FINAL PUBLISHABLE REPORT

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RMG: -		

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1 Overview

This project concerned two aspects of hearing assessment and conservation; the further development of the next generation of ear simulators that will provide measurement traceability for hearing tests on adults, children and neonates, and improvement in our understanding of human response to infrasound and ultrasound, including novel assessment methods for potential health risks.

2 Need

Virtually everyone will have their hearing tested at stages throughout their life. It is essential for effective diagnosis that these tests are accurate and quality assured. Measurement devices known as *ear simulators* provide the basis for measurement traceability, but in the past have been designed for adults only. The EMRP HLT01 EARS project made first significant steps at specifying ear simulators for other age groups and produced a prototype neonatal ear simulator. However, the concept of an all-encompassing ear simulator family needed further refinement to cover for all forms of audiometric testing before it can be adopted into clinical practice. Modern audiometric methods now use short-duration test stimuli such as tone bursts and clicks, rather than steady tones that will be familiar to most people. One specific aspect is that new calibration methods for short-duration test stimuli are needed to replace the current, technically flawed methods. The move to the next-generation of ear simulators was the ideal time to introduce improved calibration methods for these stimuli.

Noise exposure from both environmental and industrial sources is another important aspect of hearing conservation. Urbanisation and industrial innovation are often accompanied by undesirable consequences, including the generation of infrasound and airborne ultrasound. These emerging noise hazards present potentially significant new social and occupation health issues. Indeed, the health risks extend beyond hearing damage and into general areas of cardio-vascular and mental health. Effective mitigation first required a better understanding of the human perception mechanisms. Due to the inaudible nature of some of these noise sources, a multi-disciplinary approach to the research was needed, combining neuro-imaging and advanced audiological investigations to fully understand the human response. Then, to supplement this understanding, new measurement methods and instrumentation were needed to assess noise sources in both public and workplace environments.

3 Objectives

The overall objective of this project was the improvement and further development of strategies for hearing assessment, hearing diagnosis and safety, appropriate for modern society. The specific objectives of the project were:

1. To finalise the universal ear simulator concept to fulfil the whole range of audiological requirements for traceability to sound pressure, including the development of an alternative approach to transient calibration based on impulse response and adaptors for the most common devices, and realisation of demonstrator devices for the novel ear simulators.
2. To generate robust normative reference threshold data (transfer and input impedance), calibrate devices across partners, quantify the degree of equivalence with currently established practices and provide a user guide summarising features, calibration and handling for application of the novel ear simulator in practice.
3. To exploit neuro-imaging and audiology to further develop understanding of perception as well as response and loudness thresholds for ultrasound (16 kHz – 80 kHz), infrasound (4 Hz – 16 Hz), and the influence of infrasound on sound within the normal hearing range; together with the development of instrumentation and measurement methods for the determination of noise and its hazards in those frequency ranges in both public and workplace environments.

4. To determine experimentally the impact of infrasound and ultrasound on hearing, mental health, cognitive abilities and general wellbeing, and their contribution to annoyance and loudness, including the study of individuals with particular sensitivity to noise.

5. To engage and work closely with stakeholders to establish the clinical protocols and international standards proposals for the use of the universal ear simulators in the calibration of audiometric equipment used for hearing assessment and hearing aid fitting for both children and adults; and to create the knowledge for future guidelines and policy framework to enhance the wellbeing of European citizens and protect them from health hazards associated with infrasound and ultrasound.

4 Results

Objective 1: Finalising the universal ear simulator

The human senses are fundamental in enabling us to lead fulfilled and productive lives, so it is vital that necessary steps are taken to preserve, protect and where necessary, restore our hearing. Hearing testing is therefore carried out at stages throughout our lives. In particular, universal hearing screening programmes for neonates and infants have been in place on a global scale since the end of first decade of 2000s. Given the young age of the test subjects, advanced audiometric methods such as evoked auditory brainstem responses (ABR) and otoacoustic emissions (OAE) are used widely. These methods do not require a deliberate response from the test subject but make use of complex non-tonal test signals.

Ear simulators are devices that are used to set up the equipment used to conduct these hearing tests, but those in routine use today were designed only for adult test subjects and for tonal test signals. The greater focus on testing neonates and children, and the expanded range of hearing assessment methodologies used, have created new use requirements for ear simulators, which this objective has addressed.

In the course of development, it became clear that to introduce the benefits targeted by this research, a new approach to hearing assessment overall would be required.

Definition of age groups

The goal to create new ear simulators for infants and young children leads quickly to the questions of which age groups to provide for and how many devices are practical. There is also the issue of anatomical variations, especially amongst neonates and young children which can result in a poor match between actual ear canal characteristics at a given age and the characteristics of the designated ear simulator.

In consultation, arranged during this project, with health service policy makers, clinical audiologists and calibration service providers, and taking into consideration the balance between practicality and additional precision, a scheme restricted to three ear simulators was agreed, appropriate for:

- young infants at 3 months of age
- infants at 24 months of age
- adults (including children over 7 years old).

The chosen ages of 3 months and 24 months represent key stages in ear canal growth and allow a focus on the early development of the auditory system. Clinical assessment and, where necessary, hearing aid fitting also target the period between these two age-points. These ear simulators provide for three calibration points on the audiometric test equipment.

An outline for a further automated procedure has also been proposed, to be carried out as part of a hearing test, that will allow an individual's physical ear canal characteristics to be measured and matched to the ear simulator with the closest characteristic. While implementation is beyond the scope of this research, a range of normative corrections and a process to interpolate between the calibration reference points based on the result of the in-test procedure, will complete the process leading to individualised calibration.

The major resulting benefit is that when the test stimulus is tailored for the test subject, inter-subject variation in results is considerably reduced. Ultimately this reduces the band where test results are neither a certain pass or a certain fail, leading to improved confidence of test results and reduced false-positive results. In the

case of neonatal and infant screening, unnecessary referrals for further testing and the associated parental anxiety from false-positive results is also avoided.

Specifications and manufacturing

In essence, an ear simulator is a device that has a microphone in a cavity and enables an estimate to be made of the level of sound that would be produced by an earphone when coupled to a real ear. The level of sound produced by the earphone during a hearing test is important and depends on a number of factors. In the case of a real ear, it is governed by particular characteristics of the ear canal (for example the volume and length). The full range of relevant characteristics can be described precisely in technical terms which are the basis for designing the ear simulator, where a microphone represents the ear drum. The task is to match all of these characteristics, i. e. technical terms as best as possible.

Deriving the required characteristics from measurements on test subjects of the appropriate age, was outside the scope of the project. However, data can be found in the scientific literature, that while not originally acquired for the specification of ear simulators, can be re-used for that purpose, albeit with some lengthy reprocessing.

Following this approach and accepting significant remaining uncertainty, it was possible to derive the specifications for the three ear simulators from published data sources. The derivation required assumptions to be made on the internal geometry of the ear canal of infants, and in the absence of actual data, scaled detailed from adults were used. This resulted in a set of target responses to be achieved by the actual ear simulators.

Based on these details, five sets of the family of three ear simulators were designed and professionally manufactured. They are shown in Figure 1.1. These prototypes were then used in the remainder of the project. They are available from one of the project partners and can be borrowed for further experiments and use.

Figure 1.1: Five sets of the prototype ear simulator family (top row adult, middle row 24-months and bottom row 3-months).

Figure 1.2 shows the generally close agreement between the target specification (up to 10 kHz) and that actually achieved by the manufactured prototype ear simulators.

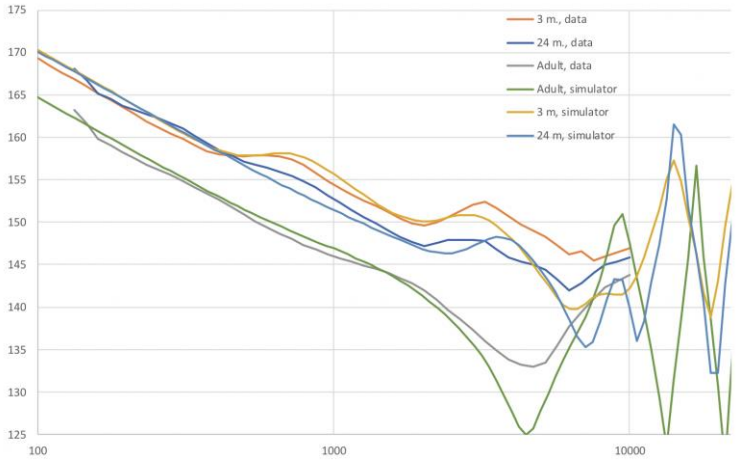


Figure 1.2: Modelled and measured characteristics of the prototype ear simulators

Adapters

As they are, the ear simulators can be used with audiometric earphones designed for insertion directly into the ear canal. However, other common types of audiometric earphones are intended to be placed on or around the outer ear when used. To extend the application of the ear simulators to these other earphone types, a range of adapters have been produced to change the external configuration. These are shown in Figure 1.3. The adapters do not provide direct compatibility with conventional ear simulators, but they do provide a means for measuring the full range of earphones commonly used in clinical practise.

Figure 1.3: Adapters for earphones intended to be placed on the ear (left) and for converting to the IEC 60318-4 occluded-ear simulator configuration (right)

A second type of adapter that was produced, enabled the external configuration of the adult ear simulator to be converted to that of the equivalent conventional ear simulator, known as the IEC 60318-4 [1] occluded-ear simulator. There is already a large body of know-how available for attaching and measuring both, audiometric earphones and hearing aids with this device, so the ability to adapt the new adult ear simulator to this configuration provides valuable backward compatibility.

New calibration method

Aside from the development of the ear simulator themselves, the increasing reliance on advanced methods of audiometry noted above, leads to concerns over calibration and traceability arising from the non-tonal, or short-duration test stimuli used for such tests.

Many will be familiar with the type of hearing test where the test subject responds to a series of ‘beeps’ or pure tones which is still the test most convenient in audiological practise. By contrast advanced and novel audiometric methods may use much shorter tone bursts, a series of clicks or other complex short duration stimuli. The advantage is that they need no action by the test-subject to respond.

Just as with pure-tone audiometry, the stimulus level of these short-duration signals needs to be known, and traceability should be assured through appropriate calibration. However, the meaning of the parameter stimulus level is currently not well defined. From an auditory perspective it is clear that the level somehow corresponds to the loudness of the stimulus as perceived by a nominal test subject. However, the way the stimulus level is currently quantified derives more the available measurement capability than from auditory considerations.

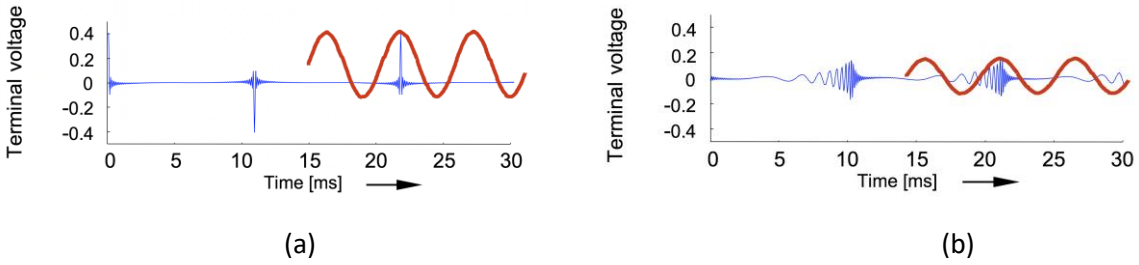


Figure 1.4: Two types of short-duration signals producing anomalous loudness levels.

Figure 1.4 illustrates the problem. It shows two types of test stimuli and illustrates how the stimulus level is currently quantified (following international standards), by the level of a matching pure-tone (in red) having the same peak-to-peak magnitude as each burst (maximum value) in the test stimulus. This process indicates that the signal in (a) has a higher level and should therefore produce a stronger sensation of loudness in the test subject. In fact, the signal in (b) being active for a longer time period overall, is actually perceived as being louder. There are many features of the stimulus that may influence its perceived loudness, but a scheme that takes into account the total energy and duration of the stimulus seems necessary and more appropriate.

So, it is fair to argue that developments in appropriate calibration methods and instrumentation have not kept pace with the rapid development in hearing assessment methods. The development of the next generation of ear simulators provides an opportunity to also review the calibration process for short-duration stimuli and overcome such problems as illustrated above and a first step was made in this project.

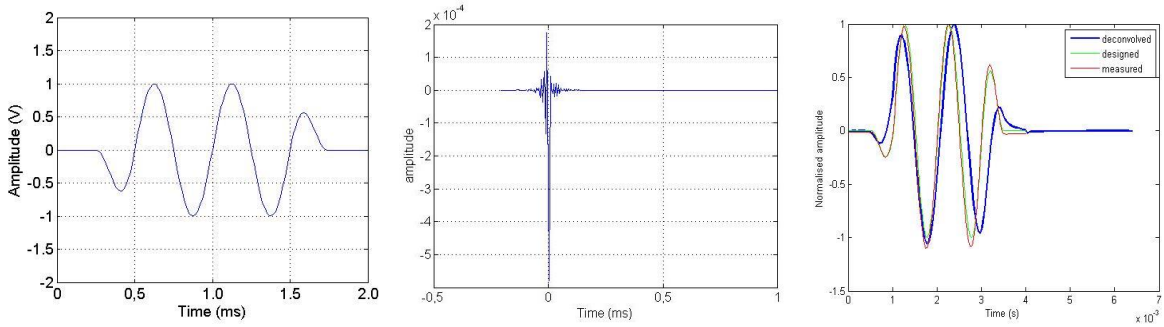
Expressing the stimulus level by comparison with the amplitude of a pure tone as illustrated in figure 1.4, is described in the international standard IEC 60545-3 (2017) [2] whereupon, the derived level is referred to as the peRETSPL (peak-equivalent, reference equivalent threshold sound pressure level).

The method is easy to implement, even with rather basic instrumentation. However, as seen in figure 1.4, this concept frequently results in calibration values which do not correlate at all with either the behavioural hearing thresholds or the spectral energy of the periodically repeated stimuli often connected with loudness. Elberling and Esmann [3] therefore proposed an alternative approach that better correlates with perceived loudness by taking account of the time duration and overall energy of the stimulus. This approach describes how to calibrate short-term stimuli by directly measuring the unweighted root-mean-square (RMS) sound pressure level (L_{Zeq}) of the short-term stimulus presented periodically at a given repetition rate and representing a variable accompanied with the energy content of the signal. In the following, this measure is referred to as *L*ZeqETSPL. This procedure was adapted to measurements with both conventional ear simulators and the new ear simulator family, to develop new methods for defining reference hearing thresholds. The results are described in the Section for Objective 2.

One prerequisite of such a new and better metric was to develop an ear simulator calibration method that enables the waveform of the sound pressure acting on the microphone to be determined, when the ear simulator is driven by an audiometric earphone producing a short-duration acoustic stimulus. The microphone represents the ear drum in the real ear, but any alteration of the sound waveform by the microphone itself needs to be accounted for, so this was the calibration challenge.

The response of the microphone to any short-duration stimulus can then be derived from the waveform of that stimulus and the response of the microphone to the idealised impulse. The calibration method is therefore based on a mathematical process that enables the response to this idealised impulse to be deduced from the wideband frequency response. The calibration method therefore reduced to relatively straight-forward measurements of the response to individual frequencies, for example by sweeping through

the frequency range, coupled with some post-processing of this measurement data to implement the said mathematical process.



(a) (b) (c)

Figure 1.5: Examples of (a) a short-duration stimulus, (b) microphone impulse response and (c) the influence of the microphone on the stimulus.

Figure 1.5(a) shows the waveform of a tone-burst that might be used as a hearing test stimulus, and Figure 1.5(b) shows the impulse response of the microphone derived from the newly developed calibration process. Figure 1.5(c) shows the signal produced by the microphone in response to the tone-burst, and the result of removing the influence of the microphone itself to obtain the waveform of interest. Thus, the influence of the microphone, which is inevitable during measurement of transient signals, can be corrected.

Notice that the impulse response of the microphone lasts only for a very short time (less than 0.2 ms). This is a good indication that this high-quality microphone is unlikely to distort the waveform shape significantly. However, this may not necessarily be the case for other microphones used in future ear simulators designs. Therefore, the calibration method described here remains valid and necessary for the general use of the ear simulator.

Summary

Specifications for a new family of ear simulators were deduced from literature data for anatomical and acoustical properties of ear canals. For defining the age ranges a stakeholder survey was made using a questionnaire. Three age ranges were defined, and the ear simulators were constructed and manufactured by a professional company and so the universal ear simulator concept was finalised. In addition, adapters were designed and manufactured to allow ear phone types currently in use to be applied. For implementing new calibration methods for transient stimulus signals a technique based on impulse response was developed and tested which allows the correction of microphone response.

With the specifications, the ear simulator demonstrators and the new calibration method this objective has been fully achieved.

Objective 2: Generate normative data for the novel ear simulator

In objective 1 the basic development work was made for designing and manufacturing the new ear simulators and to develop new methodologies for calibration. Objective 2 focuses on the generation of data, methods, and knowledge necessary for the implementation of the ear simulator in practice.

Test and calibration procedures for ear simulator transfer impedance, practical implementation in different NMIs, influence of different adapters

A first and important step is to ensure that the acoustic parameters that govern the performance of the ear simulators can be determined with high reliability. This requires a well-defined test procedure that enables results to be compared between laboratories, and conformance with the design specifications to demonstrated. Ultimately the design specification will be standardized, and the test procedure used to verify ear simulators on a routine basis as part of a calibration service.

Such a procedure suitable for the new ear simulators was devised and implemented by four test laboratories. Each facility was developed independently using different equipment and subject to local operating procedures, and would provide the basis for an interlaboratory comparison.

Figure 2.1 shows an example of the calibration setup, and the configuration of the sound source that was found to provide optimal performance.

Figure 2.1: Proposed configuration of the reference microphone that minimizes the additional volume on the ear simulator. To the left the WS3 microphone mounted in a quasi-flush adapter; to the right, the microphone mounted on an earlier prototype of the ear simulator.

Intercomparison, environmental dependence, definition of equivalence

Following manufacturing of the EARS family occluded-ear simulators, an interlaboratory comparison was carried out to verify their key performance characteristics and produce normative data for input into the standardisation process. The verified methods described above were used for this purpose. Independent measurements at four laboratories performed in a wide frequency range not completely covered by any comparisons before, showed excellent reproducibility in the measured performance characteristics indicating that the ear simulator design and manufacturing process was highly reliable, that the devices can be calibrated consistently, and that their characteristics can be standardised. All of these factors are essential qualities for reference devices.

An expected dependence of the ear simulators' characteristics on static pressure and temperature variations was also investigated by means of independent measurements at three laboratories. The acoustic characteristics of each ear simulator was measured over the range of pressures and temperatures expected in normal use (i.e. covering normal variations in ambient environmental conditions). The resulting data will be incorporated in proposed new international standards and support the routine implementation of calibration services in the future.

An important consideration when proposing major changes to hearing assessment methodology is that the test outcomes should not be altered. Therefore, the terms used to evaluate the level of equivalence were defined at the outset and measurements carried out to quantify those terms. While the EARS family occluded-ear simulators provide traceability for all test subjects regardless of age, current practices only cover adult test subjects. Therefore, the demonstration of equivalence was necessarily restricted to the adult group, where results from a study that compared the performance of the standardized occluded-ear simulator with that of the adult member of the EARS family showed levels of agreement significantly below normal test margins. Thus, a smooth transfer from current practise to the propose new methods was assured.

New reference data and calibration approach for short-duration stimuli

When conducting a hearing test or calibrating an audiometric device, it is necessary to know the magnitude of the sound produced by a given type of earphone within the ear simulator, that corresponds to the typical hearing threshold of potential test subjects. These characteristics define the zero setting on the audiometric equipment which in-turn corresponds to normal hearing and serves as reference for every treatment of a patient. For steady signals the magnitude of the sound is relatively easy to quantify, but for short-duration stimuli there are different ways this can be specified.

This procedure was applied for determining *L*ZeqETSPL values (see Section for Objective 1), of the periodically repeated short-term stimuli by a high-performance sound level meter (IEC-61672 Class-1 [4]) for

a new type of insert earphone, a RadioEar IP 30. Excellent agreement was found between measured and estimated levels, with typical differences of 0.2 dB and a maximum deviation of 0.5 dB. Thus, the concept for specifying equivalent hearing threshold levels by this RMS-based metric turned out to be highly appropriate for this new model of insert earphone.

In a next step a series of measurements on selected test subjects were carried out to determine their individual hearing thresholds, again using the RadioEar IP30 insert earphone. The tests were made with both steady tones, tone bursts and clicks. For the latter two, being short-duration stimuli, the magnitude of the sound was calculated using the currently established peak-level approach (peRETSPL) and the proposed new approach (*L*ZeqETSPL). Measurements were also made in the EARS occluded-ear simulator for adults and the corresponding conventional ear simulator. The results of this study have been presented to the standardisation bodies responsible for specifying hearing assessment methodology for further consideration by the international audiometric community.

Use of appropriate age-related ear simulator for stimulus calibration

Hearing threshold reference data, as they are behavioural data, need to be determined by means of listening tests with otologically normal test subjects. The international standard ISO 389-9:2009 [5] specifies an age range from 18 to 25 years for these test subjects. Hence, for the determination of the reference zero ear simulators that represent the adult age range need to be applied.

If one assumes, simply by lack of proof to the contrary, that the hearing ability, i. e. thresholds of healthy children are virtually equal to those of young, normal-hearing healthy adults, then also the sound pressure at threshold near the eardrum can be assumed to be equal between children and young adults. Hence, in principle, the task of a proper ear simulator is to emulate the sound pressure level at the eardrum with the sound pressure level in front of its built-in microphone. This, however, will only succeed if the volume as well as all other acoustic features of the ear simulator, represented by its input impedance and transfer impedance, match those of the peripheral ear of the human target age group.

If, supposedly, one measured the equivalent threshold sound pressure levels (SPLs) of the adult subject group in an infant ear simulator – by applying the adult group's median threshold terminal voltage of the insert earphone to the latter when it is connected to the infant ear simulator – the measured SPLs would be much higher than those measured in the adult ear simulator with the very same terminal voltages. The enhancement in SPL would be essentially equal to the enhancement of SPLs in the real ears of infants if the earphone and the audiometer to which it is attached were (erroneously, as we know now) calibrated using the (correct) adult ETSPLs and the (inappropriate) adult ear simulator for that purpose. The SPL enhancement due to the usage of adult calibration for infant applications is shown in Figure 2.2 for the RadioEar IP30 insert earphone. To measure this enhancement, the (inappropriate) measurement described was really performed. The tube of the respective earphone was coupled to both the 24-month and the 3-month EARS occluded-ear simulator. The difference shows how much greater the SPL in 3-month and in 24-month ears is than the nominal value, if the (inappropriate) calibration method described is applied. On the other hand, if the appropriate calibration is applied, using a non-adult ear simulator for calibration when non-adult hearing is to be assessed, the terminal voltage level of the earphone must be lower by just that very difference to induce the very same correct threshold SPL both at the non-adult ear simulator's microphone and at the real non-adult's eardrum.

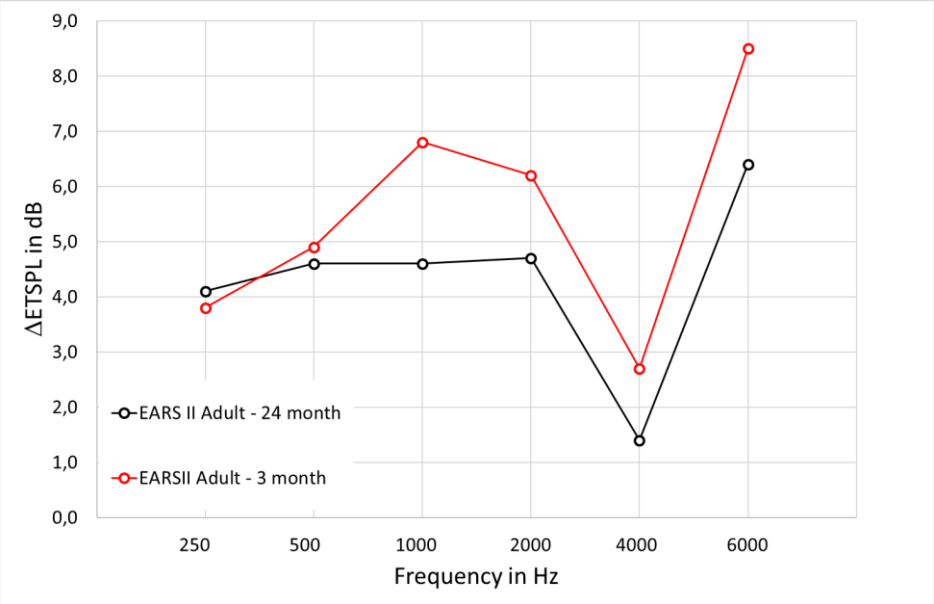


Figure 2.2: Differences between ETSPLs measured in an adult occluded-ear simulator and the EARS occluded-ear simulator prototypes for 24-month and 3-month infants for the RadioEar IP30 insert earphone.

The following recipe can be derived for calibrating stimuli for infants:

a) Determine reference data in adult ear with adult occluded-ear simulator
b) Calibrate stimuli for non-adult ear with suitable member of the EARS occluded-ear simulator family (with corrections, if applicable, see Section 5 above)

This recipe, however, is based on the general assumption that the hearing thresholds for non-adults belongs to the same ear drum sound pressure as for adults.

Guidance document

The research on Objectives 1 and 2 covered many measurement-related aspects of hearing assessment, that have an impact across a wide range of stakeholders from health service policy makers, and hearing assessment practitioners, to instrumentation manufacturers and calibration service providers. To enable the research findings to be disseminated effectively, a guidance document has been produced summarising the key achievements and future recommendations.

It covers the initial rationale for the project and from the metrology perspective, the improvements in calibration and traceability aimed for. However, it also points to the expected impact on the wider audiometric community, including enhanced service quality for clinicians, new technical drivers for manufacturers of instrumentation, and most importantly greater assurances for patients and their families.

The document is comprehensive in covering all of the aspects of the research that the various stakeholder groups need to be informed about. There is a description of the proposed new approach to hearing assessment that flows from having ear simulators covering different age points for the first time, and consideration of the continuity issues that may arise from introducing such significant changes. It covers innovations in calibration and in specifying the level of short-duration test stimuli that calibration service providers and the standardisation community alike can adopt and build upon. Importantly it also defines the scope of further audiological research needed to help establish the new ear simulator specifications and see them become embodied in international standards and gain acceptance.

The guidance document is available from the project website.

Summary

A key comparison showed both, that project partners have appropriate calibration facilities to calibrate the new ear simulators and that the manufacturing process of the ear simulators was highly reliable, that the

devices can be calibrated consistently, and that their characteristics can be standardised. Necessary data for application and standardisation as transfer impedance, input impedance and environmental coefficients were determined. In another step the equivalence to currently established practise was shown. A new calibration methodology for transient signals was successfully tested and it could be shown that the new ear simulators can appropriately account for age dependent differences in calibration of audiometers.

With the calibration capability, data sets and documentation noted above, this objective has been fully achieved and the key research achievements are summarised in the guidance document.

Objective 3: Development of further understanding of perception of infrasound and airborne ultrasound

Development of a measurement procedure to determine the exposure to airborne ultrasound at the workplace

In today's industry, ultrasound is a widespread technology used in applications such as the welding of plastics, the cutting of foodstuffs and the cleaning of objects [6]. Frequently, these ultrasonic applications generate airborne ultrasound as a side-effect and the operators are being exposed to airborne ultrasound. There are complaints about various adverse effects which are related to the exposure to ultrasound at the workplace [7]. According to national [8] and international [9, 10] regulations on the protection of workers against noise and vibrations, it is necessary to determine and assess the exposure to sound occurring at a workplace. So far, no measurement procedure for airborne ultrasound has been developed that would be suitable for practical applications.

Compared to the measurement of audible sound in the frequency range from 16 Hz to 16 kHz, the measurement of ultrasound (i.e. sound with frequencies higher than 16 kHz) is challenging. Due to the higher frequency, ultrasound has special properties and these properties should be considered by using dedicated measurement techniques and procedures. As a first step in development of a measurement procedure, a reference workplace was set up at laboratories of two partners of the project to investigate a representative sound field for properties and conditions particular to ultrasound frequencies. The sound source used for this purpose was an ultrasonic welding machine that was made available by an industrial cooperation partner (Herrmann Ultraschalltechnik GmbH & Co. KG). Using time consuming measurements which were impossible at a real industry workplace the complete sound field was measured with high spatial resolution and specific sound field variables were deduced from the data.

The measurements at the reference workstation revealed that the sound field (shown in Figure 3.1) is characterized by high sound field levels and strong spatial variations. Measurement points spaced by just one or two centimetres may have sound level differences of more than 15 dB. So, individual measurement points may not be representative of the total sound field. Consequently, a measurement procedure was developed which makes use of spatially averaged measurements. Spatial measurement paths on which the microphone is moved were defined considering the positions the person working at the workplace is exposed due to a potential movement during work. Besides specifications on how and where measurements must be performed at the workplace, technical requirements on measuring instruments have been defined for the novel measurement procedure. This includes specifications on measurands which must be evaluated during measurement or in the off-line analysis. The list of measurands may be updated in the future according to new insights concerning the human perceptual mechanism of ultrasound and the impact of ultrasound on humans.

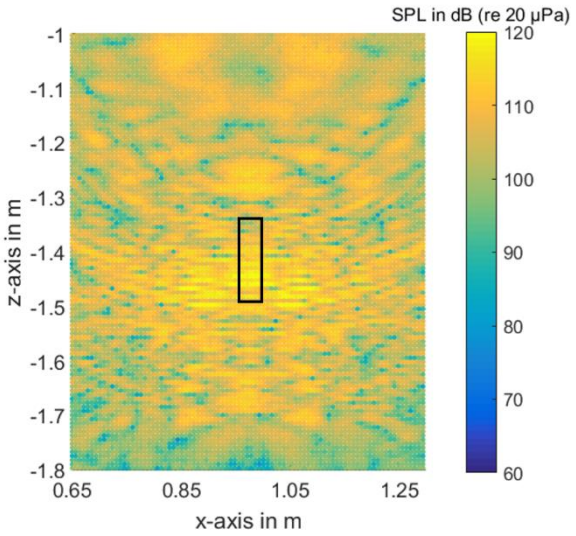


Figure 3.1: Airborne ultrasound field in front of the welding machine; black box represents the ultrasound source within the machine.

Based on the measurement procedure developed, initial measurements have been carried out at three 'live' industrial workplaces in Germany where ultrasonic modalities are implemented in ultrasonic cutting of food, ultrasonic leakage testing and ultrasonic welding [11]. These field tests served as a proof-of-concept for the developed measurement procedure and satisfactory results could be obtained although several details need further development. The procedure is envisaged to be introduced into the responsible standardisation body. These developments enable a significantly improved characterisation and assessment of airborne ultrasound at workplaces and are a step forward for a better occupational health and wellbeing of persons involved.

Investigation of ultrasound exposure in the public

Several sites were identified where devices emitted sounds with frequencies between 16 kHz and 40 kHz, and where the public can be exposed to the sound. Recordings of five devices were made. Two were pest deterrents designed to produce ultrasound or very-high frequency sound (one for birds and one for mosquitos). The other three emitted high-frequency sound as a by-product of their operation: one was an ultrasonic automatic door sensor, one was a surveillance screen using a cathode ray tube, and the third was a hand dryer found to emit considerable high-frequency sound, as shown in Figure 3.2.

Measurements of the sound pressure levels and spectra were made using protocols and devices like those developed for workplace measurements. These measurements will be useful in estimating the levels of exposure to high–frequency sound that the public may experience.

A particular difficulty with ultrasound measurement in public spaces is that the location of sources, and therefore the best place to make the measurement, is not always obvious. To help with this, a multi-microphone device was developed using the latest miniature microphone technology that allows ultrasound sources to be identified and visualised. Unfortunately, due to significant technical challenges the device was not ready in time for the field surveys but is part of the capability now available for future studies.

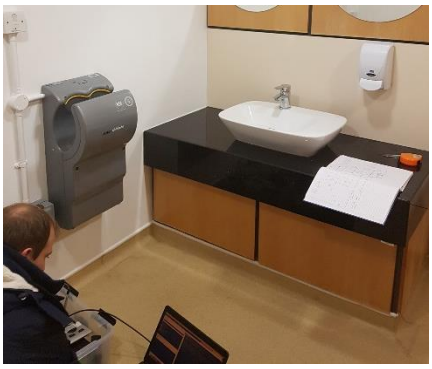


Figure 3.2: Measuring high-frequency sound emitted by a hand dryer.

Perception: Development of sound sources

Various perception mechanisms of ultrasound and infrasound are the subject of controversial discussion amongst experts, and this issue was also addressed in the project. As a first step, special sound sources had to be developed that couple directly to the ear canal, i.e. insert earphones. The most challenging factor for the development of these sound sources was that infrasound and ultrasound must be presented at a very high sound pressure level in order to be audible albeit with strict requirements for low distortion. In addition, the sources were to be used inside a magnetic resonance imaging (MRI) scanner and system for magnetoencephalography (MEG), and therefore had to be electrically and magnetically compatible with these test environments.

One device was a new high-power ultrasound source with in-ear monitoring that allowed a controlled ultrasound exposure up to 40 kHz. The ultrasound source has a cubic body with an ultrasonic piezo loudspeaker at each of the six side faces. United through horns into a central volume inside a cubic body (Figure 3.3), the six loudspeakers enable a stimulation with ultrasound at sound pressure levels (SPL) up to 130 dB (re 20 µPa) with sufficiently low signal distortion. As intended, the ultrasound source proved to have the necessary MEG- and MRI-compatibility and was applied to these investigations successfully.

The other device (Figure 3.4) was used to study the effect of infrasound on audible sound and vice versa. A combination of sound-sources was therefore needed that could simultaneously deliver infrasound and sound within the normal hearing range without audible interference. Such intermodulation was avoided by introducing an additional loudspeaker behind the actual audio sound loudspeaker. It successfully compensated for the modulating effect that the infrasound pressure in front of the audio sound source would otherwise have on the audio sound stimuli [12]. The sound source system was applied in the psychoacoustics experiments that required infrasound stimulation up to 120 dB SPL, in combination with audio sound between 100 Hz and 4000 Hz, presented up to 80 dB SPL.

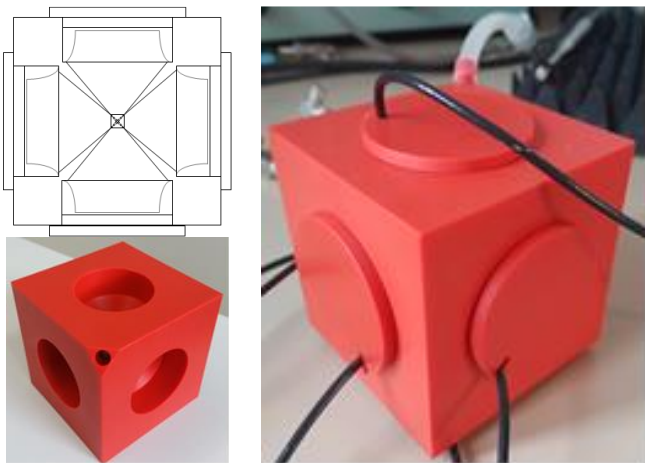


Figure 3.3: Cubical source array for airborne US; Upper left: Cross section; Lower left: empty housing with horns; Right: Complete source with 6 piezo loudspeakers.

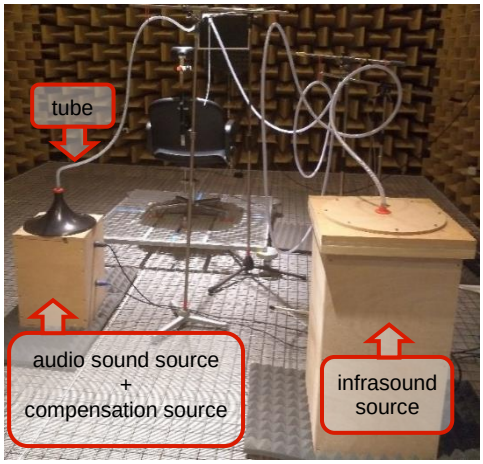


Figure 3.4: Infrasound source and compensated audio sound source were combined by tubing to connect to the subject ear canal.

Perception: Brain imaging including optical sensor techniques

One way to investigate the sensory pathway of ultrasound and infrasound perception is brain imaging. In the project functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG) and electroencephalography (EEG) were used with varying success.

Using fMRI, activation of the auditory cortex in response to infrasound stimulation was measured, but no brain response to ultrasound was detected although these stimuli were reportedly audible to many of the participants. The reasons behind this are unclear at the moment. The fMRI responses were compared with unpleasantness ratings and are therefore reported with more detail below, (objective 4).

For the recording of MEG response to ultrasound, a novel sensor technology using optically pumped magnetometers [13, 14] was established using a very new and prospective technology. Whereas conventional MEG systems based on so-called superconducting quantum interference devices (SQUIDs) are bulky and troubled by sound source artefacts, it could be shown that that the novel optical sensors are completely immune to magnetic fields above 1 kHz.

Fifteen of these sensors were mounted into a 3D-printed helmet (see Figure 3.5, left) specifically fitted to the test subject that can be worn like a cap, and thus, allows the subject to move. Since the measurement conditions are highly reproducible, several measurement sessions could be combined to increase the statistical power. Despite of various technical problems with this cutting-edge technique, the research resulted in the first ever demonstration that acoustically evoked magnetic fields could be successfully elicited (see Figure 3.5, right). An audible sound signal was applied as stimulus and activation of the auditory cortex could be seen. From the comparison with conventional SQUID-based measurements these experiments demonstrated a signal-to-noise ratio sufficient for ultrasound stimulation studies.

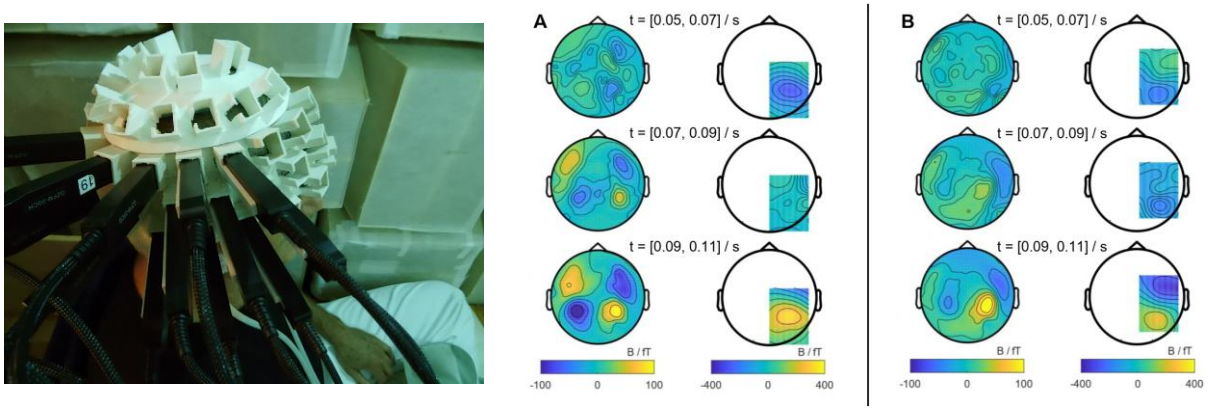


Figure 3.5: left: OPM MEG system with subject inside magnetically shielded room. Right: Magnetic field distribution maps for two subjects (A and B) obtained with SQUID-MEG (left column) and OPM-MEG (right column) for an audible sound stimulus.

Another aim of the project was to develop a practical objective correlate of individual sensitivity to low-frequency sound and infrasound, measuring the brain response. Because of their long periodicity, steady-state EEG responses to continuous infrasound tones were recorded, the so-called frequency-following response (FFR) of the brain which can reveal spectrally resolved brain responses. FFRs to monaurally presented infrasound (11 Hz) and low-frequency (38 Hz) tones over a 30-phon range for 11 subjects [15] were detected. Surprisingly, 11 Hz FFRs were often significant already at a loudness level of 0 phon (i.e. near the hearing threshold) and saturated already above 20 phon (which is still very quiet). The FFR growth with 38 Hz stimulation was shallower than that with the 11 Hz stimulation, and continued to 60 phon. The same loudness level (30 phon) elicited 11 Hz FFRs that were on average 4.5 dB higher than 38 Hz FFRs, possibly reflecting a higher synchronisation of neural activity across the entire auditory pathway, which phase-locks better to the slow periodicity of the 11 Hz than the 38 Hz tone. Unfortunately, these findings make questionable an interpretation of the FFR strength in terms of perceived loudness. Nevertheless, it was a surprise to observe a significant brain synchronisation to infrasound at barely perceptible levels (Figure 3.6). This contrasts with the normal hearing range, which requires 30 – 40 phon stimulation to elicit an FFR. We conclude that the FFR can be useful as a positive confirmation of a brain response to barely audible infrasound. However, the absence of such response must not lead to the conclusion that a person does not perceive such stimulus.

Detection of vestibular-evoked myogenic potentials

Because some of the reported symptoms of infrasound exposure are similar to motion sickness, the hypothesis is commonly discussed whether the balance system (the inner ear vestibular system) contributes to infrasound perception. To test this argument in this project the vestibular-evoked myogenic potential (VEMP) were investigated, which represent an acoustically evoked response from the vestibular system [16]. Whereas VEMPs to 500 Hz tone burst (as also used clinically) could be measured in almost all 15 subjects, the number of significant responses gradually decreased as the stimulus frequency was lowered. (All stimuli were at a loudness of 90 phon.) Few responses were seen at 40 Hz and 16 Hz pure tone stimulation. No vestibular activation could be measured at 4 Hz (Figure 3.7). These results do not then support the hypothesis of perception of infrasound via the vestibular system.

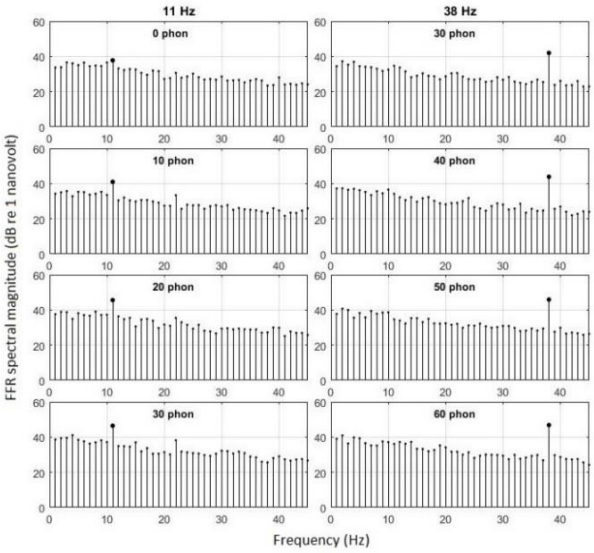


Figure 3.6: FFR EEG spectra averages across all 11 subjects obtained for each stimulus condition.

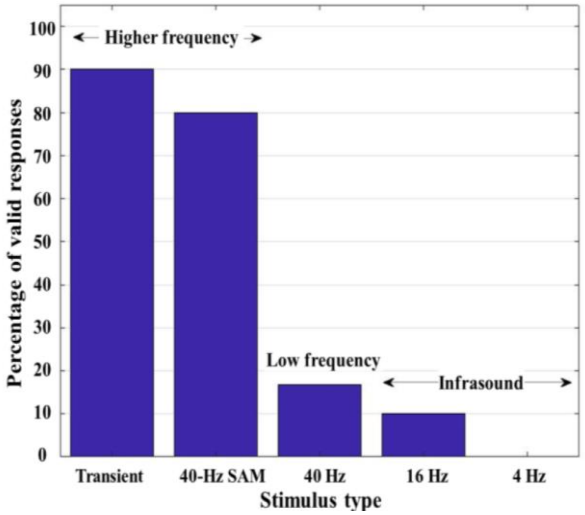


Figure 3.7: Percentage of statistically significant VEMPs to the various acoustic stimulus types.

Interaction between audible sound and infrasound

Many experiments have previously revealed that low-frequency acoustic stimulation affects sound processing over a surprisingly wide frequency range. To quantify these effects, we measured the suppression of otoacoustic emissions (OAEs) evoked at a wide frequency-range of eliciting tones. OAEs are acoustic by-products emitted by a healthy ear, which are measurable with a miniature microphone in the ear canal. They are commonly used in the audiological clinic as a means of assessing hearing function. We measured the suppression of distortion-product otoacoustic emissions (DPOAE) in response to 15 Hz and 30 Hz tones in 18 subjects. The result shows that the effect of these low-frequency tones decreases by 8-9 dB/octave with increasing OAE-eliciting frequency. These findings confirm the slope of the cochlear excitation pattern predicted by our finite-element model (FEM), which was especially developed in this

project to study cochlea response to low-frequency and infrasound (Figure 3.8) and help us to understand the effects that infrasound stimulation has on hearing in the mid-frequency range.

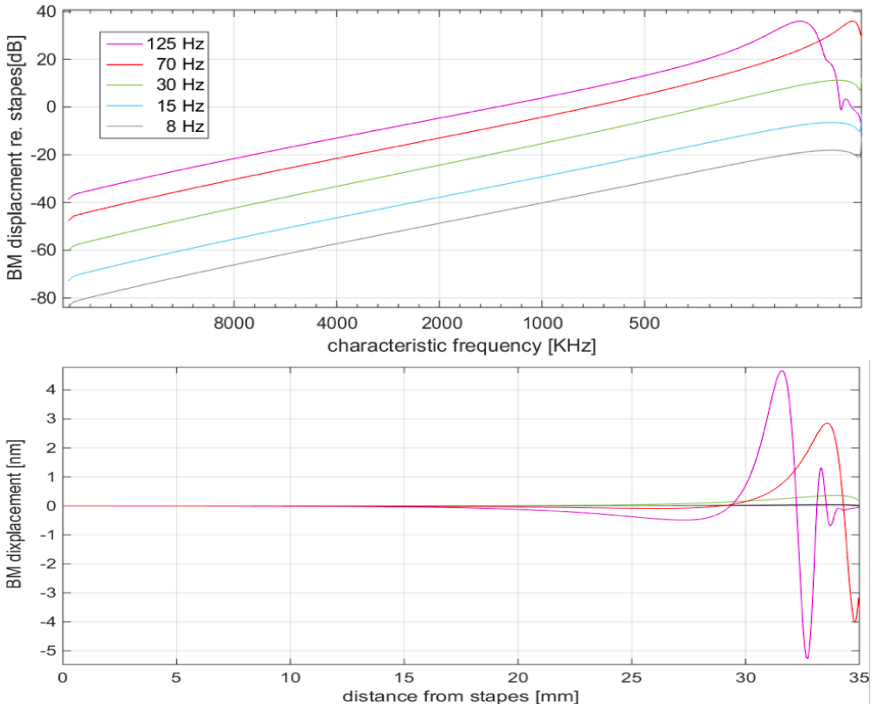


Figure 3.8: Results of a finite-element model of the cochlea, which was fitted to known physiological data. Panel above: displacement of basilar membrane in dependence on frequency, panel below displacement of basilar membrane in dependence on the distance from the stapes

Because infrasound also displaces the mid-frequency range of the basilar membrane (Figure 3.8), one hypothesis is that infrasound might affect sound perception in the normal frequency range due to mechanical biasing of the resting position of the basilar membrane. The modulation of the audible tones might make infrasound better detectable. Whereas modulation is evident for high-level infrasound, no evidence of such benefit could be found in this project for subthreshold infrasound. Contrarily, it *was* found that higher frequency sound can increase the sensation threshold to infrasound. Hearing thresholds for 13 normal hearing subjects were determined for infrasound and audible sound separately and, in a second step for both sound types with the respective other sound as background noise [17]. It was found that a significant infrasound threshold increase occurred when audible sound was present. Vice versa the hearing threshold for the audible sound remained unaltered when infrasound was present (Figure 3.9). This was a quite unexpected result because the hypothesis was that infrasound leads to improved perception of audible sound and becomes perceivable by this process.

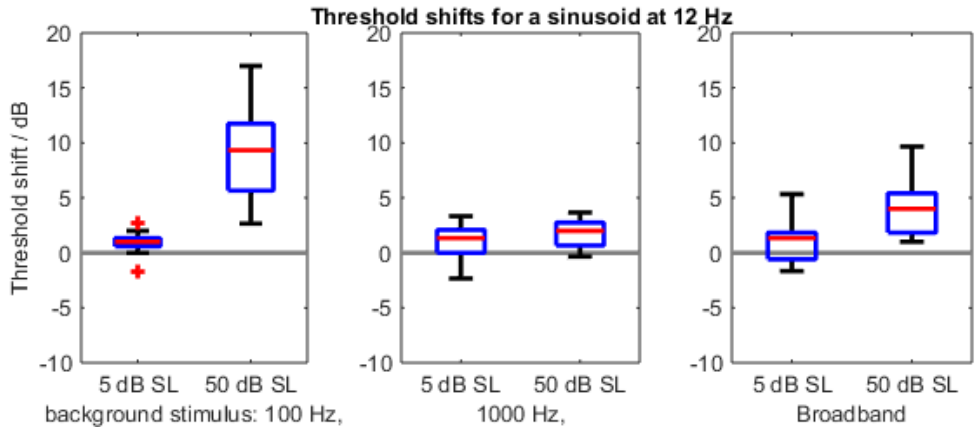


Figure 3.9: Boxplot of the threshold shifts for an infrasound stimulus (sinusoid at 12 Hz) of 13 normal hearing subjects. The threshold shifts were calculated as the difference between the threshold for infrasound in quiet (reference value) and the threshold for infrasound simultaneously presented with a background stimulus in the higher frequency range: 100-Hz tone (left), 1000-Hz tone (centre), broadband noise (250 – 4000 Hz pink, right panel), each at 5 dB and 50 dB above sensation level. Note the large variability (error bar) of the threshold increase (especially with the 100 Hz background tone), indicating that the masking effect was strongly subject-dependent.

We also hypothesised that low-frequency and audible sound above 20 Hz could be mistaken as infrasound if it is amplitude-modulated at rates less than 20 Hz (heard as fluctuation in loudness). This might explain the many infrasound complaints in the absence of measurable infrasound above detection threshold. A study in this project tested whether listeners can distinguish a 63 Hz carrier tone, amplitude modulated at 8 Hz, from a 63 Hz pure tone that was perceptually loudness-modulated by an 8 Hz biasing tone [18]. The twelve participants first adjusted the intensity of the 8 Hz tone so that the perceived modulation of the pure tone matched that of the amplitude-modulated tone. Both stimuli types were then presented in random order, and participants had to identify presentations which contained the infrasound tone. About half the participants performed close to chance. The best had only 81% responses correct. Experiments with a 125 Hz carrier tone gave similar results. Contrary to the expectation, the reason for the similar percept of the two types of stimuli was not that the amplitude-modulated tone sounds like containing infrasound, but it turned later out that, again, the higher frequency tones very effectively mask the infrasound.

Summary

The metrology infrastructure for determination of ultrasound at workplaces and in the public was established in this project. Measurement techniques and instrumentation, including microphone measurement chains, calibration techniques and microelectromechanical systems (MEMS) microphone arrays were developed and built-up. Novel measurement methods for noise determination were developed and tested at real industrial workplaces and at five representative public sites where airborne ultrasound was present. Thus, the current situation of ultrasound noise exposure can be better judged now.

Several studies and setups were built up in this project to investigate the perception processes of infrasound and ultrasound, including the investigation of loudness and the determination of hearing thresholds. They showed that infrasound can be effectively suppressed and masked by higher frequency sound. The masking is well explained by the developed cochlear FEM model. It could show that the lowest frequency that is resolved by the cochlear spectral analyser is just below 100 Hz, and not as generally assumed 20 Hz. Although all these findings do not exclude the possibility that at higher intensities other modalities contribute to its sensation, the masking and suppression effect, in addition with the fMRI observation of auditory cortex activation and the lack of VEMP responses to infrasound, are hard evidence that excitation of the inner ear and the auditory nerve as the pathway is the most sensitive modality to perceive infrasound.

With the studies described the objective has been fully achieved.

Objective 4: Impact of infrasound and ultrasound on hearing, mental health, cognitive abilities

There have been several reports in the literature, part of them anecdotic, that the exposure to infrasound (at frequencies below 20 Hz) may cause various adverse effects in human listeners, ranging from being particularly annoying to causing negative effects on health and well-being. There is no question that the individual sensitivity to infrasound is very different across listeners. In a similar way, the sensitivity to airborne ultrasound at frequencies just above the common audio frequency range (20 - 30 kHz) is very different across individuals, and adverse effects such as headaches have also been reported. With regard to objective 4 of this project, the interrelation of detection thresholds, loudness perception, annoyance and corresponding brain activation was investigated in a set of several psychoacoustic studies as well as brain activation studies using functional magnetic resonance imaging. In parallel, a comprehensive questionnaire in three different languages was developed that is specifically targeting individual sensitivity to sound at very low frequencies as well as very high frequencies. The questionnaire also includes questions about the awareness of possible sound sources at these frequencies in the individual living environment. This questionnaire was designed to allow for the extraction of personal factors that may explain part of the variance found in psychoacoustic as well as brain activation data.

Psychoacoustic results

For very low frequency tones and tones in the infrasound range, the main psychoacoustic findings are:

- Detection thresholds for infrasound frequencies vary considerably across normal hearing listeners, to a greater extent than detection thresholds in the common audible frequency range.
- As expected, the dynamic range between detection thresholds and uncomfortable loudness is shrinking to less than 40 dB (in contrast to 100 dB or more in the typical audio frequency range for normal hearing listeners) on average for frequencies below 20 Hz, see Figure 4.1 A, with some participants exhibiting particularly steep slopes for the increase of loudness with level. These listeners supposedly represent a group with particularly sensitivity to low-frequency sounds.
- The annoyance for isolated tones - in our studies acquired by means of rating sensory unpleasantness, a precursor of annoyance - is clearly highly correlated with loudness ratings. Still, even for the same loudness, infrasound stimuli (8 Hz, 16 Hz) are rated as more annoying than tones in the common audible-frequency range (64 - 256 Hz), see Figure 4.1 B. Sensory unpleasantness can therefore not be predicted by the perceived loudness only. There is an interaction with stimulus frequency.
- Since human exposure to infrasound is usually accompanied by common audible-frequency sound, we were also interested in investigating the annoyance for combined infrasound and audible-frequency sound stimuli. Hearing tests with a sample of 19 participants showed that the combination of infrasound (12 Hz), presented above-threshold, with audible-frequency sound (tones at 1000 Hz, broadband pink-noise 250-4000 Hz) can increase the perceived annoyance compared to the same stimuli presented alone.

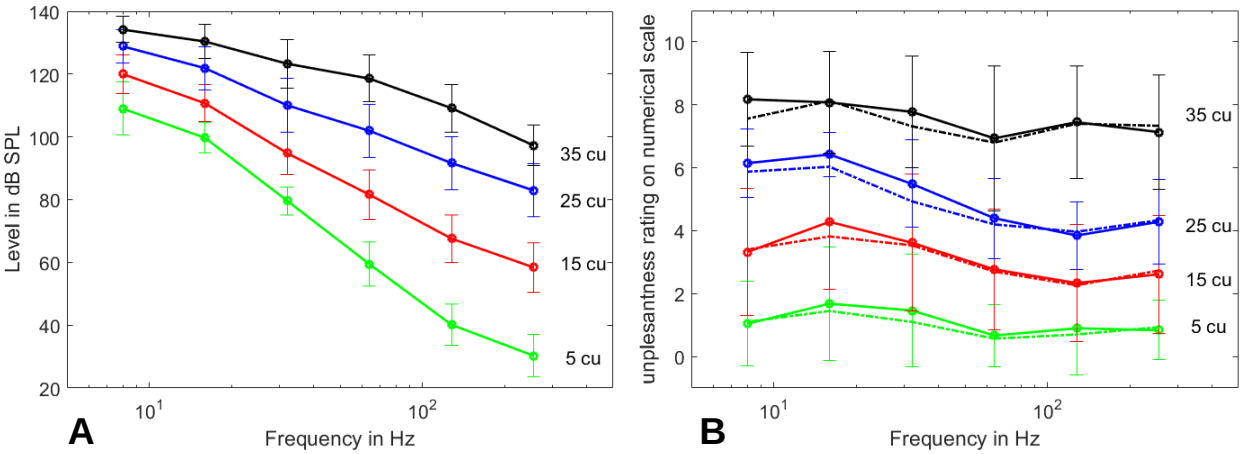


Figure 4.1A: Results of adaptive loudness scaling for low frequencies: Data points indicate mean levels (with standard deviations) across listeners required to cause a loudness rating of 5, 15, 25 or 35 categorical units (corresponding to verbal categories “very soft”, “soft”, “medium”, and “loud”. **B:** Results from two unpleasantness rating tasks for low-frequency sounds. Symbols connected by solid lines are mean values across listeners for the 11-step numerical scale (ranging from 0 to 10), while the dash-dotted lines indicate the results from the 5-step verbal categories-task for comparison (transformed to numbers 0 to 4 and multiplied by a factor of 2.5 to expand to the same range). Error bars indicate standard deviations for the 11-step numerical scale.

For tones at very high frequencies and ultrasonic frequencies, psychoacoustic measures of detection thresholds, subjective loudness, and sensory unpleasantness were obtained for two groups of subjects: those who self-reported having experienced adverse reactions to high-frequency sound in the past (the “high-sensitivity group”), and those who did not (the “normal-sensitivity group”). The main psychoacoustic findings are:

- Detection thresholds vary to a greater extent across listeners for very-high frequency tones than for 1 kHz tones.
- For both participant groups, curves of equal loudness between 14 and 18 kHz were compressed relative those at 1 kHz, indicating that subjective loudness increased with sound pressure level more steeply at these very high frequencies than at 1 kHz. For example, for tones that are 10 dB above a person‘s detection threshold, the sound was typically judged to be louder for very-high-frequency tones than for 1 kHz tones.
- For both participant groups and for sounds that were equally loud, ratings of sensory unpleasantness were considerably greater for very-high-frequency tones than for 1 kHz tones. This increase in unpleasantness at very-high frequencies was more marked for participants with high sensitivity than for those with normal sensitivity. For example, for the range of levels tested, the 1 kHz tone was rarely rated as being more than “slightly unpleasant”, while at 16 kHz, for a similar loudness rating, the tone was typically rated as ”moderately unpleasant” by the normal-sensitivity group, and as between ”moderately” and “very unpleasant” by the high-sensitivity group.

Brain activation in relation to loudness and annoyance

Individual psychoacoustic findings on loudness and annoyance were then used as input for the data analysis of brain responses to low-frequency and infrasound stimulation as acquired by means of functional MRI. The main findings are:

- Brain activation maps in response to infrasound stimuli, indirectly represented by increases of the recorded MRI signal caused by changes in the oxygenation of blood, are largely in line with what is typically found for common audible-frequency sound, with activation regions distributed across auditory areas in the superior temporal lobes, and no consistent activation in areas outside these common auditory regions. There was no significant difference in activation between 8 Hz (infrasound) and 32 Hz stimulation (that is, sound just at the lower limit for musical pitch). This

suggests that infrasound stimulation, at least when stimuli are delivered directly to the ear canal via the silicone tubes employed in this project, does not involve other sensory pathways than the ascending auditory pathway.

- fMRI signals in the auditory regions of the brain increase with increasing presentation level, increasing loudness, and, to a lesser extent, with increasing annoyance, all of which was expected.
- Results of within-participant cross-validation analyses for different ways to predict the fMRI response show that individual loudness and annoyance are better predictors than the level only, for the 8 Hz stimulus and the 32 Hz stimulus. This suggests that the brain activation linked to both auditory stimuli is indeed a correlate of the perceptual quantities of loudness and annoyance rather than just a representation of sound pressure level. Therefore, functional MRI of the auditory system appears to be a useful way to identify particular effects caused by the stimulation with infrasound stimuli. In future, the incorporation of responses from the questionnaire developed in this project (see below) should allow for a more detailed description of the interrelation between individual sound sensitivity and additional personal and environmental factors.

Binaural loudness summation of infrasound

For this study, the infrasound source system, described in objective 3 was duplicated so that left and right stimuli were completely independent. We compared the loudness of infrasound presented to one (monaural) and to both (binaural) ears. In the latter case the phase-relationship between the tones at either ear was varied in order to study to what extent the stimulus-locking of the neural response influences the loudness of infrasound stimuli. This is informative in designing the time-integration stages of models that predict loudness (e.g. ISO 532). In a study with five participants with normal hearing ability, loudness matching experiments were used to adapt the level of binaural test stimuli to the level of monaural (left and right) reference stimuli with the same frequency. The stimuli had pure frequencies of 125 Hz, 32 Hz and 8 Hz; 125 Hz is the lowest frequency used in clinical audiometry and was used to compare the results in the audiometric frequency range with those of low-frequency (32 Hz) and infrasound (8 Hz) stimuli. Binaural stimuli were presented with 0°, 180°, +90° and -90° interaural phase difference (IPD) between left and right stimulus. Care was taken to match the loudness perceived with monaural left and right stimuli to exclude any influence due to a different perception of both ears. In addition, also the hearing thresholds of all stimulus configurations were determined.

The binaural tones at 125 Hz had to be approximately 5 dB lower in order to be perceived equally loud as a monaural 125 Hz tone (Figure 4.2, second box group from left). This was in accordance with previous studies. For the infrasound tone of 8 Hz, however, this loudness discrepancy decreased to only 2 dB when left and right stimuli were out of phase (180° IPD, third group from left). Interestingly, the hearing thresholds show a similar tendency (not shown).

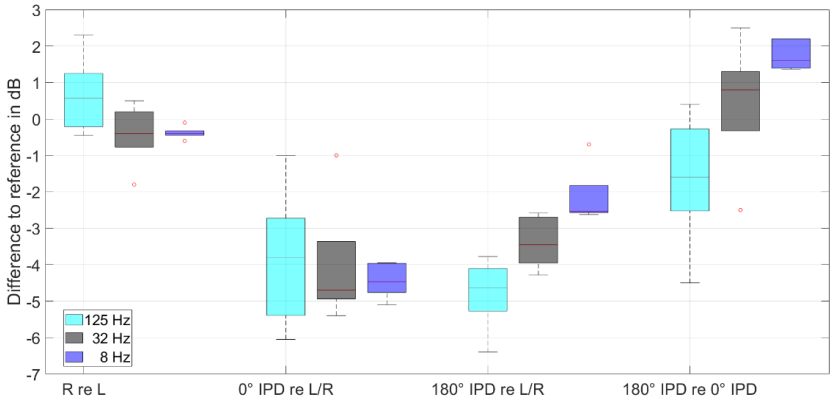


Figure 4.2: Results of the loudness matching experiment are shown as the difference in sound pressure level between the adapted test stimulus and the reference stimulus when both are perceived with the same loudness (nomenclature on abscissa: test stimulus re reference stimulus). The colours indicate the different test frequencies. The data of different test subjects are summarized as boxplots.

Long-time impact of infrasound and ultrasound on humans – mental health and effects on cognitive performance

In a longitudinal study (i.e. over the course of 4 weeks) investigating the long-term impact of infrasound and ultrasound on human mental health, cognitive function, and brain, different types of sound sources were successfully installed in private households (dormitories) all over the city of Hamburg and surrounding areas. In total, a sample of forty-two healthy subjects (age range between 18 and 40) - twenty-one each assigned to the infrasound or ultrasound condition (13 verum, 8 placebo each) - was fully assessed and statistically evaluated concerning potential changes in psychiatric symptomatology (e.g. depressive symptoms or symptoms of anxiety), somatic symptoms (e.g. headache, nausea, vertigo) and cognitive function (e.g. sustained attention, working memory performance).

The study was single-blinded (i.e. the participants were unaware of their treatment allocation) with randomized group assignment (i.e. they were randomly assigned to either the treatment group with true sound or a sham sound source group). We followed a standardized study protocol for all stages as well as manualised assessment procedures, meaning that the investigators had a strict procedure how to instruct and assess all participants. This allows for high reliability of all procedures and assessments. Participants were exposed to either a sham (placebo) source (the appearance of these sources was identical to the verum = true sound sources), a 6 Hz infrasound or a 22.4 kHz ultrasound source. These sources were particularly developed and manufactured in the project team and could produce sufficient power without noticing by the participants while operating. In the verum conditions, the sound was emitted for 8 consecutive hours, customized to the self-reported night-sleep interval of each individual. This individualized exposure proceeded for 28 nights.

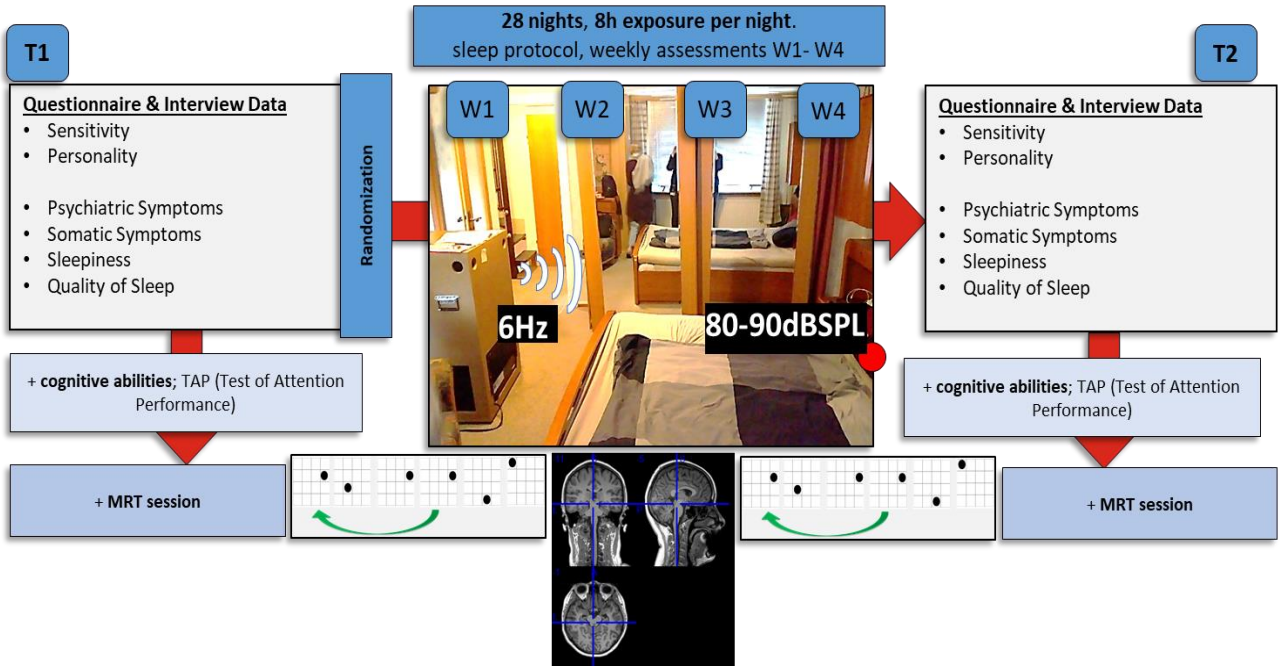


Figure 4.3: Schematic overview of the study. See explanation in the text.

As visualised in Figure 4.3, in between the pre (T1) and post (T2) assessments, that included psychological and psychiatric symptom questionnaires, a computerized cognitive abilities assessment, and an MRI session with a functional 3-back-task for determination of working memory performance (see also Figure 4.4), the sound sources (here: a 6 Hz-infrasound source) was placed and at baseline calibrated to a local SPL (head side) of 80-90 dB in a participant's dormitory. The W1 to W4 symbols indicate that data was assessed on a weekly basis to assure the participants' compliance and in order to track any meaningful changes (e.g. room constellation, onset of any illness/ medication, absence from bedroom during the night, etc.).

Analysing the data in the preliminary sample as described above no conclusive evidence was found for harmful effects of 6 Hz infrasound or 22.4 kHz ultrasound. On the contrary, evidence for the null hypothesis (i.e. the hypothesis that states that there is, in fact, no effect) was observed. On a descriptive level, for infrasound there were four variables (somatic symptoms, stress, noise sensitivity, speed-accuracy trade-off in a cognitive flexibility task) showing moderate (although non-significant) changes, potentially attributable to the experimental manipulations. The direction of these effects seemed to be, however, quite mixed; with some variables improving and others deteriorating over time. Due to their non-significance they should not be interpreted at this point. There were also three (descriptively) large (although non-significant) changes, potentially attributable to the infrasound experimental manipulation: the covert shift of attention performance index (i.e. this measures the ability to re-orient the attention based on cues) increased (suggesting an improvement) within the verum and decreased (slightly) within the placebo condition, the median reaction time in a GoNoGo task decreased within the verum condition, and sleepiness was constant in the verum while decreasing in the placebo condition. In sum, this pattern of descriptive changes seems inconclusive at this point.

For ultrasound, there were seven variables showing moderate (general noise sensitivity, anxiety, sleep quality, phasic arousal, phasic alertness index, total performance index cognitive flexibility task) changes, and two variables exhibiting large changes (somatic symptoms, stress), potentially attributable to the ultrasound experimental conditions. Interestingly, in all the symptomatic variables (general noise sensitivity, anxiety, stress, somatic symptoms) there were descriptive increases only in the placebo condition, pointing towards potential nocebo (i.e. negative effects emerging due to according negative expectations; such as dangerousness of inaudible sound) effects. Only sleep appeared to descriptively worsen within the verum group (constant in placebo). Concerning cognitive parameters, effects were also pointing towards descriptive changes mainly within the placebo group: phasic arousal (i.e. readiness and fastness of response increasing after a warning tone) and cognitive flexibility (total performance) increased on a descriptive level.

As a critical side note, none of the above-reported effects would have survived an alpha-level correction (i. e. combined significance test) and should hence not be interpreted at this point. Nonetheless, it might be possible that enhanced statistical power (i.e. a common rule in statistics: effects are easier to detect with larger samples) with a larger sample size could reveal the presence of statistically significant, robust effects. Nevertheless, this work provides a significant contribution for the estimation of health risks conveyed by infrasound and ultrasound and for further, more precise study of this matter. It also provides an ecologically highly valid and feasible experimental procedure to study the daily-life impact of inaudible infrasound and ultrasound from which future studies can surely benefit.

Questionnaire

Across different European countries, a questionnaire that is suited to assess high- and low-frequency sound sensitivity was developed, assessed and evaluated within a sample of more than two-hundred participants from the adult population. The questionnaire is available in English and German language. It provides a new tool for the scientific community for further evaluation, which should allow the identification of sub-populations of individuals who are particularly responsive to high- or low frequency sound. This could be very useful for more fine-grained analyses of potential adverse health- or other effects in environmental, experimental, audiological, psycho-acoustic or other types of studies. Our present analyses with the questionnaire reveal that low- and high-frequency sensitivity only correlate to a moderate extent with each other, and only weakly to moderately with noise sensitivity in the common audio-frequency range. This suggests that they might indeed reflect different aspects of sound sensitivity. In addition, both types of sensitivity are associated with different symptoms (psychiatric and somatic; self-report), pointing towards their potential role in the emergence of adverse reactions to high- and low-frequency emissions.

Functional MRI for ultrasound exposure

Little is known on the perception mechanism and potential health effects of airborne ultrasound (US). This study was performed to find out if a potential cognitive effect due to the presence of US may be expected. This may, for example, affect situations in which high cognitive performance is necessary. In this study, the influence of ultrasound (US) stimulation on the cognitive processing was investigated by functional magnetic resonance imaging (fMRI).

We collected fMRI data of a healthy sample of participants who were able to hear ultrasound at 21.5 kHz frequency. The participants were preselected according to this criterion.

Participants performed a spatial working memory task (3-back) in which 10 black dots appeared at varying locations in a 4 by 4 grid. This task can be used to assess the capacity of an individual to memorize meaningful information, and update it, for a short time period, which is thought to also represent short-term memory performance in real-life. The task of participants was to indicate by means of button presses (index and middle finger of the right hand) whether each dot was in the same position as the dot three steps earlier in the sequence (3-back) or not (Figure 4.4). Dots appeared for 500 ms at random locations with the constraint of not appearing in the same location in consecutive steps. The inter-stimulus interval between the dots was 2750 ms. During fMRI acquisition after ten trials a fixation period of 20 s was inserted. The latter is done in order to provide a 'baseline' where participants are inactive, in order to compare this with the activity during active phases of the fMRI trial. Overall participants went through three runs with 10 blocks each during the fMRI acquisition. During n-back blocks one third of the blocks were accompanied by the presentation of ultrasound at 21.5 kHz (on each trial presented with a duration of 3 s) at a sound pressure level of 5 dB above the hearing threshold; another third of the blocks were accompanied by the same sound presented 10 dB below the hearing threshold and another third of the blocks were not accompanied by tones. The blocks with and without tone administration were identical – to allow direct comparison- but presented at random. The task is described in more detail in Weichenberger et al., 2015 [19].

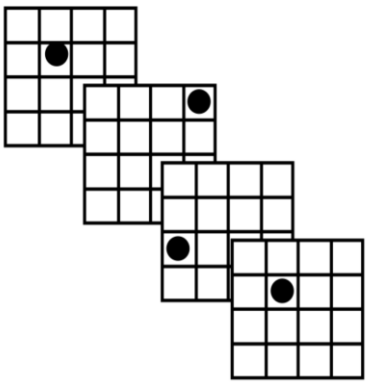


Figure 4.4: Schematic drawing on 3-back task

The fMRI data were analysed using a widely accepted software analysis tool to evaluate blood oxygenation level dependent activity (BOLD) during fMRI tasks. The BOLD signal indicates how strongly oxygenized a given brain region is in the moment of the task – hence hinting towards the neuronal activity. When focusing on brain activity during 3-back performance compared to fixation activation in the typical so-called cognitive control network was observed, including prefrontal and parietal brain regions (both brain regions together 'control' so called executive functions which are functions crucial for planning and control of actions). Then we directly contrasted the two-tone conditions (5 dB above, 10 dB below threshold) with the no tone conditions, but found no significant differences between conditions, even when focusing on regions of interest in primary auditory cortex no significant differences were observed. The same was true when contrasting only the 5 dB above threshold condition against the no tone condition.

However, interestingly a significant difference was found when contrasting the 10 dB below threshold condition with the 5 dB above threshold condition. Here higher brain activation was observed for the 10 dB below threshold stimulation in bilateral inferior prefrontal cortex – an area crucial for instance for inhibition (i.e. the oppression of a dominant/ strong impulsive action tendency). Interestingly, when focusing on the behavioural performance during the working memory task, we found an almost significant difference in reaction times between the no-tone condition and the 10 dB below threshold condition with the 10 dB below threshold reaction times being faster than the ones during the no tone condition. Although this is only a tendency for a difference, the direction of the effect is interesting and suggests that the higher activation in bilateral prefrontal cortex may not necessarily a "negative" effect but may reflect an enhanced effort to focus

on task performance. No correlation between reaction time differences and brain activity differences was observed. Since data analysis is not yet finished, these results should be considered as preliminary findings. However, it is highly interesting that the results seem to point in a similar direction as the almost significant superior performance in the same working memory task observed under infrasound exposure.

Summary

Psychoacoustic studies were carried out to investigate the impact of infrasound and ultrasound on hearing and mental health. Mainly annoyance and loudness and their interrelation were addressed, and it could be shown that infrasound and ultrasound tend to behave like audible sound and similar strategies can be applied. A questionnaire was developed and evaluated with more than two-hundred participants which allows the determination of subjective responsivity to infrasound and ultrasound. This could be very useful for more fine-grained analyses of potential adverse health- or other effects in environmental, experimental, audiological, psycho-acoustic or other types of studies. Experiments for determining the binaural loudness were made showing that the situation at infrasound changes significantly because the loudness gain typically at audible frequencies is lost. A long-time study to investigate the impact of infrasound and ultrasound on humans was carried out using specially developed sound sources. At the present point from this study could concluded that concerning infrasound, there could be singular variables affected by it, but the evidence overall speaks for a null-effect. Concerning ultrasound, there appears to be evidence for nocebo effects, but more data is needed to confirm this impression, which was based on descriptive post-hoc examination of the data. Finally, the impact of ultrasound on cognitive abilities was investigated by a memory test and fMRI investigation but also no significant effect could be detected although a slight influence was observed.

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5 Impact

The objectives and outputs outlined above have been formulated to meet the declared needs. Therefore, delivery of these outputs will enable a significant impact in key areas to be created.

Impact on industrial and other user communities

The consortium worked with industry and clinicians directly, to enable early adoption ahead of the research outputs becoming mainstream. Clinical users have been consulted about the practicalities in using the ear simulators, and their feedback was incorporated in the final specifications. They were given access to the ear simulators in order to assess their impact alongside established protocols. There is close contact with

companies involved in calibration and testing of audiological equipment as the main users of the new ear simulators and calibration procedures.

The research on objectives 1 and 2 covered many measurement-related aspects of hearing assessment, that have an impact across a wide range of stakeholders, from health service policy makers, and hearing assessment practitioners, to instrumentation manufacturers and calibration service providers. A guidance document has been produced summarising the key research achievements and future recommendations, for dissemination to the above stakeholders.

New measurement techniques for infrasound and ultrasound have also been demonstrated within the project and now form the basis of new measurement capability and services. In case of airborne ultrasound at workplaces, new measurement methodologies were developed and successfully tested in three German companies with ultrasound technology. These new methods now form the basis of a significantly improved assessment methodology of noise at ultrasound work places leading to a higher level of occupational safety in this field.

New understanding of human factors such as perception and annoyance will also assist industry and local authorities in mitigation of noise hazards in a systematic way with scientifically robust approaches. Regular training and awareness raising of noise in the workplace now includes the topic of ultrasound as a direct result of this work. This is the basis for an appropriate and sustainable noise protection at workplaces, ensuring safety for machine operators and avoids unnecessary, bulky, and expensive noise isolation equipment and setups.

Impact on the metrology and scientific communities

A virtual centre of excellence in metrology and measurement capability for infrasound and airborne ultrasound has emerged from the project activities, providing an open resource for the metrology and scientific communities across Europe, and making duplication in this highly specialised area unnecessary. The project consortium is already in contact with other NMIs with an interest in these activities.

The newly developed psychometric questionnaire provided a new tool for evaluating an individual's susceptibility to annoyance and other impacts from infrasound and ultrasound with respect to acoustic, psychoacoustic and psychological factors. This has the potential to identify sub-populations of individuals who are particularly responsive to high- or low frequency sound and for more fine-grained analyses of potential adverse health- or other effects in environmental, experimental, audiological, psycho-acoustic or other types of studies.

The research on infrasound perception produced various interesting results. There is no apparent difference in infrasound sensitivity per-se while many properties and issues are not that strictly different to audible noise. The new finding of masking will give future research, into the infrasound problem, a completely new direction, such as whether the efficiency of the discovered masking effects is individually different.

The use of novel optical sensors in MEG studies has been successfully demonstrated, paving the way for further studies on human behavior and perception, not just for auditory studies but with the full range of stimulus types.

Impact on relevant standards

Many project outputs have directly or indirectly targeted the standardisation activities of the International Standardisation Organisation (ISO) and the International Electrotechnical Commission (IEC).

For ear simulator standardisation, it is essential for the new technology to gain recognition and ultimately be taken up in clinical practice to yield quality assurance and reliability improvements in hearing assessment, particularly for children and neonates. Members of the project team are also involved in the IEC working group that prepares the standards so there has been regular contact between the groups. An early draft document was presented to the working group around the mid-point of the project but concerns about the robustness of the anatomical data and the tentative nature of the specifications stalled the standardisation project. However, feedback from the dissemination workshops led to the preparation of a Publicly Available Specification that has been submitted to the working group. This will allow others to pursue their own ear simulator developments building on the project outputs.

A communication has been sent to another IEC working group dealing with audiometric equipment. This concerns the use of the new metric for specifying the level of short-duration test stimuli, and its relationship with existing metrics.

Another communication has been sent to the ISO working group dealing with the specification of hearing thresholds, on the measured data for the new earphone type used in the hearing threshold studies. This is the first data of its kind and was measured in full compliance with the requirements necessary for it to be adopted as normative data. This will increase the reliability and consistency of clinical measurements made with the new earphone type.

At the national level, contributions have been made to the German standardisation body on the new model of how infrasound is detected by the inner ear, which will ultimately contribute to international standards on loudness and perception.

Likewise, contributions have been made on the new recommendations and protocols for measuring airborne ultrasound in the context of general assessment of industrial noise exposure. These are expected to feed-forward to the corresponding international working group under the auspices of ISO in due course, fostering widespread recognition and take-up of research outputs from the project.

Longer-term economic, social and environmental impacts

The project will have long-term effects since many of the initiated changes, technology and methodology will take time to evolve. The transition to the new arrangements for hearing assessment involving the EARS family occluded-ear simulators will take many years before standards are finalised and health policy is changed. Individualised calibration ultimately reduces cases where test results are neither a certain pass or a certain fail, leading to improved confidence and reduced false-positive results. In neonatal and infant screening, unnecessary referrals for further testing and the associated parental anxiety from false-positive results are also reduced.

Although the methods are already in use, for example at the measurement groups of the German insurance companies, the development of measurement methods for ultrasound at workplaces will continue because of the large variety in source types, usage and external environment. The core findings of this research will help build a greater wealth of experience necessary to formulate widely applicable methods. This will finally bring the level of occupational safety at ultrasound frequencies to that in the audible frequency range.

The significant progress made in our understanding of the perception of infrasound now enables new mitigation strategies to be suggested, especially for those known to be very sensitive. The masking effects that have been discovered in the auditory sensing mechanism, now indicates how the external acoustic environment can be changed to reduce the impact of the infrasound itself.

The consortium has been active in many dissemination activities to complement the research work. 14 journal papers and conference proceedings have been published, 57 presentations have been made to 20 different organisations or groups at conferences, events or meetings, and 1 article has appeared in the popular press. In addition, the project website will be retained for the foreseeable future.

6 List of publications

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