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REVIEW

Shedding Light On The Human Auditory Cortex: A Review Of The Advances In Near Infrared Spectroscopy (NIRS)

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Samantha C Harrison[1,2]
Douglas EH Hartley[1–3]

[1]NIHR Nottingham Biomedical Research Centre, Nottingham, UK; [2]Hearing Sciences Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK; [3]Department of Otolaryngology, Nottingham University Hospitals National Health Service Trust, Nottingham, UK

Abstract: Imaging the auditory cortex can prove challenging using neuroimaging methodologies due to interfering noise from the scanner in fMRI and the low spatial resolution of EEG. Optical imaging provides a new and exciting option for exploring this key cortical area. This review presents a brief history of optical imaging, followed by an exploration of how advances in optical imaging technologies have increased the understanding of the functions and processes within the auditory cortex. In particular, the benefits and limitations of using functional near infrared spectroscopy (fNIRS) on complex populations such as infants and individuals with hearing loss are explored, along with suggestions for future research developments.

Keywords: optical imaging, hearing loss, superior temporal gyrus, plasticity, auditory processing

Introduction

The primary auditory cortex is located bilaterally in the temporal lobes, and corresponds to Brodmann areas 41 and 42. It is situated in the superior temporal gyrus (STG) and extends into Heschl's gyrus and the lateral sulcus. Surrounding it is the auditory association area. Together these areas form the auditory cortex of the human brain. As its name suggests, the auditory cortex's primary role is to process incoming auditory signals – this can include speech, non-speech sounds and music. Imaging of the human auditory cortex, to date, has been somewhat restricted by the limitations of traditional neuroimaging methodologies, such as the noisiness of magnetic resonance imaging (MRI) that often interferes with the presentation of experimental sounds. However optical imaging, a relatively novel neuroimaging methodology, overcomes many of these limitations, not least optical techniques are silent (see Benefits and Limitations of Optical Imaging section for more details), meaning our understanding of the human auditory cortex is advancing in new directions.

Optical imaging refers to the use of light to investigate tissue within the body and is increasingly used in neuroscience fields to image the human brain. The focus of this review is on near infrared spectroscopy (NIRS) methodologies; other optical imaging methodologies are less-often used to image the living human brain, and are beyond the scope of the current article.

In this review of optical imaging of the auditory cortex, we first discuss fNIRS and the history of optical imaging, followed by the benefits and limitations of this

Correspondence: Samantha C Harrison
NIHR Biomedical Research Centre, Ropewalk House, 113 The Ropewalk, Nottingham NG1 5DU, UK
Tel +441158 232640
Email Samantha.Harrison@nottingham.ac.uk

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method compared to other neuroimaging methodologies. These include fMRI, which measures changes in blood flow throughout the brain, electroencephalography (EEG) which measures electrical signals, and positron emission tomography (PET), which measures the trace of a radioactive substance as a molecule of interest (typically glucose) is metabolized in the brain. Subsequently, we will discuss work confirming the base utility of functional optical imaging techniques for imaging the human auditory cortex. After, we explore the optical imaging of complex auditory processes such as language discrimination and music processing. Furthermore, we look at the work being conducted to explore what happens to the auditory cortex when the brain adapts following environmental changes or sensory deprivation, such as hearing impairment. We also review the role of the auditory cortex in speech production and discuss multimodal imaging work, with a focus on how this can be used to cross validate methodologies, and overcome some of the limitations of optical imaging. Finally, we conclude with a brief look at how ongoing advances of optical imaging technologies can benefit future research into the human auditory cortex.

Functional Near Infrared Spectroscopy

The following is a brief description of fNIRS; for more a more in depth discussion of the fNIRS technique, and for an overview of the different instrumentation techniques available, see Saliba et al.[1]

fNIRS is a neuroimaging methodsology whereby two types of optodes, light sources and light detectors, are placed on the scalp. These optodes are connected to a base computer via fiber optic cables. Typically, multiple sources and detectors are used to record over the area(s) of the brain in question; a source-detector pair is referred to as a channel and multiple channels can be measured at once. For adequate depth penetration, the distance between each probe should be roughly 30-50mm in adults or 20-30mm in infants.[2] The depth penetration is approximately half of the distance between probes (for further details, see Benefits and Limitations of Optical Imaging section).

The wavelengths of light emitted by the source probes are from the near infrared range of 650-1000nm, though they may vary somewhat depending on the NIRS system and settings used. This light spectrum is used because some tissue, such as the scalp and skull, are relatively transparent at this spectral level, allowing for measurements to be collected from deeper tissue structures.[3] However, it is important to note that measurements from the scalp can still be collected, and caution must be applied when interpreting the data (for further discussion on this, see Benefits and Limitations of Optical Imaging section). As oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) demonstrate different absorption of light in the near infrared spectrum,[4,5] two wavelengths are used to enable the measurement of both chromophores.

O_2Hb and HHb are measured as an indirect measure of neural activity. That is, when an area of the brain is particularly active, the metabolistic requirement of oxygen is met with a vascular response of an increase in O_2Hb. In turn, HHb is removed from the area. By measuring changes in the volume of these chromophores, fNIRS allows for an estimation of the level of underlying neural activation occurring. This relationship between brain activation and blood flow is called neurovascular coupling and also forms the basis for the BOLD response used in fMRI.

Brief History Of Optical Imaging

The use of continuous light to non-invasively image human tissue, such as the brain, has been in practice since the early nineteenth century.[6] By the mid-nineteenth century this work developed further with the first descriptions of the absorption spectrums of oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) in 1862 and 1864 respectively.[7] This prompted some of the first works into the absolute and relative amounts of O_2Hb and HHb.[8] However, by the turn of the twentieth century, this area of work had diminished, and a paucity of relevant research was published again until the 1930s.

In 1938, Matthes and Gross, as cited in Scholkmann et al,[6] began utilizing two wavelengths of light rather than the single wavelength seen prior. The work during this time covered a variety of tissue types, yet it was not until much later, in the 1970's that focus turned towards the brain. Jobsis[9] first demonstrated continuous and non-invasive monitoring of O_2Hb and HHb concentrations in the brain using near-infrared light on cats. It is believed that this is the first instance of NIRS, as we know it today, being used. In 1993, 4 different research groups demonstrated investigations into brain activity using functional NIRS (fNIRS).[10–13] Whilst Chance[10] and Kato's[12] teams utilized single-channel fNIRS machines, Hoshi and Tamura uniquely used five single-channel fNIRS machines to explore simultaneous measurements at multiple brain

regions.[11] Their early work featured region specific tasks, including auditory-based tasks.

Whilst Hoshi and Tamura's novel use of multiple machines provided promising early results,[11] the feasibility of using multiple machines in future research and clinical settings was limited due to economic factors and difficulties with data collation. For these reasons, work turned towards developing multi-channel instruments where one machine had the ability to cover a large area, or multiple areas, of the head.[14,15] As optical imaging is non-invasive, these technical advancements made it a feasible method for use in both research and clinical settings across the human lifespan. By the turn of the 21st century, the use of fNIRS was extended to infant studies.[16,17]

As the technology and uses advanced, the demand to refine the understanding of the data increased. In early work, signal detection typically involved basic data processing or simple visual inspection.[18,19] These techniques, however, were prone to error. The uniqueness of fNIRS data required more rigorous pre-processing and analyses, and so Schroeter et al applied the general linear model,[20] which has since been utilized in a number of studies and is particularly popular for multi-level or group analysis.[21] Much work has, additionally, gone into refining the NIRS signal so that the effects of extraneous hemodynamic changes are limited. For example, Bauernfeind et al explored a number of approaches for reducing the influence of this systemic noise.[22] They concluded that whilst the signal-to-noise ratio (SNR) of the O_2Hb improved with spatial filters, adaptive filtering and transfer function models, only the transfer function model improved the SNR of HHb. For a comprehensive review of the development of fNIRS analyses, see Tak and Ye.[23]

Due to the development of these methodologies, optical neuroimaging uses now include cognitive rehabilitation,[24] drug monitoring,[25] seizure monitoring,[26] and psychiatric applications,[27] to name but a few. As this exciting methodology continues to develop, so does our understanding of brain function.

Benefits And Limitations Of Optical Imaging

Whilst optical imaging remains a relatively novel concept, it has a number of benefits over other neuroimaging methods with regards to imaging the auditory cortex. For example, optical imaging techniques are significantly quieter than fMRI, which is limited in auditory research by the effects of the associated mechanical noise from cryogen pumping, slice selection and MR gradient interference.[28,29] In comparison, the only mechanical noise during optical imaging comes from the running of the base computer. Whilst researchers have, and are, exploring ways to minimize the impact of MRI scanner sound on auditory research,[30–34] optical imaging techniques negate this step due to much quieter overall volume of the equipment.

Moreover, fNIRS is compatible with hearing devices, including cochlear implants. Deafness and subsequent cochlear implantation is an interesting sub-topic in terms of functional processing in the auditory cortex, as it allows researchers to explore cortical plasticity with regards to a loss and reinstation of a key sense. However, all neuroimaging methodologies except for optical imaging techniques and PET are sensitive to artefacts from cochlear implants, particularly from electrical signals. For fMRI, many types of implant must be surgically removed before scanning, as the implant components are not safe to enter the scanner. This not only poses additional risks, but also means the participant cannot listen to auditory stimuli during scanning. To combat these issues, MRI-compatible implants are now available, however there are still risks of discomfort, heating and implant displacement. Additionally, implants can interfere with scanner signal, distorting areas of the scan particularly over the temporal areas where the auditory cortex is situated. Similarly, with EEG and magnetoencephalography (MEG) recordings, electrical and magnetic artefacts can contaminate the data. As fNIRS does not require the use of magnets and does not measure electrical signals, these limitations do not extend to this methodology, making it suitable for exploring changes in cortical activation after implantation (for more details, see the Hearing Loss/Impairment section).

In addition, optical imaging methodologies have a number of strengths that are beneficial for imaging the human auditory cortex and other cortical areas of interest. For example fNIRS is able to detect two chromophores: O_2Hb and HHb, whereas fMRI is only able to detect the blood oxygen level dependent (BOLD) signal.[35] In some circumstances, this allows for a more detailed exploration of the precise metabolic hemodynamic processes which occur in the cortical areas in response to stimulation.

Additionally, fNIRS has a much higher temporal resolution than fMRI, with sampling rates of up to 100Hz compared to fMRI's 0.5 Hz.[36] This allows for both event-related[35,37] and block designs.[38] However, it is

important to note that this is still much slower than methods such as EEG that do not rely on sluggish hemodynamic responses, and instead measure more instantaneous electrical pulses. However, with careful considerations regarding event-related or block-design and adequate time to return to baseline between trials, as well as an understanding of the hemodynamic delay during data analysis, fNIRS' temporal resolution need not prevent it from being a valuable neuroimaging methodology.

Whilst EEG's temporal resolution is desirable, it's spatial resolution of between 5cm and 9cm[39] is poor. In comparison, fNIRS' spatial resolution lies around the 10-20mm mark,[15,40] which allows for more precise conclusions to be drawn about activity in regions of interest in various study designs. However, stronger spatial resolution can be seen in both PET (5-10mm) and fMRI (typically 3mm, although 100–150 microns is achievable).[41] Importantly, both PET and fMRI also have strong depth penetration, allowing for measurements from sub-cortical areas, whereas fNIRS typically records to a depth of approximately 15mm from the scalp - although the exact depth is contingent on factors such as the distance between the source and detector optodes, and the thickness of the scalp and skull and the cerebrospinal fluid.[42,43] Therefore, imaging is generally restricted to the outer layers of the cortex, and imaging areas partially or totally submerged within sulci (such as the primary auditory cortex) can be problematic, whilst sub-cortical imaging is beyond the reaches of this technique. Furthermore, fNIRS provides no structural brain information, which poses difficulties in concluding which exact cortical areas an fNIRS signal arises from when this technique is used in isolation.[44] The use of standardized co-ordinates such as the international 10–20 system can offset this limitation, with further power added during multimodal imaging.

Another advantage of optical imaging techniques is that they are useful for lengthy procedures (up to approximately one hour of continuous imaging) and research which requires repeated testing. This is due to the use of safe, non-ionizing infrared radiation as opposed to the ionizing radiation seen in PET. This also gives optical imaging strength with regards to imaging vulnerable populations, including infants and children. Of further note, particularly for pediatric populations, is fNIRS' tolerance for moderate amounts of movement compared to traditional neuroimaging techniques. Whilst researchers should still seek to limit movement where possible, advances in motion correction algorithms[45] allow less data to need to be rejected on the grounds of movement artefacts (for a comparison of common algorithms, see Brigadoi et al.)[46] This allows participants to be awake, alert and interacting with a task of stimuli, as opposed to fMRI or MEG imaging which requires most pediatric participants to be asleep or sedated during scanning.

However, it is important to be aware of extraneous data that may be collected using optical imaging, such as signals from respiration and cardiovascular activity in the scalp.[47] As only some of the light emitted penetrates and re-emerges from the brain, but all of the photons record extraneous signals from the tissues between the probes and the cortex, fNIRS has a low SNR.[48] Therefore, it is important that researchers consider ways to control for these systemic variables, either with careful design of tasks that avoid potentially evoking variations in them, or by monitoring them independently and extracting them from the functional component of the signal with appropriate analysis techniques.[49–51]

On a more general note, optical imaging methodologies have increased portability when compared to their counterparts such as MRI and PET. Their compactness allows the technology to be moved between laboratories in a research setting, and between clinics and wards in clinical settings. This extends the applicability of this method to a range of scenarios and uses, including medical monitoring and research outside of traditional laboratory settings. Furthermore, optical imaging technologies are relatively cheap to procure and run. For example, currently an fNIRS machine can cost under USD100,000 depending on the number of channels, whereas an MRI scanner costs significantly more and also requires a specialist shielded room and expensive installation fees. This extends the feasibility of neuroimaging work to a wider set of basic-science and clinical researchers, who do not have access to funds required for fMRI studies.

fNIRS In Auditory Research

As briefly mentioned, Hoshi and Tamura uniquely used five single-channel fNIRS machines to explore simultaneous measurements at multiple brain regions.[11] The optodes from one of the machines were placed on the head adjacent to Brodmann's area 41, with the aim to record from auditory brain areas. Whilst the participants listened to classical music, fNIRS detected an overall increase in blood flow to the region, with both O_2Hb and HHb increasing during stimulation and rapidly restoring to baseline once the music had ceased to play. A similar pattern was also

detected during trials requiring mental arithmetic, where the equations were given verbally. This simple, yet crucial, early work clearly demonstrated the ability of fNIRS to detect changes in cerebral blood flow in, or near, the auditory cortex in response to auditory stimulation.

Similarly, Ohnishi et al utilized single channel fNIRS to measure cortical responses to tone bursts in the left temporal lobe of a male participant.[52] The optodes were placed using coordinates gathered using MEG to ensure accurate positioning. To explore optimal imaging depth, two different optode spacings were trialed: 15mm apart giving a depth of 10-20mm, and 20mm apart giving a depth of 20-30mm. Ohnishi's results demonstrated the ability of single channel fNIRS to detect changes in total Hb and HHb in the auditory cortex caused by auditory stimulation, but only at a depth of 20-30mm. This was expected as the MEG data in this study suggested the participant's auditory cortex was ~25mm below the scalp, which again strengthened the authors support for the fNIRS data's validity. This comparison of optode spacing highlighted the importance of considering factors that influence cortical depth, such as age and head region, when deciding optimal optode layout. Light from optodes placed too close together may not reach the intended cortical areas, and instead measure more shallowly from the space between the optodes and cortex, which includes the cerebrospinal fluid.

Similarly to Ohnishi et al, Chen et al (2015) employed multimodal imaging in their exploration of auditory cortical activation.[53] By utilizing concurrent fNIRS and EEG, this work was able to reveal a correlation between the signals from each technique with regards to auditory-evoked activation. Importantly, this work also explored area specificity and stimulus selectivity with regards to auditory and visual information. Area specificity is the notion that there is greater activation in the auditory areas than the visual areas to auditory stimulation, and vice versa for visual stimulation. Stimulus selectivity is the notion that auditory stimulation evokes more activation in the auditory areas than visual stimulation, and vice versa for visual areas. For a methodology to be suitable for use on a functionally specialized area such as the auditory cortex, it must be able to demonstrate both. Chen's work demonstrated both area specificity and stimulus selectivity in the auditory domain, which shows that fNIRS is a suitable methodology for this area. Further, this work also compared hemodynamic responses to the auditory stimuli presented at different volumes. Results revealed cortical activation is modulated by perceived loudness, which demonstrates that it is possible for optical imaging to measure differences in how an auditory stimulus is presented and processed by the brain.

Following these studies on the hemodynamic functions of the adult auditory cortex, Zaramella et al's work sought to replicate the findings in a group of 19 infants.[17] An increase in total Hb and O_2Hb was observed in response to a tonal sweep in 13 of the infants. Out of these 13, variations were observed in the HHb changes, with 8 participants displaying an increase in HHb and 5 displaying a decrease. These variations may have been due to the different phases of brain development across the sample, as the gestational age range was very broad, between 28 and 41 weeks. Nevertheless, Zaramella's work revealed that the auditory system is mature at birth, supporting findings from non-optical imaging research[54,55] and is able to be measured successfully using fNIRS.

Despite evidence confirming the utility of fNIRS in auditory research, as described above, it was not until 2014 that the test-retest reliability of auditory-evoked fNIRS recordings was assessed (for test-retest reliability outside of the auditory domain, see visual[35] and motor[56] work). Blasi et al assessed the test-retest reliability of fNIRS responses to auditory stimuli in an infant population.[57] Blasi found that, with a retest interval of almost 9 months, there was excellent test-retest reliability at the group level. However, the reliability levels were variable at an individual level. Whilst this work demonstrated fNIRS' reliability when measuring auditory responses in infants, this population is subject to rapid neural development which is not seen in adults. Subsequently, Wiggins et al assessed the test-retest reliability of fNIRS responses to speech in the temporal lobe of healthy adults, with a retest interval of 3 months.[58] Results showed test-retest reliability to be good-to-excellent at a group level, mirroring the results from Blasi and colleagues.[57] These studies demonstrate the utility of optical imaging the auditory cortex, at least at a group level.

Complex Auditory Processing

The work discussed above confirms that fNIRS can be used successfully in research on the auditory cortex as it is supported by previous fMRI and EEG research. Further to this, fNIRS can be used explore complex auditory processing such as music perception and sound discrimination.

Music Perception

Santosa, Hong and Hong used fNIRS to investigate how the well-known right-lateralization of music processing in

the auditory cortices alters in the presence of noise.[59] Participants listened to segments of music, and music with concurrent quiet and loud noise segments. Results revealed that the extent of right-hemispheric lateralization in the auditory cortices during music processing was strongest with the addition of modest noise interference, and reduced with the addition of high levels of noise interference or in quiet. This evidence, derived from using the fNIRS technique, is in line with work into the effects of noise during speech perception,[60] and adds strength to the suggestion that noise interference leads to altered representation of complex sounds in the auditory cortex.

Sound Discrimination

fMRI studies have shown neurobiological data concerning how the auditory cortex processes different sound categories.[61,62] However, the noise associated with scanning complicates the interpretation of these fMRI studies. To overcome this concern, Hong and Santosa explored cortical sound discrimination using fNIRS due to its relatively silent recordings.[63] Hong and Santosa measured cortical activation to four types of auditory stimuli: English speech, non-English speech, annoying sounds and nature sounds. This allowed for comparisons between and within two sound groups – speech and non-language sounds. The results revealed different regions of interest for the respective sound categories, suggesting that different areas of the temporal regions are involved in processing different types of auditory stimuli. As fNIRS does not create an image of the cortex, the precise locations of these regions of interest cannot be determined from this research. However, as the fNIRS headset was positioned bilaterally with a central channel positioned using the international 10–20 system over T3 and T4 respectively, it can be strongly suggested that data was collected from the auditory cortex. Using averaged O_2Hb data, this research was able to calculate the classification accuracies of a latent Dirichlet allocation (LDA) algorithm. The LDA algorithm was able to accurately distinguish between cortical responses to the speech-based stimuli at an accuracy of 70.53%, and the sound-based stimuli at an accuracy of 73.39%. This work demonstrates that, not only is speech processed differently to sounds at a cortical level, but also that different types of speech and different types of sounds show different cortical activation within the stimuli groups.

The future of this field of work, when advancements in technology and analysis may be able to increase this accuracy further, has important implications for clinical work with groups such as cochlear implant (CI) recipients. Providing fNIRS data can discriminate between the brain's processing of good or poor speech, or clear or unclear sounds, on an individual level, it has the potential to eventually be used during implant programming appointments and follow-ups. This would be particularly beneficial for patients who cannot reliably undergo behavioral or self-report measures of CI outcome, such as individuals with severe learning disabilities, young children, and infants.

The ability of fNIRS to discriminate between clear and unclear speech is explored in more detail in Pollonini et al's work.[64] Pollonini explored whether fNIRS is detailed enough to provide an objective measure to discriminate between whether an individual is hearing normal or distorted speech. This research uncovered that a larger area of activation was more synonymous with participants listening to normal speech, and this activation area decreased as the degradation of the speech stimuli increased. However, as this research only used two discrete levels of speech distortion, a linear pattern could not persuasively be observed. Lawrence et al's work used five levels of speech stimuli in their intelligibility study.[65] Indeed, this research revealed results in line with that of Pollonini et al,[64] with a positive linear relationship between group-level activation in the auditory cortex and the intelligibility level of the speech stimuli. However, at present, we are unaware of an fNIRS study to date that has shown discrimination of speech from non-speech responses at an individual level, which would be prerequisite for the creation of a clinically useful tool. It is also important to note that this research used normally hearing participants, who are unlikely to display the same cortical responses as individuals with hearing loss due to the impact of cross-modal plasticity.

Hearing Loss/Impairment

As well as advancing our understanding of the typical auditory cortex, optical imaging has a unique advantage when it comes to imaging the auditory cortex of individuals with hearing loss. Since fNIRS is relatively quiet, compared with fMRI, cortical responses to auditory stimuli can be made without the scanner noise impacting more on the normally-hearing participants, compared with deaf individuals.

In their 2015 study, Dewey and Hartley compared responses in the auditory cortex to auditory, visual and

tactile stimulation in a group of 30 profoundly deaf and 30 normally-hearing participants.[66] They revealed that stimuli-evoked responses in the visual trials were stronger in the right auditory cortex in the profoundly deaf individuals, compared with controls. In contrast, there were no group differences in responses to the tactile stimuli. Subsequent studies have shown that this cross-modal plasticity within the auditory cortex impacts on an individuals' success with cochlear implants (CIs).[38,67–72]

However, there have been contradictions within the literature regarding the role of cross-modal plasticity on CI outcome.[67,68] For example, some research revealed that cross-modal plasticity before cochlear implantation is correlated with poor CI success.[69–71] Contrastingly, other research has found that strong visual activity measured with PET correlated with auditory speech recovery following cochlear implantation.[72] Whilst the differences in the research may be due to stimulus type and imaging method, Anderson and colleagues have additionally suggested that changes in cross-modal activation post-implantation may be more successful determiners of CI success.[38]

Until recently, measurement of cortical activity post-cochlear implantation was restricted due to incompatibility of most neuroimaging methods with cochlear implants. For example, fMRI is not easily possible due to the risks of putting an implant into a strong magnetic field, and is susceptible, along with EEG and MEG, to interference from electrical and magnetic signals from the implant. Contrastingly, fNIRS is fully compatible with CIs.

In 2017, Anderson et al used fNIRS to study changes in cortical responses to visual language from pre- to post-implantation.[38] Specifically, they explored the activation of the superior temporal cortex in profoundly deaf adults before and after they received their CI. Following 6 months of CI use, participants completed speech perception testing to explore the relationship between the patterns of cortical activation and CI success. A strong positive correlation was found between pre-post implantation changes in activation to visual stimuli and speech understanding scores after implantation. This suggests that increased cross-modal plasticity within the auditory cortex following the reintroduction of hearing with a cochlear implant can be beneficial for CI success.

However, Anderson et al's (2017) work also revealed that neural adaptation post-implantation is at least somewhat dependent on an individual's clinical history, with individuals who had experienced a shorter duration of deafness showing a pre-post increase, and those with a longer duration of deafness showing an overall decrease.[38] Whilst their analyses revealed this did not strongly impact upon the correlation discussed above, it is an interesting point for future research to consider; in particular, for comparing cases of congenital deafness and individuals who developed deafness later in life.

An important area for future research would be to extend this work to younger age groups, as fNIRS is suitable for use on children and infants and they are less likely to be impacted by factors such as duration of deafness due to their age. Preliminary work showed fNIRS' utility when assessing the auditory function of children using CIs. Sevy recorded responses to speech in normally-hearing children, children who have >4 months experience using a CI, and children whose implants were switched on upon the day of testing.[73] Their results revealed similarities in the hemodynamic responses across all groups, demonstrating that children's cortical responses to speech are similar, whether hearing normally or through CIs. However, this research did not assess how well the children with implants could perceive and understand speech, nor did it follow up on the newly implanted children to see if and how their cortical responses to speech changed as they adapt to their implant. Ongoing work, including longitudinal studies of fNIRS responses in infants before and after cochlear implantation in own laboratory are attempting to address these issues.

Speech Production

The research discussed so far has primarily been based around the role of the auditory cortex in sound perception, whether those sounds be noise, music or speech. However, the auditory cortex also plays an important role during speech production, possibly due to auditory feedback from speech[74,75] and from the forward predictive coding – ie motor plans pre-articulation leading to predictions of sensory output, which serve to detect potential errors in speech.[76,77]

It is important to study the role of the auditory cortex in speech production, as it may help with the future understanding and diagnosis of speech disorders including aphasia and stuttering. A common task used within speech production work in clinical and experimental settings is the confrontational naming task. In this task, participants are shown an object on a screen or card and must name each object as presented. This task has been used during neuroimaging, but to limit the risk of motion artefacts disrupting the MRI or MEG data, the task has typically been limited to covert naming, where participants say the

object name internally, as opposed to the traditional overt naming where the participants speak aloud as normal.

The emergence of optical imaging techniques have allowed the overt naming task to be used during imaging. Hull, Bortfeld and Koons utilized 2-channel fNIRS over the left and right auditory cortices to measure temporal activation during overt naming, and revealed that O_2Hb increases in the left temporal area during speech production.[78] This contrasts the pattern seen during covert naming, in which the changes in cortical activation are located more in the prefrontal area.[79] Moriai-Izawa et al extended this work using multi-channel fNIRS to explore the responses to the overt and covert tasks in specific temporal areas of 30 healthy adults.[80] Their results revealed increased activation in the left STG in both tasks, with the overt naming task recruiting additional cortical areas in the pre-/frontal regions. This work shows that the auditory areas are activated in both the overt and covert versions of the task, but are recruited in parallel to other cortices to deal with the additional processing required for verbalization. Not only does this work demonstrate differences in neural processing during overt and covert versions of the confrontational naming task, it may also pave the way for future fNIRS work to explore the utilization of optical imaging for the diagnosis of aphasic, apraxic and anarthric patients.

Optical imaging has also been used to investigate stutter, another problem with speech production. In adults who stutter, MRI studies have found activation of the auditory cortices during speech production differs in its degree and symmetry when compared to controls.[81] However, similar explorations in a child population have been limited by neuroimaging restrictions such as the need for children to often be sedated during scanning. Walsh et al used optical imaging to explore cortical activations during speech production in children who stutter.[82] Results suggested a difference in activation patterns over the STG between children who stutter and controls, with less and slower activation noted in the former. This suggests that there is atypical functional organisation for speech production in children who stutter, with a potential lack of, or delay in, forward predictive coding in the auditory regions which leads to uncorrected and repetitive articulatory errors.

Multimodal Imaging

Whilst there is a wealth of research available where optical imaging is used successfully in isolation, the benefits of multimodal imaging cannot be overlooked. In this section, we discuss a small number of studies where optical imaging has been used concurrently with an additional non-optical neuroimaging methodology to showcase the benefits multimodal imaging can bring to research.

Multimodal imaging has been employed to cross-validate recording techniques and add strength to conclusions. For example, Horovitz and Gore explored the feasibility of simultaneous EEG and fNIRS imaging during a semantic processing task.[83] In previous EEG research, the N400 wave is seen as a correlatory response to anomalous sequences of words.[84] However, whilst EEG spatial localization techniques are valuable, it is still beneficial to use this technique alongside a method that can more accurately locate cortical activity.

Therefore, Horovitz and Gore employed optical imaging, which has a spatial resolution of around 10-20mm, alongside EEG whilst presenting anomalous and expected word pairs to healthy adults.[83] Results revealed increased vascular responses around Wernicke's area, which correlated highly with the event-related potentials (ERP) data, suggesting that this section of the auditory cortex is likely to be the origin for the N400 wave. This study is believed to be the first to demonstrate the feasibility of simultaneous multimodal imaging utilizing optical imaging and EEG with regards to language functioning. In particular, this novel work demonstrated the ways concurrent imaging can increase the precision (in this example, by locating the likely broad origin of the N400 wave) and validity (by supporting the vascular results with the N400 data) of research into the auditory cortex.

Additionally, Telkemeyer et al used concurrent EEG and fNIRS neuroimaging to explore the cortical response to sounds in 3-day old infants.[85] Telkemeyer utilized four stimuli types with differing temporal structures (12, 25, 160 and 300ms). Their vascular data from optical imaging revealed differing responses to the different stimulus types, suggesting that the newborn auditory cortex is sensitive to the temporal structure of sounds. Interestingly, the greatest bilateral cortical response was produced during the 25ms stimuli, which Telkemeyer argue is the closest to the temporal modulation required for the perception of phonemes. Contrastingly, for the two stimulus conditions with slower temporal modulation, cortical responses were mostly lateralized to the right hemisphere. This shows a tendency for functional asymmetry to exist within the first days after birth, which may help contribute to the development of speech perception. If Telkemeyer had just used fNIRS imaging, it could be argued that these differences could be explained by a simple change in perception; however, as concurrent EEG data was collected, this additional layer

adds strength to the conclusions made based on the vascular results. Their electrophysiological results showed a similar AEP to stimulus onset across all stimulus types. These AEPs were considerably slower than those seen in adult studies but were in line with prior infant work.[86]

Multimodal imaging data collected has also been used to help overcome some of the limitations of optical imaging. For example, Funane et al developed a method for discriminating deep (from the cortex) and shallow (from the scalp) contributions to fNIRS signals, namely the multi-distance independent component analysis method (MD-ICD).[87,88] Briefly, this method uses multiple receiver optodes placed at distances of 15- 16- and 30mm from a source optode to separate out the fNIRS signal during analysis. This increases the validity of the signal, by limiting the effect of extraneous data as discussed in the Benefits and Limitations of Optical Imaging section. Whilst this and similar strategies (for example, see Kohno et al)[49] have been utilized in optical imaging studies, the spatial separation validity of the method was not initially established. Therefore, in 2015, Funane et al employed simultaneous fNIRS-fMRI imaging to assess the correlations between the separated fNIRS data and the BOLD signal which is less affected by shallow signals.[89] Funane revealed significantly stronger correlations between the deep signal and BOLD response than between the shallow signals and BOLD response. This supports the use of the MD-ICA method for improving the accuracy and reliability of fNIRS signals in future research.

An additional limitation of fNIRS which can be somewhat overcome by multimodal imaging is that of the slow temporal resolution when compared to electrophysiological data from EEG. By combining the two methodologies, it is possible to generate a combination of temporal and spatial information, which is not possible using each methodology in isolation. This coupling of neural and vascular information may be particularly useful in a clinical diagnostic and monitoring setting.[90] Further, as demonstrated in Ohnishi's early work into optical imaging, the use of additional imaging techniques to locate precise co-ordinates for optode placement during fNIRS can help overcome the lack of structural imaging capabilities.[52]

Future Technical Directions

As the wealth of research using optical imaging expands, so do the technological improvements. fNIRS research is heading in the direction of wireless technology. This development increases the portability of this methodology, allowing it to be used in real world environments, such as noisy restaurants, as opposed to lab created scenarios (for an overview, see Piper et al).[91] This development also increases the suitability of this methodology for clinical applications. With regards to auditory cortex research specifically, this could be useful for testing auditory processing in emergency situations such as after a stroke or traumatic brain injury, where lesions in the temporal lobes may lead to cortical deafness, hearing loss or auditory neglect.[92–94] Finally, wireless headsets are also suitable for pediatric research, and are particularly useful when testing older infants and toddlers who may want to touch or pull on the wires of a traditional headset. By removing this distraction or source of data corruption, wireless headsets allow for easier testing of this age group, which is important for testing language processing as this age group cannot easily complete traditional behavioral testing.

Another interesting direction that optical imaging is taking is that of "hyperscanning". Hyperscanning is a technique whereby the brain activity of two individual's is recorded in unison as they complete a task or are exposed to particular stimuli. The first fNIRS study using this technique is believed to be Funane et al,[95] and its current popularity stems from an influx of work around social interaction (for a review see Koike, Tanabe & Sadato),[96] including research into cooperation,[97] sensorimotor synchronization,[98] leader-follower relationships during music performance[99] and communication.[100]

However, as of yet no research has explored this technique when exploring the auditory cortex. This novel technique could allow for research into understanding how atypical processing of sounds and speech impacts upon social interactions, and vice versa.

Conclusion

Near infrared spectroscopy is an optical neuroimaging technique with multiple benefits highlighting its suitability for imaging the human auditory cortex. These include, but are not limited to, a quiet operating noise level and suitability for imaging pediatric and clinical populations. However, NIRS is somewhat limited by its poor temporal resolution as it relies on the notoriously sluggish hemodynamic response, and its lack of structural imaging capabilities. However, these limitations may be reduced with multimodal imaging methods.

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