR waves,

and one[10] provides the following values for FFR latencies in young adults: 6.72 ms for wave V, 7.64 ms for wave A, 22.92 ms for wave D, 31.07 ms for wave E, 39.52 ms for wave F, and 48.39 ms for wave O. Again, our FFR that was collected in the home data aligns with these normative values. Moreover, the waveforms provided in Figs. 1 to 4 show the individual waveforms for neurotypical children (Fig. 1), children with ASD (Fig. 2), and neurotypical adults (Fig. 3), as well as the grand average waveform plotted for each group (Fig. 4). All waveforms were peak picked by three to four members of our research team, and show the morphology expected of ABRs and FFRs.

Furthermore, we were interested in examining the SNR of the recordings as a metric of data quality. Our prior work examined the SNR data of our in-home recordings on the adult group presented here, in comparison to the SNRs of their in-laboratory recordings.[68] We found that SNR was robust both in the home and the laboratory setting, without significant differences between the two locations. Here, we present the SNR data in our neurotypical adults in tandem with our neurotypical children and a group of children with ASD. Skoe and Kraus[70] explained that when the SNR is less than 1, the "response" activity is smaller than the pre-stimulus activity, provoking them to recollect FFR data or exclude the patients when their SNR is less than 1.5. Generally, SNR falls into the range of 2.5 to 3 but can be even higher.[70] Table 2 shows the mean SNR values across our three groups of participants: 3.13 in neurotypical children, 2.95 in children with ASD, and 4.22 in neurotypical adults. For comparison, when the same sample of adult participants had their FFR recorded in our laboratory,[68] the average SNR was 4.164, comparable to their average SNR in the home setting. While children with ASD have, on average, the lowest SNR of our three groups, their SNR is still above the 1.5 "retest" or "favorability" threshold. Overall, only four participants had SNRs less than 1.5 (three in the neurotypical children group, one in the children with ASD group, and none in the adult group). It is difficult to determine whether the location was the primary factor in the unfavorable SNR in those four participants; however, our previous work[63] would suggest not, and that it may be a participant (e.g., they were fidgety during testing), rather than location, matter. No participants had an SNR of less than 1.25.

Finally, we presented the relationship between age and wave V latency in our child participant sample. Children show a statistically significant, positive correlation between age and wave V latency. We consider this proof-of-concept of the quality of in-home ABR recordings, as these results are similar to that found in previous laboratory-based studies,[10] suggesting that even outside of a controlled laboratory setting, high-quality, reliable data can be collected.

In our studies of home-based ABRs, we found that with proper techniques, children and adults can (1) sit comfortably, with minimal movement for a 30-minute session and (2) provide useable, high-quality ABR and FFR data (Figs. 1, 2, 3, 4). Participants could also tolerate the electrode application and sound stimulation, particularly important for children with ASD. Our results, thus, demonstrate the feasibility of recording early neural responses to sound in a home setting in both typical and difficult-to-test populations. With these in-home ABR/FFR datasets, we replicate latencies published as normative values[23,77,78] and we show that it is possible to collect recordings with favorable SNRs,[70] even in an environment less controlled than a laboratory setting. The simple set of analyses we present on these small datasets provide critical, proof-of-concept data that open the field to larger, more exhaustive investigations in which early auditory neural function is measured in the home.

The limitations of this study should certainly be noted. First, the sample sizes for all three groups are small, ranging from 12 to 14 participants each. Studies examining the clinical utility of in-home ABRs should include a larger sample size. Moreover, while the ABRs/FFRs conducted in children were all recorded in their own homes, those recorded in adults were all conducted at one, static, specific home environment belonging to a member of our research team. With this, interpreting the data between the children and adults should be done with caution.

The current dataset adds to the growing body of literature on mobile electrophysiological measures and to the literature on brainstem structure and function in individuals with ASD (for a recent review and meta-analysis see Talge et al[80]). Neuroanatomical studies have revealed that individuals with ASD have reduced brainstem volume and other dysmorphologies,[81–84] with a higher incidence of immature cell types within the brainstem.[84] Consistent with this neuroanatomical data, evidence of prolonged ABR latencies has been repeatedly (although not consistently) observed in ASD[80] with findings being strongest for infants and young children.[80–86] Our in-home data show nominal prolongations in ABR latencies at all waves for the group of children with ASD versus neurotypical children—no waves show statistically significant differences.

GUIDELINES FOR IN-HOME ABRS

Based on our experience collecting ABRs in a home setting, we offer practical guidelines. These commonsense guidelines are the product of our successes, and they also reflect our experiences both with children and adults, including with two child participants with ASD where we were not able to obtain usable ABR data, even on a revisit.

Start-up considerations, investments, and equipment transport: *Invest in durable carrying cases and hardware, insurance, isolation transformer, and a sound level recorder.*

- Many of the AEP systems that are on the market have a small form factor—and each generation of equipment is getting smaller—that makes them lightweight and transportable, avoiding the need to purchase new, specified equipment.[92] For such systems, the stimulus presentation and the averaging software are bundled into a single software interface that can be run from a single laptop computer. To ensure greater durability with transport (between laboratory/clinic, the car, and into the home), we recommend using a laptop with a solid-state hard drive and investing in a sturdy carrying case and reusable foam sheets/wrapping to give each individual piece of equipment an extra layer of protection. The testing team should be made aware of the delicate nature of the equipment and trained on packing procedures before being trusted to take it into the field. Taking out an insurance policy on the equipment is also recommended so that equipment can be replaced in cases of damage or loss.
- When recording AEPs outside a controlled laboratory environment, there are two potential sources of contamination: electrical noise and environmental noise. The latter will be discussed later, and to combat the former, medical-grade EEG equipment often includes an isolation transformer and should be purchased one to suppress line noise and prevent electrical shock.
- Develop a checklist of all the equipment and materials that are needed and travel with extra supplies.
- Establish precise responsibilities of each team member ahead of time and develop routines for packing so that equipment can be packed and unpacked in an organized fashion.
- Perform a dress rehearsal before the first home visit, when a new research member joins the team and when there are long intervals between test sessions. For these staged practices, we recommend packing up the equipment and all supplies and taking them to a site outside the laboratory (e.g., a classroom on a university campus) to practice moving the equipment, unpacking and setting up the equipment in unfamiliar settings, and making recordings under constraints where the furniture in the space might not be moveable. This guideline is critical to follow because small issues with the test procedures can have inflated consequences in the field. This dress rehearsal will also identify issues with the transportation of the equipment including whether the equipment is too heavy or large to be transported

(depending on the size of the car and the physical limits of the research team). Be prepared for a situation, where the equipment must be carried up multiple flights of stairs (e.g., in an apartment building).

- To be able to measure the ambient noise level of the house, we recommend investing in a sound level meter. If such equipment is outside the budget, a smart-phone–based application could be used.[93]

Appointment preparation: *Familiarize the participant with the testing procedure before arriving for the appointment, and the research team with the testing environment.*

- Prior to booking the visit, arrange a phone call to describe the procedures to the participant and their family. We recommend providing the participant/family with a video of the procedures to watch ahead of time to familiarize the test procedures, especially in those prone to test-related anxiety.
- Discuss the specific challenges of the individual, the family, the home, and the geographic location prior to entering the home. Moreover, ask the participant/family who, besides the research participant, will be present for the testing and if other children or pets might be in the house during testing. We have found that it can be helpful to involve the family in the testing and knowing who will be present for testing can guide visit preparations.
- Ask the family to describe the home environment including places where (1) the participant could sit comfortably, (2) the research team has sufficient room to set up, and (3) that are close to an outlet or a table for the equipment.
- In cases where there is a potential concern that the participant might not tolerate having something applied to their head, sample electrodes and ear inserts can be mailed to the family ahead of time, and the home visit can be scheduled once the family has had a chance to acclimate to the test materials.

In-home set-up: *Prepare the testing environment data collection which does not require turning the house upside down.*

- Bring the equipment into the home with, using extra caution when unloading from the car, and entering the home.
- In cases where it is not possible to locate a table in the home, we have set up the equipment on the floor using our equipment carrying case as a makeshift table. Traveling with a small, collapsible table is advised.
- Consider using separate locations for the electrode application process and the ABR testing. For example, during the electrode application process, we have found it helpful to have the child sit in a kitchen/dining room chair in the middle of a room so that it is easier to reach their head from multiple angles. Once the electrodes have been secured, the participant can be moved to a more comfortable setting (e.g., a couch, recliner chair, bed).
- Ask the participant (or their guardian, if running a child) about the electrical system in the home, and if the electrical system is outdated, ask for permission to unplug appliances or other electrical equipment that might compete for amperage. In modern homes, the electrical systems did not interfere and beyond turning off the lights in the home, appliances (the refrigerator, oven, televisions, etc.) were kept plugged in and WI-FI was kept on. However, on one occasion, our ABR system did overload the home's electrical circuit. Running the laptop computer on battery power and using a battery-powered amplifier (such as is available through Brain Vision, LLC and BioSemi) would bypass concerns about the home's electrical system.
- In a home setting, we recommend developing a team-based approach with a two-person or three-person research team, in which one team member has the responsibility of setting up the

equipment and controlling the testing software/hardware, and other team members are on hand to interact with the participant and family, put electrodes on, etc. Even in cases where the participant population may not fall under the label of "difficult to test," we would still make this recommendation so that someone is always available to troubleshoot the equipment.

Testing: *Keeping the participant calm, comfortable, and occupied.*

- Ask the participant if they have a favorite movie or video so that the movie selection can occur before the appointment to streamline the testing session. We recommend playing their movie choice on silent with subtitles to prevent artifact, but in cases where a child is too young or unable to read, the volume can be kept just barely audible.
- Environmental noise can be distracting to the participant, and if sufficiently intense could mask the acoustic stimulus leading to diminished amplitudes and prolonged latencies.[94] The use of foam inserts earphones to deliver the stimulus is one line of defense against such masking effects, assuming that the acoustic environment cannot be controlled. With deep insertion into the ear canal, the amount of attenuation (~30 dB) is roughly equivalent to a single-walled sound booth.
- Allow the participant a moment to move, stretch, and get comfortable between testing blocks, and check impedance before starting a new block.
- For some families, we have learned that food is used as a reinforcer or an intervener for a child, especially those with ASD. Because facial and oral muscle movements, such as chewing, are particularly detrimental to recording ABRs, parents should be advised ahead of the home visit to use a different type of behavioral support during the ABR session, if possible. But if food is to be used, it should be consumed only during breaks and be easy to swallow (like pudding). In such cases, the participant should also be given the opportunity to have a sip of water before testing resumes, to rinse the mouth of food residue so that s/he does not engage in movements during testing to clean food from the mouth.
- When scheduling the home visit, in cases where compliance of child participants has been previously challenging, ask their guardians for suggestions to focus or calm the child. Even in cases where the participant is compliant, having the family participate in the process can ease everyone's anxiety about the process. For example, it can be helpful to use a parent as a model for demonstrating the electrode application process.
- In our specific case, we were often visiting the families on weekends when more family members were present. We have found that siblings are often quite interested in the process and want to watch but were not always adept at staying quiet during the test procedures. To optimize testing conditions in the home, and to avoid uncomforable situations, it is best to forewarn the family that siblings and pets might be asked to move to another location during testing.[95]
- Similar to when packing the equipment to prepare to visit a home, develop routines for packing the equipment back up to return to the laboratory.

We present these guidelines with the caveat that the families who participated in our study were already accustomed to having a research team visit their homes, or were adults who were familiar with ABR protocols, and this inevitably shortcuts gaining the family's and participant's ease with the process, and our recruitment efforts. That said, in our child study, families were not previously familiar with the specific team members who visited them for the ABR testing nor, to our knowledge, had they previously participated in any EEG studies. We have also found that a child's comfort level with the testing environment, in some instances, worked against the research

team and hindered study compliance because the expectation of behavioral compliance is different between an unfamiliar laboratory or clinic setting and the more familiar home environment. Thus, for some children, it may potentially be more difficult to test them at home than in a laboratory environment. We have also learned from more than a decade of recruiting families for the LSEL study that not every family will be interested in participating in this type of research and some may be uncomfortable with a team of unfamiliar researchers entering their home. That said, from our experiences talking with families, we can imagine cases where a reluctant family might, for the sake of convenience, be more willing to participate in home-based testing than travel to the laboratory.

CONCLUSIONS: THE FUTURE OF AUDITORY NEUROSCIENCE FIELDWORK FOR RESEARCH AND CLINICAL APPLICATIONS

Our application of in-home auditory neuroscientific techniques is just one illustration of how this method could be used to study and evaluate the neural processing of sound. Based on our experiences implementing this in-home technique in adults and children with and without ASD, we envision research and clinical applications in a wide array of populations, including populations who have difficulty traveling due to limited mobility, chronic pain, or social anxiety. Testing in a home setting would also facilitate the implementation of family-based association designs. In our particular case, a natural extension would be testing high-risk siblings of children with ASD.

We note that this work was performed with the long-term vision of integrating neurophysiological measures into an existing multihour test battery. This motivated our short-test sessions (30 minutes, including 10 minutes of preparation). The passive nature of the testing, and the ability to make measurements during sleep,[96,97] could allow such sessions to be tailored to the participant's natural schedule within their natural environment. This opens the field to many research questions, including, but by no means limited to, deeper investigations into circadian rhythms within the human auditory system,[98,99] the impact of environmental stimulation within the home (including parental language and noise levels) on auditory neural function,[100,101] and, reciprocally, the impact of auditory neural function early in life on subsequent child language development and adult–child interactions.

In-home ABRs also hold promise clinically because of the potential to expand current clinical services. In many states, children younger than 3 years are eligible for special services if they have significant developmental delays or disabilities, including hearing loss. Such "birth to three"[102] services are often provided in the home and involve a team of specialists that includes social workers, occupational therapists, audiovisual therapists, psychologists, and speech and language pathologists. Audiologists, however, are not currently part of the in-home care team, and because of this, an appointment with an audiologist requires a trip to a hospital or clinic. When hearing loss is suspected but behavioral audiometry is not feasible, because the child is too young or has diminished language and/or cognitive capacity, ABR testing may be performed by the audiologist. Common clinical practice involves sedating[103] children between 6 months and 6 years, because of the difficulty of having them remain still during testing and because of concerns that they will not spontaneously nap during testing. However, sedation requires significant preparation including minimizing food intake beforehand, in addition to potential health risks. Being able to test children in their natural environment, and during their natural sleep cycles, might minimize the need for sedation. Indeed, a recent string of research suggests that sedation is not necessary for testing preschool children when the testing conditions are tailored to them[104,105] or specialized mobile equipment is used.[92] Another potential application of in-home ABRs is testing children born out of hospital (who therefore did not go through the newborn hearing screening) or to reevaluate children who did not pass their initial hearing screening. In both cases, parents are referred to an audiologist or otolaryngologist for testing. Unfortunately, however, a high number of children (estimated 40%) are lost to follow-up,[106] leading to potential delay in

services for pediatric hearing loss. Providing this service in the home or daycare, therefore, could help decrease the number of children who fall through the cracks following the initial newborn hearing screening.

The appeal and utility of in-home or mobile ABR testing are not limited exclusively to infants and children. Adult individuals may prefer in-home healthcare to travel to a testing site for reasons including motor dysfunction or disabilities (e.g., Parkinson's disease, arthritis), vision issues, cognitive or communication disabilities (e.g., dementia, ASD, stroke), or equilibrium disorders, or even due to transportation limitations, restricted schedules, or childcare needs.[107]

In addition to opening the doors to new lines of research and research populations, as well as providing hearing services to populations who are unlikely to seek out medical professionals on their own, neurophysiological field testing also leads to greater public exposure to the scientific process. Deploying a research study in a home or another natural setting allows the research participants to see science in action. This increases public awareness about science and demystifies the scientific process and sparks curiosity about the research process, which in turn could reduce one of the major roadblocks to recruiting underrepresented populations.[52] The current body of work adds to an expanding set of literature on mobile healthcare in audiology and EEG research, and how recording high-quality data is achievable outside of a controlled laboratory or clinic environment.

CONFLICT OF INTEREST

None declared.

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