Relationship between Cochlear Mechanical Dysfunction and Speech-In-Noise Intelligibility for Hearing-Impaired Listeners

PH.D. THESIS

Patricia Pérez González

Instituto de Neurociencias de Castilla y León

Universidad de Salamanca

July 2017

Enrique Alejandro Lopez Poveda, con documento nacional de identidad nº 07.953.786-H, Profesor Titular de la Universidad de Salamanca, adscrito al Departamento de Cirugía (Facultad de Medicina), al Instituto de Neurociencias de Castilla y León y al Instituto de Investigación Biomédica de Salamanca,

CERTIFICA

Que la tesis doctoral titulada "*Relationship Between Cochlear Mechanical Dysfunction and Speech-in-Noise Intelligibility for Hearing Impaired Listeners*" describe el trabajo original de investigación realizado por Dña. Patricia Pérez González en los últimos años en mi laboratorio y bajo mi dirección.

La tesis demuestra que, una vez compensada la pérdida auditiva mediante amplificación, las personas hipoacúsicas tienen peor discriminación verbal en ambientes ruidosos cuanto mayor es su disfunción coclear mecánica. Esta relación, sin embargo, sólo ocurre cuando el ruido es estacionario; en ruido fluctuante, la discriminación verbal no está correlacionada con el grado de disfunción coclear mecánica. La tesis demuestra, además, que el grado de disfunción coclear mecánica puede variar desde un 30% a un 60% entre personas con un mismo tipo y grado de hipoacusia. También apoya los supuestos del método psicoacústico de las curvas de enmascaramiento temporal empleado habitualmente para inferir el grado de disfunción coclear mecánica en humanos. Los resultados se han descrito en tres artículos publicados en prestigiosas revistas científicas internacionales.

Considero que esta tesis doctoral reúne la calidad y el rigor científicos necesarios para ser defendida públicamente en nuestra Universidad como requisito parcial para que Dña. Patricia Pérez González opte al grado de Doctor.

Salamanca, 3 de Julio de 2017

Enrique Alejandro Lopez Poveda

Director de la Tesis Doctoral

AGRADECIMIENTOS

Cómo decíamos ayer…

Hace mucho que empecé esta etapa de mi vida y ahora toca cerrarla para dar paso a nuevas experiencias. Durante este tiempo, han sido muchas las personas que me han ayudado y acompañado en este camino, y a todas ellas quiero dedicar este trabajo, que sin su ayuda no hubiera sido posible. También debo pedir perdón y extender mi agradecimiento a aquellos de quienes me olvide en las siguientes líneas (seguro que de alguien me olvidaré).

Empecemos por el principio. Gracias a los Manolos (Manuel Malmierca y Manuel Gutiérrez). Ellos fueron los que me dieron la oportunidad de entrar en el mundo de la investigación con mi primer proyecto de fin de carrera. Y, por su puesto, gracias a todo el laboratorio de Neurofisiología de la Audición. Sin ellos, las horas y horas, tanto en medicina como en el INCyL, no hubieran sido iguales.

Un tiempo después, y con mi segundo proyecto de fin de carrera, tuve la oportunidad de empezar a trabajar en el Laboratorio Audición Computacional y Psicoacústica, donde he pasado los últimos años y donde me he sentido en familia. Muchas gracias en especial a Peter por esas 'siestas' tan buenas después de comer; a Almudena por esos congresos ¡ya sabes cuál es nuestro próximo negocio!; y, por su puesto, a Enrique, por enseñarme todo lo que me has enseñado y por aguantarme todos estos años a pesar de que a veces me hubiera merecido más de una colleja.

No quiero olvidarme del equipo del proyecto de Starkey. José Luis: gracias por enseñarme tanto, fue un auténtico placer. Joseba: muchas gracias por todo. To Bill and Sridhar: it really was a pleasure to work with you; thank you guys! Y, por supuesto, a todos mis participantes: muchas gracias por vuestra ayuda; sin vosotros, esto no tendría ningún futuro. A Marcelino, Toñi, Jesús, Rubén…, y así hasta 68, mil gracias!

Por último agradecer a todos los demás…

A todos mis amigos que en algún momento me preguntaron que para cuándo me tocaba y siempre estaban allí con unas cañas o perdonándolas cuando he

tenido que apretar. A mis jerezanos favoritos: ¡no me voy a olvidar de vosotros, ni ahora ni en el 2020!

Al doctor Colino, a la doctora Blanco y al doctor Rodríguez, que son muy graciosetes, pero que ya se les acabó el chiste… mala suerte. Siempre nos quedarán las taquillas del Pryca.

A mi familia, en especial a mi madre, que siempre me ha apoyado o tirado de las orejas para que saliera para adelante, ambas cosas igual de importantes. A David, gracias por todo, me has ayudado muchísimo ¡y lo sabes! A Pili, porque he conseguido seguir nadando. Y, por supuesto, a Rober, sin quien no hubiera sido posible terminar esto ni nada. Gracias.

¡Ah! Y, por supuesto, a mis gorditos, las cositas que hacen seguir para adelante, Patán, Bullma y Melé, mi canija que nos cuida a todos desde arriba, gracias por estar ahí y ser como sois, tenemos mucho que aprender de vosotros.

Y, para terminar, dar las gracias a los que han puesto la pasta. Esté trabajo ha sido financiado por la empresa Starkey Ltd, (USA), por la Junta de Castilla y León (Orden EDU/1204/2010, de 26 de agosto*)* y por el Ministerio de Economía y Competitividad (ref. BFU2012-39544-C02).

GRACIAS A TODOS

ABSTRACT

We aimed at investigating why hearing impaired (HI) listeners vary widely in their ability to understand speech in noisy environments, even when their hearing loss is compensated for with amplification. We hypothesized that outer hair cell (OHC) dysfunction affects the intelligibility of audible speech in noise, and that HI listeners with identical audiometric loss can vary widely in their degree of OHC dysfunction. To test these hypotheses, we inferred the proportion of the audiometric loss that is due to cochlear mechanical gain loss (HL_{OHC}), and investigated the correlation between HL_{OHC} and residual cochlear compression with the speech reception thresholds (SRTs) in noise. HL_{OHC} and residual compression were estimated from comparisons of cochlear input/output (I/O) curves for HI listeners with reference curves for normal-hearing listeners. I/O curves were inferred using a psychoacoustical technique known as the temporal masking curve (TMC) method. Therefore, for completeness, a third objective was to validate the assumptions of this method.

68 listeners with symmetrical sensorineural hearing losses participated in the study. For each of them, we measured air and bone conduction thresholds, temporal masking curves, and distortion product otoacoustic emissions at multiple test frequencies (0.5, 1, 2, 4 and 6 kHz). We also measured SRTs for speech-shaped noise and a (time-reversed) two-talker masker.

Results showed that (1) it is reasonable to use TMCs for inferring cochlear input/output curves in humans; (2) the large majority of HI listeners suffer from mixed inner hair cell and OHC dysfunction; (3) HL_{OHC} contributed between 30–40 and 60–70% to the total audiometric loss, and the contribution was approximately constant across the frequency range from 0.5 to 6 kHz; (4) the contribution of HL_{OHC} to audiometric loss varied largely across listeners, particularly at low frequencies or for mild-to-moderate hearing losses; (5) estimated OHC dysfunction is uncorrelated with SRT in steady-state noise; (6) residual cochlear compression, however, is correlated with SRT in speech-shaped steady noise but not in a (time-reversed) two-talker masker; (7) age *per se* reduces the intelligibility of speech in any of the two maskers tested here, regardless of absolute thresholds or cochlear mechanical dysfunction.

ABBREVIATIONS AND ACRONYMS

ANSI	American National Standards Institute
BM	Basilar Membrane
BMCE	Basilar Membrane Compression Exponent
CF	Characteristic Frequency
dB	Decibels
DPOAE	Distortion Product Otoacoustic Emissions
f_1, f_2	DPOAE primary frequencies
f_M	Masker Frequency
f_P	Probe Frequency
HI	Hearing Impaired
HINT	Hearing In Noise Test
HL	Hearing Level
HL_{IHC}	Amount of audiometric loss (in dB) due to IHC dysfunction
HL_{OHC}	Amount of audiometric loss (in dB) due to OHC dysfunction
I/O	Input/Output
IHC	Inner Hair Cell
L_1, L_2	Levels of the f_1 and f_2 primary tones
L_M	Masker Level
NH	Normal Hearing
OHC	Outer Hair Cell
PPT	Audiometric Pure-Tone Thresholds
R2TM	Time-reversed Two-talker Masker
RMS	Root Mean Square
SD	Standard Deviation

SII	Speech Intelligibility Index
SPL	Sound Pressure Level
SRT	Speech Reception Threshold
SSN	Speech-Shaped Noise
TFS	Temporal Fine Structure
TMC	Temporal Masking Curve

Index

1. Introduction 1

Speech Intelligibility in Noise for Listeners with Impaired Hearing 1

The Potential Importance of Cochlear Mechanical Dysfunction for Understanding Speech in Noise 2

Assessment of Cochlear Mechanical Dysfunction from Input/output Curves . 4

Inference of Cochlear Input/output Curves in Human 5

Hypotheses 7

Aims and Objectives 8

2. Material and Methods 9

Subjects 9

Ethics 10

Speech Reception Thresholds 10

TMC Stimuli and Procedure 12

TMC Fitting 14

Inference of Cochlear I/O Curves 14

Indicators of Cochlear Mechanical Dysfunction 15

DPOAE Measurements 16

Middle-Ear Muscle Reflex Measurements 17

Statistical Analyses 18

Stimuli and Apparatus 19

3. Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss 21

Introduction 21

Hearing Loss Distributions 22

Temporal Masking Curves 22

I/O Curves Inferred from TMCs 23

I/O Curve Analyses and Taxonomy 27
HL_{OHC} and HL_{IHC} Estimates from I/O Curves 31
From I/O curves with a compression threshold 31
From linear I/O curves 34
From compressive I/O curves without a compression threshold 35
Across Listener Variability of HL_{OHC} 36
Prevalence of IHC and OHC Dysfunction 37
Verification and Extension of Model Assumptions 39
4. Forward-Masking Recovery and the Assumptions of the Temporal Masking Curve Method of Inferring Cochlear Compression 41
Introduction 41
Approach 41
TMC Analysis 43
Distortion Product Otoacoustic Emissions 43
Temporal Masking Curves 44
Forward-Masking Recovery as a Function of Probe Frequency and TMC Intercept Level 46
Possible Frequency-Level Interactions on Forward-Masking Recovery 49
5. The Influence of Cochlear Mechanical Dysfunction on the Intelligibility of Audible Speech in Noise for Hearing-Impaired Listeners 53
Introduction 53
Speech Reception Thresholds 54
Pairwise Pearson Correlations 56
Potential Predictors of Speech-in-Noise Intelligibility 57
Stepwise MLR Models 58
6. Discussion 61
Behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss 61

Potential Methodological Sources of Bias 62
Comparison with Earlier Studies 67
On the validity of the TMC method for inferring cochlear input/output curves 68
Limitations of the Present Data 68
Relationship With Earlier Studies 71
Implications for Estimating Compression From TMCs 71
The influence of cochlear mechanical dysfunction on speech-in-noise intelligibility 73
7. Conclusions 77
8. References 79
Publications and conference communications resulting from this thesis 89
Peer-reviewed papers 89
Other papers 89
Conference communications 90
Appendix A. Reprints of published articles
Appendix B. Summary in Spanish

1. INTRODUCTION

A person who is not able to hear as well as someone with normal hearing is said to have hearing loss or is referred to as hearing impaired (HI). More technically, a person is said to have a hearing loss when his/her audiometric thresholds for pure tones, expressed in decibels hearing level (dB HL), and averaged over the frequencies of 0.5, 1, and 2 kHz, exceed 25 dB HL in the two ears. Disabling hearing loss refers to a hearing loss greater than 40 dB HL in the better hearing ear in adults and a hearing loss greater than 30 dB HL in the better hearing ear in children.

According to the World Health Organization (WHO, 2017), over 5% of the world's population – 360 million people – suffers from disabling hearing loss (328 million adults and 32 million children). Approximately one-third of people over 65 years of age is affected by disabling hearing loss.

A hearing loss may be mild (between 25 and 40 dB hearing loss, HL), moderate (40-70 dB HL), severe (70-95 dB HL), or profound (>95 dB HL) depending on the pure-tone average threshold (Goodman, 1965). It can affect one ear or both ears, and leads to difficulty in hearing conversational speech.

SPEECH INTELLIGIBILITY IN NOISE FOR LISTENERS WITH IMPAIRED HEARING

The ability to understand speech in noisy environments may be measured in different ways (reviewed by Schoepflin, 2012). One of them is to present lists of speech items (e.g., consonants, words, or sentences) at different signal-to-noise ratios (SNRs) and measure the percentage of items correctly identified by the

listener. Another reliable and sensitive measure of intelligibility is the speech reception threshold (SRT). The SRT can be defined as the SNR at which a listener can correctly identify 50% (or other specified percentage) of the speech material presented in quiet or noise (Nilsson, Solli and Sullivan, 1994). The later can consist of monosyllables, spondees, words, key words or sentences. When sentence material is used, the SRT for sentences is usually measured instead of word scoring. Other advantages of measuring SRTs instead of percent scores include the ease of administrating the test and its reliability, by effectively eliminating the need to calculate the number (or percentage) of words repeated correctly.

Listeners with impaired hearing show poorer word recognition scores and/or higher SRTs (in dB SNR) than listeners with normal hearing (NH), particularly in noisy backgrounds. For example, Peters, Moore, and Baer (1998) showed that the SRT for elderly listeners with moderate-to-severe cochlear hearing loss is between 2 to 19 dB higher than that of NH listeners in noise backgrounds, depending on the type of noise (see their Table I).

Hearing-impaired listeners, however, vary widely in their ability to understand speech in noise, even when the detrimental effect of their hearing loss on intelligibility is compensated for with amplification (hearing aids). While some listeners are able to recognize 100% of monosyllabic words in noise with or without their hearing aids, others, however, do not even reach 10% word recognition (e.g., see Figure 2 in Löhler et al., 2015).

The Potential Importance of Cochlear Mechanical Dysfunction for Understanding Speech in Noise

Several factors can affect the ability of HI listeners to understand audible speech in noise (reviewed by Lopez-Poveda, 2014). One of them is outer hair cell (OHC) dysfunction. OHC dysfunction would degrade the representation of the speech spectrum in the mechanical response of the cochlea, particularly in noisy environments, for various reasons. First, OHC dysfunction reduces cochlear frequency selectivity (Robles and Ruggero, 2001). This can smear the cochlear representation of the acoustic spectrum, making it harder for HI listeners to separately perceive the spectral cues of speech from those of

interfering sounds (Moore, 2007). Several behavioral studies have supported this idea (Baer and Moore, 1994; Festen and Plomp, 1983; ter Keurs, Festen, and Plomp, 1990).

Second, in the healthy cochlea, suppression might facilitate the encoding of speech in noise by enhancing the most salient spectral features of speech against those of the background noise (Deng, Geisler, and Greenberg, 1987; Young, 2008). OHC dysfunction reduces suppression and this might hinder speech-in-noise intelligibility.

Third, cochlear mechanical compression might facilitate the understanding of speech in interrupted or fluctuation noise by amplifying the speech in the low-level noise intervals, a phenomenon known as *listening in the dips* (e.g., Gregan, Nelson, and Oxenham, 2013; Rhebergen, Versfeld, and Dreschler, 2009). OHC dysfunction reduces compression (i.e., linearizes cochlear responses; Ruggero, Rich, Robles, and Recio, 1996) and thus could hinder *dip listening* (Gregan et al., 2013).

Fourth, medial olivocochlear efferents possibly facilitate the intelligibility of speech in noise by increasing the discriminability of transient sounds in noisy backgrounds (Brown, Ferry, and Meddis, 2010; Guinan, 2010; Kim, Frisina, and Frisina, 2006). Medial olivocochlear efferents exert their action via OHCs, and so OHC dysfunction could reduce the unmasking effects of medial olivocochlear efferents.

The degree of OHC dysfunction could be different across different HI listeners (e.g., Lopez-Poveda and Johannesen, 2012) and this might contribute to the wide variability in their ability to understand audible speech in noise. While seemingly reasonable, however, this view is almost certainly only partially correct. First, for HI listeners, there appears to be no significant correlation between residual cochlear compression and the benefit from dip listening (Gregan et al., 2013), which undermines the influence of compression on the intelligibility of suprathreshold speech in noise. Second, at high intensities, cochlear tuning for healthy cochleae is reduced and is only moderately sharper than that of impaired cochleae (Robles and Ruggero, 2001) and yet HI listeners still perform more poorly than do NH listeners in speech-in-noise intelligibility tests (reviewed in pp. 205-208 of Moore, 2007).

The main aim of the present thesis was to shed some light on the importance of OHC dysfunction on the ability of HI listeners to understand audible speech in steady-state and fluctuating noisy backgrounds (Chapter 5).

Assessment of Cochlear Mechanical Dysfunction from Input/output Curves

In the healthy cochlea, inner hair cells (IHCs) transduce mechanical basilar membrane (BM) vibrations into nerve signals, while OHCs amplify BM responses to low-level sounds and are thus responsible for our high auditory sensitivity (Bacon et al., 2004). A reduction in the number of OHCs or lesions to the OHCs or associated structures can reduce the cochlear gain to low level sounds and hence cause an audiometric loss. Similarly, a reduction in IHC count or lesions to the IHCs or their associated structures can increase the BM excitation required for detecting a signal, which may also cause an audiometric loss (Moore, 2007).

Although it is not generally possible to establish a one-to-one correspondence between audiometric loss and the degree of physical IHC/OHC loss or injury (Chen and Fechter, 2003; Lopez-Poveda and Johannesen, 2012), it is reasonable to assume that the audiometric loss of listeners with cochlear hearing loss may be due to combined loss or dysfunction of IHCs and OHCs. Indeed, some authors have assumed that the audiometric loss (HL_{TOTAL}) for a given test frequency may be conveniently expressed as the sum of two contributions: one associated with cochlear mechanical gain loss, or OHC dysfunction (HL_{OHC}), and one associated with inefficient IHC transduction, or IHC dysfunction (HL_{IHC}), where HL_{TOTAL}, HL_{IHC} and HL_{OHC} are all in decibels (dB) (Moore and Glasberg, 1997; Plack et al., 2004; Moore, 2007; Jepsen and Dau, 2011; Lopez-Poveda and Johannesen, 2012).

Cochlear mechanical dysfunction linearizes BM input/output (I/O) curves (Ruggero and Robles, 2001). Therefore, HL_{OHC} may be assessed by comparing BM I/O curves for a HI listener with reference I/O curves for listeners with normal hearing (NH). Plack et al. (2004) suggested that a cochlear mechanical I/O curve may be modeled by a function consisting of a linear segment (slope ~1 dB/dB) at low input levels, followed by a compressive segment at mid-level

inputs (slope < 1 dB/dB), eventually followed by another linear segment at high input levels. The breakpoint between the low-level linear segment and the compressive segment is referred to as the compression threshold (CT) and the breakpoint between the mid-level compressive segment and the high-level linear segment is referred to as the return-to-linearity threshold (RLT).

According to Plack et al. (2004), cochlear mechanical dysfunction shifts the low-level linear segment of the BM I/O curve to higher levels without changing the slope of the I/O curve over its compressive segment. Therefore, HL_{OHC} may be estimated as the horizontal shift (in decibels) between the low-level linear segment of the I/O curve for any given HI listener with respect to the corresponding segment of the mean reference I/O curves for NH listeners. HL_{IHC} may be estimated (in decibels) as the difference between HL_{TOTAL} and HL_{IHC} (Moore and Glasberg, 1997; Plack et al., 2004; Moore, 2007; Jepsen and Dau, 2011; Lopez-Poveda and Johannesen, 2012).

Theoretically, listeners with identical audiometric loss can suffer from different degrees of IHC and OHC dysfunction. One specific aim of the present thesis was to estimate the degree HL_{IHC} and HL_{OHC} for listeners with cochlear hearing loss using the approach of Lopez-Poveda and Johannesen (2012) (Chapter 3).

INFERENCE OF COCHLEAR INPUT/OUTPUT CURVES IN HUMAN

In humans, BM I/O curves cannot be measured directly and so a number of psychoacoustical methods have been developed to infer them (Lopez-Poveda and Alves-Pinto, 2008; Lopez-Poveda, Plack, and Meddis, 2003; Nelson, Schroder, and Wojtczak, 2001; Oxenham and Plack, 1997; Plack and Arifianto, 2010; Plack and O'Hanlon, 2003; Plack and Oxenham, 2000; Yasin, Drga, and Plack, 2013). A favored technique is known as the temporal masking curve (TMC) method.

The TMC method (Nelson et al., 2001) consists of measuring the level of a tonal forward masker required to just mask a fixed tonal probe as a function of the time interval between the masker and the probe. A TMC is a graphical representation of the resulting masker levels against the corresponding masker-probe intervals. Because the probe level is fixed, the masker level increases with increasing masker-probe time interval and hence TMCs have

positive slopes. Nelson et al. (2001) argued that the slope of any given TMC depends simultaneously on the amount of BM compression affecting the masker at a cochlear place whose characteristic frequency (CF) equals approximately the probe frequency and on the rate of recovery from the internal (post-mechanical or 'compression free') masker effect. By assuming that the post-mechanical recovery rate is the same across masker frequencies, BM I/O functions may be estimated by plotting the masker levels of a reference TMC (i.e., the TMC for a masker that is processed linearly by the cochlea) against the levels for any other masker frequency, paired according to masker-probe delays (Nelson et al., 2001).

The TMC method is based on two assumptions. Namely, (1) for a given probe frequency, it is independent of masker frequency; and (2) it is independent of probe frequency. These assumptions are controversial. Wojtczak and Oxenham (2009) questioned the first assumption by showing that the rate of post-mechanical recovery is actually faster when the masker and probe frequencies are equal (on-frequency condition) than when the masker frequency is about an octave below the probe frequency (reference condition). Given that masker levels are typically higher for the reference than for the on-frequency TMC, an alternative explanation for their findings is that forward-masking recovery is actually dependent upon masker level rather than masker frequency. Indeed, a third, less explicit assumption of the TMC method is that forward-masking recovery is independent of masker level. Wojtczak and Oxenham concluded that for normal-hearing listeners, the first assumption of the TMC method held for masker levels below 83 dB SPL but not for higher levels.

Stainsby and Moore (2006) questioned the second assumption of the TMC method. They showed that for HI listeners with nearly absent distortion product otoacoustic emissions (DPOAEs), and hence presumably linear cochlear responses, TMCs are steeper for low than for high probe frequencies. On the other hand, other authors have provided experimental support for the second assumption using other psychoacoustical methods that do not require a reference TMC (Lopez-Poveda and Alves-Pinto, 2008; Plack et al., 2008). In an attempt to reconcile these seemingly disparate findings, Lopez-Poveda and Alves-Pinto (2008) argued that "absence of measurable DPOAEs at low frequencies is not necessarily indicative of linear cochlear responses because it is hard to measure DPOAEs at low frequencies due to physiological and

ambient noise" (p. 1553). In other words, Lopez-Poveda and Alves-Pinto were suggesting that the absence of DPOAEs in the subjects used by Stainsby and Moore could be more apparent than real due to their using insufficiently sensitive DPOAE techniques. Indeed, Stainsby and Moore used primary tones with a single level of 70 dB SPL each even though DPOAEs depend strongly on the levels of the primary tones, particularly at low frequencies. Therefore, it is conceivable that DPOAEs may have appeared as *absent* to Stainsby and Moore but might have been present if they had used different primary levels.

In addition, Stainsby and Moore used a fixed measurement time of 2 sec. across test frequencies even though DPOAE detectability increases with increasing measurement time (on average, the DPOAE signal-to-noise ratio improves by 3 dB for every doubling of the measurement time). The use of short recording times can hinder DPOAE detectability more at low frequencies where the physiological noise is comparatively higher. Therefore, it is conceivable that DPOAEs may have appeared as absent to Stainsby and Moore but might have been present if they had used longer recording times. An additional concern about the study of Stainsby and Moore is that they used only three subjects.

Another specific aim of the present thesis is to verify the assumptions of the TMC method using an approach similar to that of Stainsby and Moore but overcoming their methodological limitations (Chapter 4).

HYPOTHESES

The present thesis is aimed at exploring three hypotheses:

1. Listeners with cochlear (sensorineural) hearing loss and with comparable audiometric thresholds may show different degrees of cochlear mechanical dysfunction.
2. The assumptions of the psychoacoustical TMC method for inferring human cochlear I/O curves are reasonable.
3. The intelligibility of hearing impaired people in noisy environments is positively correlated with their degree of mechanical cochlear dysfunction.

AIMS AND OBJECTIVES

The overall aim is to assess the importance of cochlear mechanical dysfunction for understanding audible speech in noisy environments for HI listeners.

To achieve this general aim, three specific objectives were established:

1. To infer the degree of cochlear mechanical dysfunction in a large group of people with sensorineural hearing loss from comparisons of psychoacoustically inferred cochlear I/O curves with corresponding curves for NH references. Specifically, to measure the contribution of HL_{OHC} and HL_{IHC} to the hearing loss of these people. A secondary, related aim was to investigate the distribution HL_{OHC} and HL_{IHC} across the 500-8000 Hz frequency range. A third related aim was to investigate the variability of HL_{OHC} and HL_{IHC} across listeners.
2. To validate the assumptions of the TMC method for inferring human cochlear I/O curves. In particular, to test the assumption that the post-mechanical rate of recovery from forward masking is independent of the frequency of the probe tone as well as the level of the masker.
3. To investigate the correlation between the degree of cochlear mechanical dysfunction and the intelligibility of speech in noise for HI listeners.

2. Material and Methods

Subjects

68 listeners (43 males) with symmetrical sensorineural hearing losses participated in the study. Their ages ranged from 25 to 82 years, with a median of 61 years. Air conduction absolute thresholds were measured using a clinical audiometer (Interacoustics AD229e) at the audiometric frequencies of 0.125, 0.25, 0.5, 1, 2, 3, 4, 5, and 8 kHz (ANSI, 1996). Bone conduction thresholds were measured at 0.5, 1, 2, 3, and 4 kHz. Air and bone conduction thresholds were also measured at 0.75 and 1.5 kHz for a large subset of subjects. A hearing loss was regarded as sensorineural when tympanometry was normal and air-bone gaps were smaller than or equal to 15 dB at one frequency.

The studies reported in this thesis were part of a larger hearing-aid study and hence all participants were required to be hearing-aid users or candidates and to have symmetrical bilateral loss. A hearing loss was regarded as symmetrical when the mean air conduction threshold at 0.5, 1, and 2 kHz differed by less than 15 dB between the two ears, and the mean difference at 3, 4, and 6 kHz was less than 30 dB (AAO-HNS, 1993). For the current purpose, each participant was tested in one ear. The ear was selected to maximize the number of test frequencies for wich TMCs could be obtained. For the majority of cases, this meant selecting the ear with better thresholds in the 2-6 kHz frequency range (30 left ears, 38 right ears). **Figure 1** illustrates the distribution of hearing losses.

Speech-in-noise intelligibility was assessed in bilateral listening conditions. Indicators of cochlear mechanical dysfunction, however, was measured for one ear only (typically, the ear with the better audiometric thresholds).

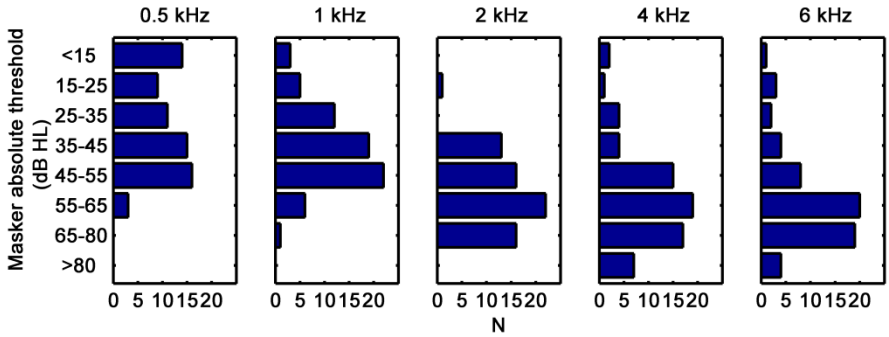

Figure 1. Distribution of absolute thresholds (in dB HL) for the 210-ms maskers used to measure the TMCs. These data give an idea of the distribution of hearing losses for the participants. Each panel is for a different test frequency, as indicated at the top.

ETHICS

All procedures were approved by the Ethics Committee of the University of Salamanca. Participans gave their signed informed consent prior to their inclusion in the study.

SPEECH RECEPTION THRESHOLDS

Speech reception thresholds were measured using the hearing-in-noise test (HINT; Nilsson et al., 1994). Sentences uttered by a male speaker were presented to the listener in the presence of a masker sound. The sentences were those in the Castilian Spanish version of the HINT (Huarte, 2008). Two different maskers were used. One masker consisted of a steady Gaussian noise filtered in frequency to have the long-term average spectrum of speech (Table 2 in Byrne et al., 1994). This masker will be referred to as speech-shaped noise (SSN) and the corresponding SRT as SRT_{SSN}. The second masker consisted of two simultaneous talkers (one male and one female) played in reverse. This masker will be referred to as time-reversed two-talker masker (R2TM) and the corresponding SRT as SRT_{R2TM}.

To generate the R2TM, the Spanish HINT sentences were uttered in a sound booth by a male and a female native Castilian-Spanish speaker and recorded with a Brüel & Kjaer type 4192 microphone with its amplifier (Brüel & Kjaer Nexus) connected to an RME Fireface 400 sound card. The recorded sentences were segmented and pauses between sentences removed. For each speaker, the sentences were equalized in root-mean-square (RMS) amplitude, time reversed, and concatenated. Finally, the concatenated sentences of the male and the female speaker were mixed digitally. A different segment (chosen at random) of the resulting R2TM was used to mask each HINT sentence during an SRT measurement. We note that the long-term spectra of the R2TM, the SSN, and the target speech could have been slightly different because the speakers used to generate the R2TM and the target sentences were different, and the filter used to produce the SSN, though speech shaped, was not based on the long-term spectrum of the specific target sentences.

To measure an SRT, the speech was fixed in level at 65 dB SPL and the masker level was varied adaptively using a one-up, one-down rule to find the SNR (in dB) at which the listener correctly identified 50% of the sentences (i.e., to find the SRT in dB SNR units). After setting the levels of the speech and the masker, the two sounds were mixed digitally and filtered to simulate a free-field listening condition where the speech and the masker were collocated 1 m away in front of the listener at eye level (i.e., 0° azimuth and 0° elevation) and had a spectrum according to Table 3 in the standard for calculation of the speech intelligibility index (ANSI, 1997). The filtering included corrections for the frequency response of the headphones. The resulting stimulus was linearly amplified individually for each participant according to the National Acoustics Laboratory Revised (NAL-R) rule (Byrne and Dillon, 1986) and played diotically to the listeners. The masker started 500 ms before and ended 250 ms after the target sentence. Twenty sentences were played to the listeners for each SRT measurement. In the adaptive procedure, the masker level was varied with a step size of 4 dB for the first five sentences and of 2 dB for the last 15 sentences. The SRT was calculated as the mean SNR used for the last 15 sentences. For each masker, three SRT estimates were obtained and the mean was taken as the final result. All other details of the procedure were as for the original HINT test (Nilsson et al., 1994). Feedback on the correctness of the listener's response was not provided.

TMC Stimuli and Procedure

Temporal masking curves were measured using stimuli and procedures similar to those used by Lopez-Poveda and Johannesen (2012). On-frequency TMCs were measured for probe frequencies (f_P) of 0.5, 1, 2, 4, and 6 kHz. Maskers and probes were sinusoids. The duration of the maskers was 210 ms including 5-ms cosine-squared onset and offset ramps. Probes had durations of 10 ms, including 5-ms cosine-squared onset and offset ramps with no steady state portion, except for the 500-Hz probe, whose duration was 30 ms with 15-ms ramps and no steady state portion. The level of the probes was fixed at 10 dB above the individual absolute threshold for the probe. Masker-probe time gaps, defined as the period from masker offset to probe onset, ranged from 5 to 100 ms in 10-ms steps with an additional gap of 2 ms. Masker levels sometimes reached the maximum permitted sound level output (105 dB SPL) after a few time gaps. If the number of measured data points was insufficient for curve fitting (see below), masker levels were measured for additional intermediate gaps (e.g., 5, 15, 25 ms). In a few cases, masker levels were atypically low for a time gap of 100 ms. In these cases, masker levels were measured for additional gaps in the range 110–140 ms.

A single 'linear reference' TMC was measured for each listener and it was used to infer I/O curves for all other probe frequencies (Lopez-Poveda et al., 2003). The linear reference TMC was for a probe frequency of 2, 4, or 6 kHz and for a masker frequency equal to $0.4f_p$ or $0.5f_p$. The selection of linear reference condition depended on the listener's hearing loss at the linear-reference probe frequency and on the maximum permitted sound level output (105 dB SPL). Following the indications of earlier studies, (Lopez-Poveda et al., 2003; Lopez-Poveda and Alves-Pinto, 2008), the linear reference conditions were sought in the order of priority shown in **Table 1**.

Table 1. Prioritized linear-reference TMC conditions and number of cases (N) where each condition applied (see also red curves in Figure 2). Note that these numbers add up to 63 rather than to the total number of participants (N=68). This is because a linear reference TMC could not be measured for four participants, and the data from one additional participant who performed inconsistently during the task were excluded from the analysis.

Priority order	①	②	③	④	⑤	⑥
Probe (kHz)	4	4	6	6	2	2
Masker (kHz)	1.6	2	2.4	3	0.8	1
N	34	6	4	4	9	6

Masker levels at threshold were measured using a two-interval, two-alternative, forced-choice adaptive procedure with feedback. The inter-stimulus interval was 500 ms. The initial masker level was set sufficiently low that the listener always could hear both the masker and the probe. Masker level was then changed according to a two-up, one-down adaptive procedure to estimate the 71% point on the psychometric function (Levitt, 1971). An initial step size of 6 dB was applied, which was decreased to 2 dB after three reversals in masker level. The adaptive procedure continued until a total of 12 reversals in masker level were measured. Threshold was calculated as the mean masker level at the last 10 reversals. A measurement was discarded if the standard deviation of the last 10 reversals exceeded 6 dB. Three threshold estimates were obtained in this way and their mean was taken as the threshold. If the standard deviation of these three measurements exceeded 6 dB, one or more additional threshold estimates were obtained and included in the mean. Measurements were made in a double-wall sound attenuating booth. Listeners were given at least 2 hours of training on the TMC task before data collection began.

Absolute thresholds for the probes and maskers were measured using a similar three-alternative, forced-choice procedure except that the adaptive procedure was one-up, two-down.

TMC and absolute threshold measurements took between 12 and 15 hours per participant in total and were distributed in several (1- or 2-hour) sessions on several days.

TMC Fitting

Linear-reference and on-frequency TMCs were fitted before they were used to infer I/O curves. Linear reference TMCs were fitted with a double exponential function with four parameters (Lopez-Poveda and Johannesen, 2012); on-frequency TMCs were fitted with a function consisting of the double exponential function fitted to the linear reference TMC plus a second-order Boltzmann function with six parameters (Lopez-Poveda and Johannesen, 2012). When fitting the on-frequency TMC, the parameters of the double exponential function were held fixed and only the parameters of the second-order Boltzmann function were allowed to vary. When the number of data points in a TMC was equal or fewer than the number of parameters of the double exponential or the second-order Boltzmann function, single exponential (two parameters) and first-order (four parameters) Boltzmann functions were used instead. A full justification of this approach can be found elsewhere (Lopez-Poveda and Johannesen, 2012).

The goodness-of-fit was assessed using the RMS error between measured and fitted TMCs. RMS errors were less than 2 dB for all linear reference TMCs, and less than 4 dB for on-frequency TMCs, except for three cases for which RMS errors were less than 6 dB.

Inference of Cochlear I/O Curves

Cochlear I/O curves were inferred for each participant by plotting the fitted masker levels of his/her linear reference TMC against the masker levels for the on-frequency TMCs paired according to time gaps (Nelson et al., 2001). For any given participant, a common linear reference condition was used to infer I/O curves at all test frequencies (Lopez-Poveda et al., 2003). A linear reference TMC could not be found for four participants because their hearing loss was too high at the linear-reference probe frequencies (**Table 1**). In these four cases, an average linear reference (mean across all other participants for the condition f_P = 4 kHz and f_m = 1.6 kHz) was used to infer I/O curves.

INDICATORS OF COCHLEAR MECHANICAL DYSFUNCTION

The cochlear I/O curves for HI listener at each of five test frequencies (0.5, 1, 2, 4, and 6 kHz) were compared with corresponding reference I/O curves for NH listeners taken from previous studies published by our group (Lopez-Poveda and Johannesen, 2012). From the comparison, we inferred three indicators of cochlear mechanical dysfunction:

1. Cochlear mechanical gain loss (HL_{OHC}).
2. Inner hair cell loss (HL_{IHC}).
3. Basilar-membrane compression exponent (BMCE).

These variables were calculated as follows.

After Moore and Glasberg (1997), we assumed that the total audiometric loss may be split into two contributions: one pertaining to a reduction of mechanical cochlear gain due to OHC dysfunction and a remaining component, which, for convenience, will be assumed due to inefficient inner hair cell (IHC) processes, or IHC dysfunction.

$$HL_{TOTAL} = HL_{OHC} + HL_{IHC}, \quad (1)$$

where HL_{TOTAL}, HL_{OHC}, and HL_{IHC} are all in decibels. In what follows, HL_{OHC} and HL_{IHC} will be referred to as "OHC loss" and "IHC loss," respectively, and should be interpreted as contribution to audiometric loss (in dB) rather than as anatomical lesions or reduced cell counts.

After Lopez-Poveda and Johannesen (2012), HL_{OHC} was estimated by comparing the CT of the I/O curve for a given hearing-impaired (HI) listener with a reference CT for normal hearing (NH) listeners, corrected for compression. HL_{IHC} was estimated using Equation (1) as the difference between HL_{OHC} and HL_{TOTAL}. Some I/O curves were linear and a CT was not present. We assumed that those cases were indicative of total OHC dysfunction and HL_{OHC} was assumed to be equal to the NH gain.

IHC dysfunction was assumed to increase the BM excitation needed for signal detection at threshold. When estimating the I/O curve with a psychophysical approach, only the part of the I/O curve that is above the cochlear mechanical

excitation required for detection can be measured. For a large increase in BM excitation, a CT may be absent and only a part of the compressive portion of the I/O curve is available. Therefore, the absence of a CT with presence of a compressive segment in the I/O curve was assumed as indicative of substantial HL_{IHC}. For these cases, it is assumed that Equation (1) does not hold and that $HL_{TOTAL} \sim HL_{IHC}$. In other words, it was assumed that even though HL_{OHC} may occur, it does not contribute to the audiometric hearing loss.

The BMCE was calculated as the mean slope (in dB/dB) of the I/O curve over the segment between the CT and the RTL threshold.

DPOAE Measurements

Pairs of primary pure tones with frequencies (f_1, f_2) and corresponding levels (L_1, L_2) were presented, and the level of the $2f_1-f_2$ frequency component of the otoacoustic emission in the ear canal was recorded and regarded as the DPOAE level. DPOAEs were measured for f_2 of 0.5, 1, 2, and 4 kHz and for L_2 values from 35 to 70 dB SPL, in 5-dB steps (4 test frequencies × 8 levels = 32 conditions). For each test frequency f_2, f_1 was set equal to $f_2/1.2$. An attempt was made to individually set L_1 so as to maximize DPOAE levels. For L_2 values of 50 and 65 dB SPL, we empirically sought the L_1 value that maximized the DPOAE level, if any. When a pair of L_1 values was found, then the values of L_1 for the other L_2 levels were obtained using linear regression. When individually optimal L_1 values were not found, we used the primary level rule of Neely, Johnson, and Gorga (2005) because it has been independently confirmed that this is the most appropriate rule to maximize DPOAE levels on average (cf. Figure 7 in Lopez-Poveda and Johannesen, 2009).

DPOAE measurements were obtained using an Intelligent Hearing System's Smart device (with SmartOAE software version 4.52) equipped with an Etymotic ER-10D probe. During the measurements, participants sat comfortably in a double-wall sound attenuating chamber and were asked to remain as steady as possible. The probe fit was checked before and after each recording session. The probe remained in the participant's ear throughout the whole measurement session to avoid measurement variance from probe fit. DPOAEs were measured for a preset measurement time of 30 s for f_2 = 500 Hz

and 10 s for other f_2 frequencies. A DPOAE measurement was regarded as valid when it was 6 dB above the measurement noise floor (defined as the mean level over 10 frequency bins adjacent to the $2f_1-f_2$ component in the OAE spectrum). When a response did not meet this criterion, the measurement was repeated. If the required criterion was not met for at least two of three successive tries, we concluded that DPOAEs were absent for that condition.

DPOAE measurements were regarded as valid only when they were 6 dB above the system's artifact response. The rationale behind this rather strict criterion and the details of the procedure for controlling for system's artifacts and calibration can be found elsewhere (Johannesen and Lopez-Poveda, 2008).

Middle-Ear Muscle Reflex Measurements

As a control, the threshold of activation of the middle-ear muscle reflex (MEMR) was measured using a clinical middle-ear analyzer (Interacoustics AT235h). Middle-ear compliance for a probe tone of 226 Hz and 85 dB SPL was measured in the presence and in the absence of ipsilateral MEMR elicitor tones with frequencies 500, 1000, 2000, and 4000 Hz and levels 75 to 100 dB HL in 5-dB steps. The MEMR activation threshold was regarded as the lowest elicitor level that evoked a detectable change in middle-ear compliance (re the non-elicitor condition) minus 2.5 dB, that is, minus half the elicitor intensity step. Measured MEMR activation thresholds are shown in **Table 2**.

Table 2. Data for the subjects used in the study reported in Chapter 4. Age is in years. Also shown is (1) the linear reference TMC condition measured for each listener, expressed as a pair of probe and masker frequencies (f_P, f_M) in kHz; and (2) the threshold of activation of the middle-ear muscle reflex (MEMR) for different eliciting frequencies. n.p.: MEMR not present; ?: MEMR could not be measured reliably.

				Reference TMC	MEMR activation threshold (dB SPL)			
Participant	**Sex**	**Age**	**Ear**	**(f_P, f_M)**	**500**	**1000**	**2000**	**4000**
S012	M	80	Left	4, 1.6	n.p.	n.p.	n.p.	n.p.
S026	F	51	Left	4, 1.6	96	95	?	?
S054	M	79	Left	2, 0.8	106	?	n.p.	n.p.
S116	M	53	Right	6, 2.4	n.p.	105	106.5	n.p.
S121	M	60	Left	6, 2.4	96	95	106.5	n.p.
S142	M	51	Right	4, 2.0	101	95	96.5	104.5
S182	F	55	Right	4, 1.6	101	90	101.5	99.5
S199	F	73	Left	4, 2.0	?	?	?	?

STATISTICAL ANALYSES

Audiometric pure-tone thresholds (PTT, in dB HL), HL_{OHC}, HL_{IHC}, BMCE and age were used as potential predictors (independent variables) of the aided SRT_{SSN} and SRT_{R2TM} (dependent variables). Pairwise Pearson correlations were first calculated between each of the four independent variables and each of the two dependent variables. Statistically significant correlations were regarded as indicative that the independent variable could be a potential predictor of the dependent variable. This type of analysis, however, does not reveal the relative importance of the identified predictors for predicting the variance in the dependent variable. Indeed, sometimes several potential predictors might reflect a common underlying factor, a phenomenon known as co-linearity. In such cases, often only one of the co-linear predictors is sufficient to explain the variance in the dependent variable. To better assess the relative importance of potential predictors while minimizing the impact of co-linearity, we conducted a stepwise multiple linear regression (MLR) analysis.

In a MLR model, it is assumed that the dependent variable may be expressed as a linear combination of independent variables. If the MLR model is constructed in a stepwise fashion (i.e., by gradually adding new potential predictors to the model in each step), the final model omits co-linear variables and, most importantly, provides information about the relative importance of the various predictors. Here, we used MLR models to predict the SRT_{SSN} and SRT_{R2TM} independently. As is common practice, the variance explained by the models was adjusted for the number of predictors used in the model (i.e., the explained variance was reduced more as more predictors were included in the model; Theil and Goldberger, 1961).

PTT, HL_{OHC}, HL_{IHC}, and BMCE were available for each of the five test frequencies. Because both the correlation and MLR analyses required that the independent variables be single valued, these multi-valued variables were combined into a single value by weighting the value at each test frequency according to the importance of that frequency for speech recognition as specified in the calculation of the speech-intelligibility index (SII) (ANSI, 1997) and summing the SII-weighted values across all frequencies. The weights were 0.18, 0.25, 0.28, 0.23, and 0.06 for the test frequencies 0.5, 1, 2, 4, and 6 kHz, respectively (from Tables 3 and 4 of ANSI, 1997).

Stimuli and Apparatus

For all psychoacoustical measurements, stimuli were digitally generated (TMC measurements) or stored as digital files (SRT measurements) with a sampling rate of 44100 Hz. They were digital-to-analog converted using an RME Fireface 400 sound card with a 24-bit resolution and were played through Sennheiser HD-580 headphones. Subjects sat in a double-wall sound-attenuating booth during data collection.

Sound pressure levels (SPL) were calibrated by placing the headphones on a KEMAR equipped with a Zwislocki DB-100 artificial ear connected to a sound level meter (Bruel & Kjaer, type 2238). Calibration was performed at 1 kHz only and the obtained sensitivity was used at all other frequencies.

3. ACROSS-FREQUENCY BEHAVIORAL ESTIMATES OF THE CONTRIBUTION OF INNER AND OUTER HAIR CELL DYSFUNCTION TO INDIVIDUALIZED AUDIOMETRIC LOSS[1]

INTRODUCTION

In this chapter, we present estimates of HL_{IHC} and HL_{OHC} for test frequencies of 0.5, 1, 2, 4, and 6 kHz. We also analyze how HL_{IHC} and HL_{OHC} vary across test frequencies to examine potential structure-function correlations; that is, to examine the potential correspondence between HL_{OHC} and HL_{IHC} with existing evidence regarding physical loss or injury and/or dysfunction of OHCs and IHCs and their distribution across frequency. Lastly, we investigate the degree of variability of HL_{OHC} and HL_{IHC} across listeners.

We used virtually the same approach as in a related study conducted by our group (Lopez-Poveda and Johannesen, 2012). The data from that study was included in the present analysis. This included reference data for 15 NH listeners and data for 18 HI listeners with mild-to-moderate sensorineural hearing loss. Results for these groups will be clearly identified below.

[1] A modified version of this chapter was published as: Johannesen PT, Pérez-González P, Lopez-Poveda EA. (2014). Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Front Neurosci*. 8:214.

HEARING LOSS DISTRIBUTIONS

Absolute thresholds for the TMC maskers were used to assess hearing losses. Masker duration was shorter for the present participants (210 ms) than for the NH reference group or the HI listeners used in our previous study (300 ms in Lopez-Poveda and Johannesen, 2012). Because absolute threshold depends on signal duration, this difference in masker duration could have introduced a small difference in threshold for the participants in each study. Given that HL_{TOTAL} was defined as the difference between masker thresholds of the HI and NH listeners, an attempt was made to correct the present masker thresholds for the influence of duration on absolute thresholds. The correction consisted of adding the difference between NH absolute thresholds for pure tone durations of 300 and 200 ms to the masker thresholds of the present HI subjects (Watson and Gengel, 1969). Corrections were smaller than 1 dB at all frequencies. **Figure 1** shows the corrected absolute thresholds for the present participants; thresholds for the HI participants from our previous study are omitted in **Figure 1** but can be found in the original publication. Clearly, on average, participants had high-frequency losses typical of presbycusis but the range of hearing losses at each frequency was quite variable.

TEMPORAL MASKING CURVES

Figure 2 shows fitted linear-reference and on-frequency TMCs for 67 participants; one participant performed inconsistently during the TMC task and her data were excluded from further analysis. Measured TMCs are omitted in **Figure 2** to avoid clutter. Each column is for a different test frequency as indicated by column title, and each row is for a hearing-loss range as indicated by the text on the right-most ordinate.

Both linear-reference (red curves) and on-frequency TMCs (black curves) had characteristics similar in most aspects to those published in earlier reports (Nelson et al., 2001; Plack et al., 2004; Lopez-Poveda et al., 2005; Jepsen and Dau, 2011; Lopez-Poveda and Johannesen, 2012). The on-frequency masker levels for the shortest time gap (2 ms) decreased with decreasing frequency and on-frequency and linear-reference TMCs were less parallel (i.e., on-frequency TMCs were steeper than linear-reference TMCs) at lower than at

higher frequencies. Both these aspects are consistent with listeners having less hearing loss (**Figure 1**) and presumably less cochlear mechanical gain loss and more compression at low than at high frequencies.

Lopez-Poveda and Alves-Pinto (2008) argued that an ideal linear-reference TMC for inferring I/O curves would be for f_p = 4 kHz and f_m = 1.6 kHz on the grounds that the slope of such a TMC would be unlikely affected by cochlear compression and would reflect only the post-mechanical rate of recovery from forward masking. As explained above, the hearing loss of some listeners was so large at 4 kHz that it was not possible to measure this preferred linear-reference TMC and alternative linear references were measured instead (**Table 1**). Before using these linear references to infer I/O curves, we verified that their slopes were statistically comparable to the slopes of the preferred linear reference. To do it, we calculated the mean slope of all measured linear reference TMCs across all available time gaps (red curves in **Figure 2**), and compared the mean slope of the preferred linear reference condition (denoted as priority ① in **Table 1**) with the mean slope for every other condition (denoted as priority orders ② to ⑥ in **Table 1**) using a Student's *t*-test. The tests confirmed that all linear references had statistically equivalent slopes (p > 0.05). The difference for conditions ① and ⑤ was close to being significant (p = 0.055) but did not reach significance. Therefore, we concluded that all linear-reference TMCs had statistically comparable slopes and that it was reasonable to use them to infer I/O curves.

I/O CURVES INFERRED FROM TMCS

Figure 3 shows the I/O curves inferred from the TMCs of **Figure 2**. Dotted lines depict linearity with no gain (input level = output level). The large majority of I/O curves had shapes typical of HI subjects: they often had a linear segment at low input levels followed by a compressive segment at mid input levels, followed sometimes by another linear segment at high input levels. Other I/O curves were best described by an almost straight line with either a compressive slope or with a slope close to linearity. Few I/O curves showed unusual characteristics. For example, their RLTs were surprisingly low (50–70 dB SPL), particularly at low frequencies. Also, some I/O curves were almost flat (e.g., at 1 kHz for hearing loss below 15 dB HL). The latter occurs because their

corresponding linear reference TMCs were very shallow. Overall, I/O curves extended to lower input levels at low than at high frequencies, a reasonable result considering that on average participants had greater hearing losses for high than for low frequencies (**Figure 1**).

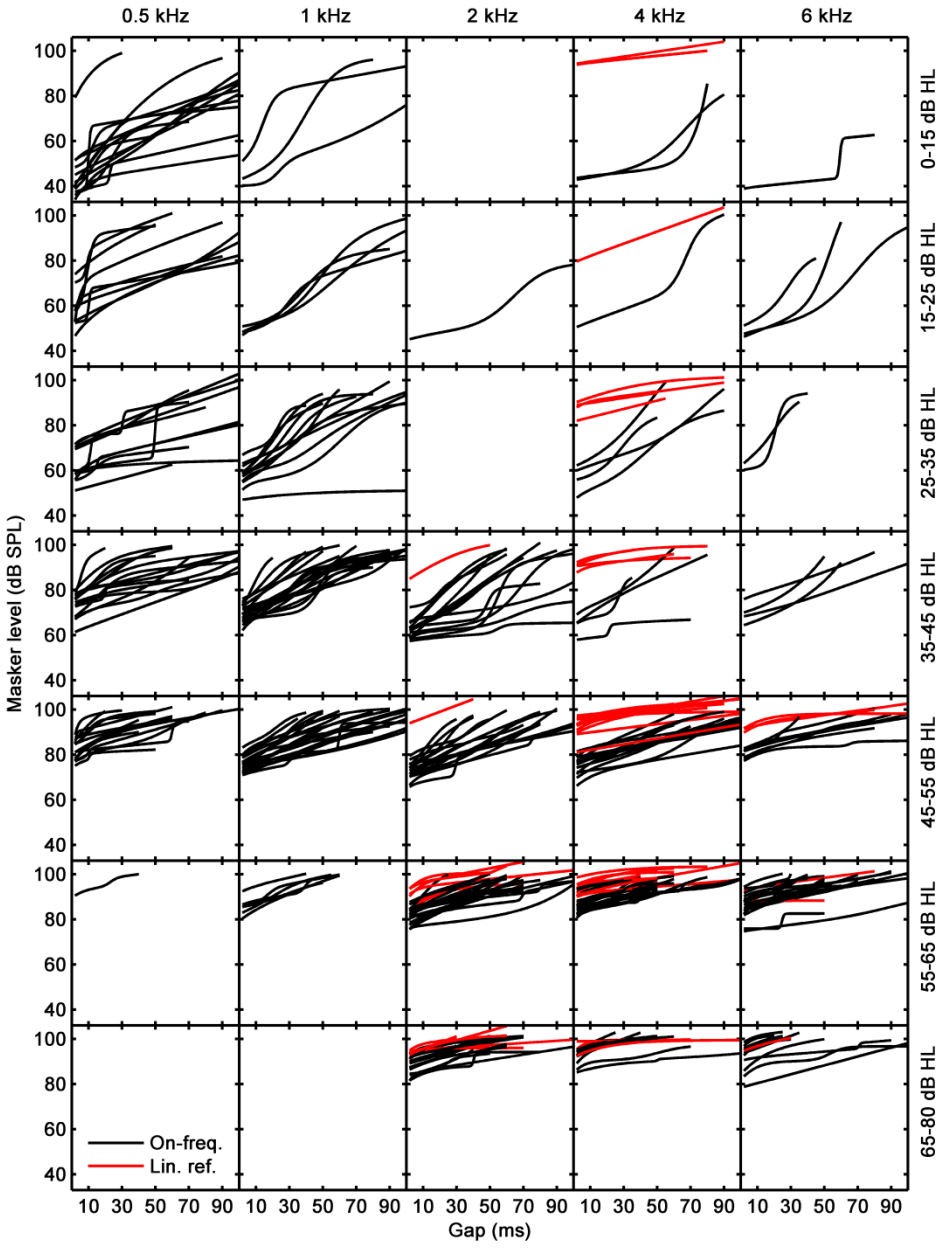

Figure 2. Fitted linear-reference (red curves) and on-frequency TMCs (black curves). Each column corresponds to a different test frequency as indicated by the column title and each row to a different hearing-loss range, as indicated by the text on the right-most ordinate.

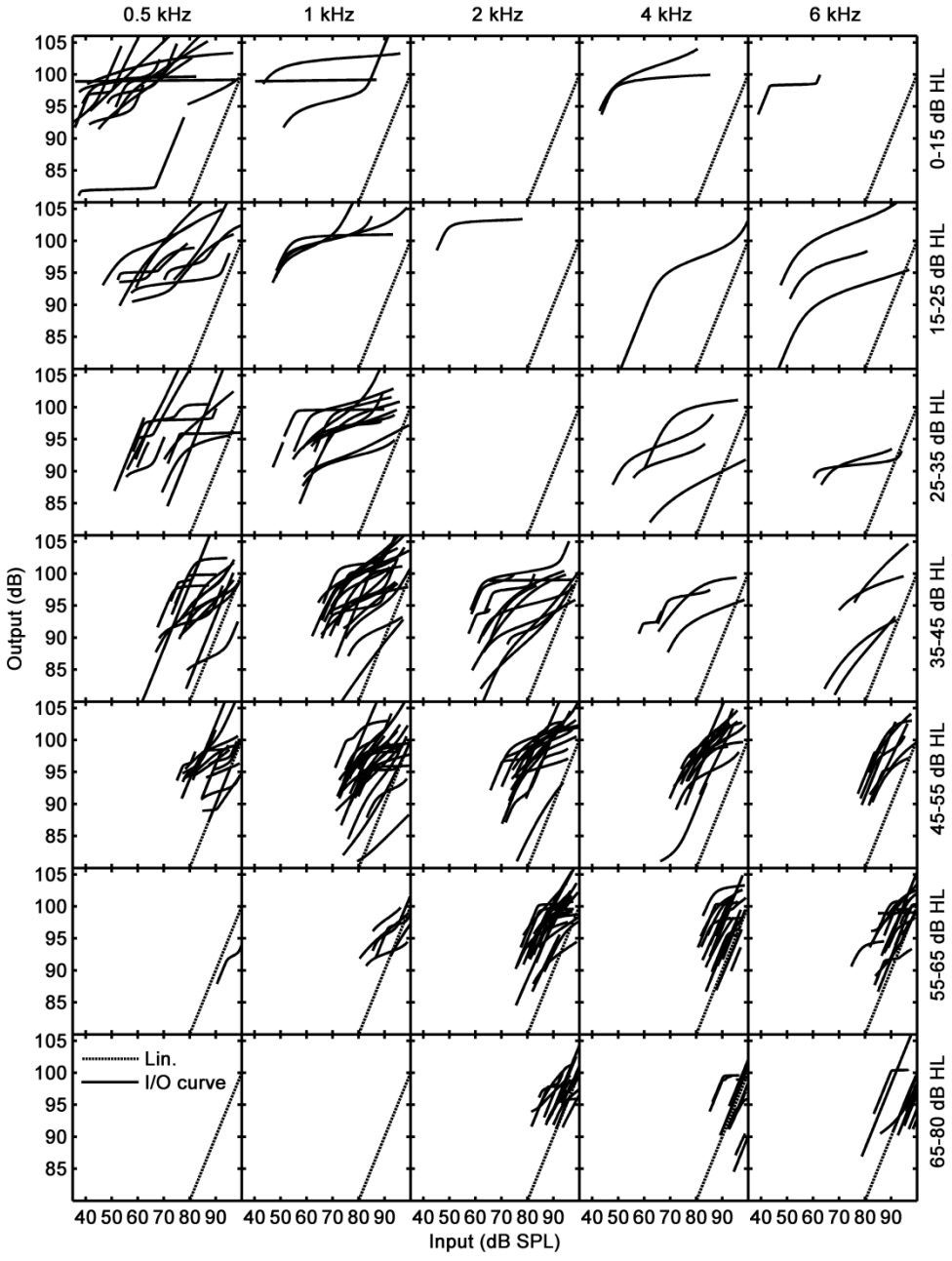

Figure 3. Inferred I/O curves. Columns and rows are as in Figure 2.

I/O CURVE ANALYSES AND TAXONOMY

Lopez-Poveda and Johannesen (2012) argued that HL_{OHC} and HL_{IHC} may be reliably obtained from an I/O curve only if the I/O curve in question shows a CT. They nonetheless hinted that the shape of the I/O curves may be indicative of the type and extent of HL_{OHC} or HL_{IHC}. Here, each I/O curve was analyzed in search for HL_{OHC} and HL_{IHC} using their reasoning and following the logic outlined in **Figure 4**.

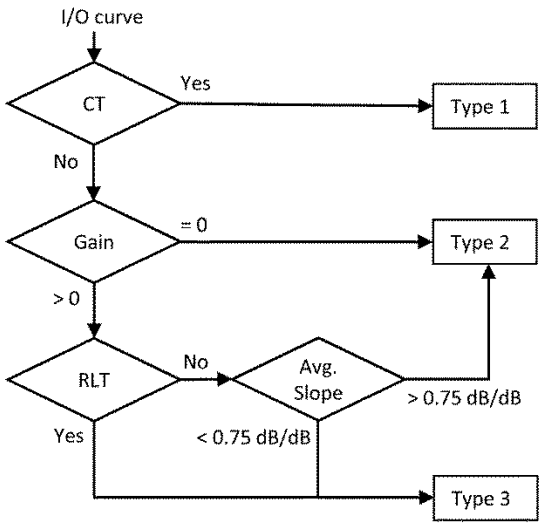

Figure 4. Flow diagram and logic used to classify each I/O curve into one of three categories: Type 1 = I/O curve with a compression threshold (CT); Type 2 = Linear I/O curve; Type 3 = I/O curve with residual compression but no compression threshold. RLT: return-to-linearity threshold.

A CT was first sought for each I/O curve. Lopez-Poveda and Johannesen (2012) arbitrarily defined the CT as the input level where the I/O curve reached a slope of 0.5 dB/dB from a higher value at lower input levels (**Figure 5B**). To take into account the experimental TMC variability on the CT estimate, rather than inferring the CT from the mean I/O curve, they simulated 100 I/O curves for each condition using a Monte-Carlo approach and used the median CT of those simulations in their subsequent analysis. They regarded the obtained CT as unreliable when it was the lowest input level in the mean I/O curve or if the mean I/O curve slope did not reach the criterion value of 0.5 dB/dB, something

infrequent in their data (see Lopez-Poveda and Johannesen, 2012). Here, we first tried to apply their same criteria but found many instances where the resulting CTs were unreliable. To maximize the number of I/O curves with valid CTs, we opted to apply slightly different criteria: (1) that 60% of the Monte-Carlo simulated I/O curves showed a valid CT; *and* (2) that the residual cochlear gain of the mean I/O curve (estimated as described below) was greater than zero. The median CT of the Monte-Carlo simulated I/O curves was taken as the final CT.

A large proportion of I/O curves showed a CT (**Table 3**). Many other I/O curves, however, were best described as straight lines with varying slopes (as depicted in **Figure 5D** or **Figure 5F**) or showed a compressive segment and an RLT but no CT (as shown in **Figure 5H**). The distinction between these cases was made based on residual gain and mean slope using the logic depicted in **Figure 4**.

Table 3. Number of I/O curves according to their shapes. The table includes the present data plus data from Lopez-Poveda and Johannesen (2012). CT: compression threshold.

Frequency (kHz)	0.5	1	2	4	6
Type 1 (CT present)	29	54	46	38	24
Type 2 (Linear)	13	4	17	23	22
Type 3 (CT absent with compression)	25	15	7	3	5
Too-high loss	3	2	2	12	20
Total	70	75	72	76	71

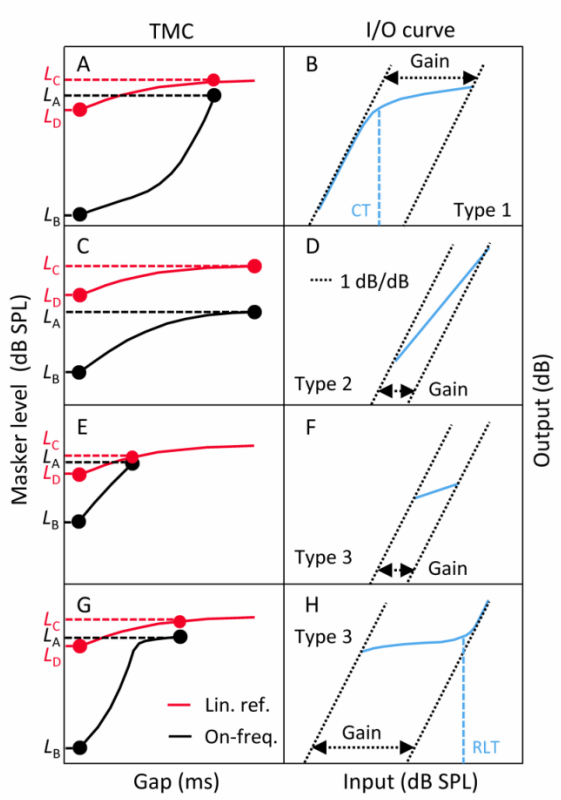

Figure 5. A taxonomy of I/O curves (blue line, right panels) and their corresponding TMCs (left panels). Left: linear-reference (red curves) and on-frequency (black curves) TMCs. Right: corresponding, inferred I/O curves. (A, B) for Type 1 I/O curves. (C, D) for Type 2 I/O curves. (E, F) for Type 3 I/O curves with little residual gain. (G, H) for Type 3 I/O curves with large residual gain. CT, compression threshold; RLT, return-to-linearity threshold. See main text for details.

Gain was defined here as the difference in sensitivity for low and high input levels, as illustrated in the right panels of **Figure 5**. That is, gain was defined as the horizontal distance between intersects with the abscissa of two lines with slopes 1 dB/dB that passed through the end points of the I/O curve. Of course, if the measured I/O curve were only a segment of the actual underlying I/O curve, as would happen for instance for straight-line I/O curves like those shown in **Figure 5D** or **Figure 5F**, this gain estimate would be smaller than the actual residual gain. Actually, insofar as an I/O curve is inferred from an on-frequency and a linear-reference TMC (compare the left and right panels of

Figure 5), gain for all types of I/O curves was directly obtained from the corresponding TMCs as follows:

$$gain=(L_{\mathrm{A}}-L_{\mathrm{B}})-(L_{\mathrm{C}}-L_{\mathrm{D}}), \quad (2)$$

where L_A, L_B, L_C, and L_D were defined as in **Figure 5**.

If gain was not significantly different from zero[2], then the I/O curve was regarded as linear, hence indicative of total gain loss. If, however, gain was greater than zero, we tried to find an RLT[3] in the I/O curve (as shown in **Figure 5H**). If absent, the I/O curve was regarded as linear when its average slope was steeper than an arbitrary value of 0.75 dB/dB. This criterion prevented cases with small amounts of residual gain and a moderate degree of compression from being erroneously classified as total gain loss; that is, it served to distinguish cases like that shown in **Figure 5F**, almost certainly indicative of significant IHC dysfunction, from cases like that shown in **Figure 5D**, almost certainly indicative of total gain loss. If, however, a RLT was present or if the average slope of the I/O curve was <0.75 dB/dB, then we assumed that compression was present and that the I/O curve was indicative of significant IHC dysfunction.

Table 3 shows the number of I/O curves in each of the three categories (Type 1: CT present; Type 2: linear; Type 3: CT absent with compression). The proportion of linear I/O curves was greater at and above 2 kHz than at lower frequencies. The proportion of Type 3 I/O curves was greater at lower than at higher frequencies. In a few cases, the hearing loss was so high (greater than ~70 dB HL) that measuring the TMC needed to infer an I/O curve would have required masker levels beyond the maximum sound pressure output of our system. These cases, classified as "too-high loss" in **Table 3**, increased slightly in number with increasing frequency.

[2] Because each TMC was measured at least three times, we could assess the variance in L_A, L_B, L_C, and L_D, hence the gain variance (Equation 2). A Student's *t*-test was then used to verify if the mean gain estimate was statistically greater than zero at the 5% significance level.

[3] The return-to-linearity (RLT) was defined as the input level at which the slope of the I/O curve reached an arbitrary value of 0.5 dB/dB from a lower value at lower input levels. It was obtained using the same method and criteria that were used to obtain the CT.

Once classified, different I/O curves types were analyzed in search of HL_{OHC} and HL_{IHC}. Type 1 I/O curves were analyzed as suggested by Lopez-Poveda and Johannesen (2012); Type 2 and Type 3 I/O curves were analyzed differently, as described below.

HL_{OHC} AND HL_{IHC} ESTIMATES FROM I/O CURVES

FROM I/O CURVES WITH A COMPRESSION THRESHOLD

For I/O curves with a CT (Type 1), HL_{OHC} was calculated as the difference between the CT and the mean CT for the reference NH group multiplied by (1–*c*) (Equation 2 in Lopez-Poveda and Johannesen, 2012), where *c* is the mean compression exponent over the compressive segment of the NH I/O curves. HL_{IHC} was obtained as HL_{TOTAL}–HL_{OHC} (Equation 1). This procedure required having mean reference CT and *c* values for NH listeners at each of the test frequencies (0.5, 1, 2, 4, and 6 kHz). Lopez-Poveda and Johannesen (2012) provided reference values for 0.5, 1, and 4 kHz but, to the best of our knowledge, reference data are still lacking at 2 and 6 kHz. For this reason, in the current analysis, the reference values at 4 kHz were used to infer HL_{OHC} and HL_{IHC} also at 2 and 6 kHz. The impact of this approximation on the results is discussed below.

Figure 6 illustrates HL_{OHC} (top) and HL_{IHC} (bottom) as a function of HL_{TOTAL}. Note that HL_{TOTAL} is defined here as the difference between a participant's absolute threshold for the masker and the mean absolute masker threshold of the reference NH group (the latter was not 0 dB HL as noted by Lopez-Poveda and Johannesen, 2012). Each column illustrates results for a different test frequency, as indicated at the top of each column. The lower insets in each panel show corresponding linear-regression functions and the number of data points (N) used in the regression; the upper insets show regression statistics, where R^2 is the proportion of variance explained by the regression line, and the *p*-value is the probability of the relationship between the two variables occurring by chance. Red dashed lines depict 95% confidence intervals for a new observation rather than the confidence intervals of the regression lines.

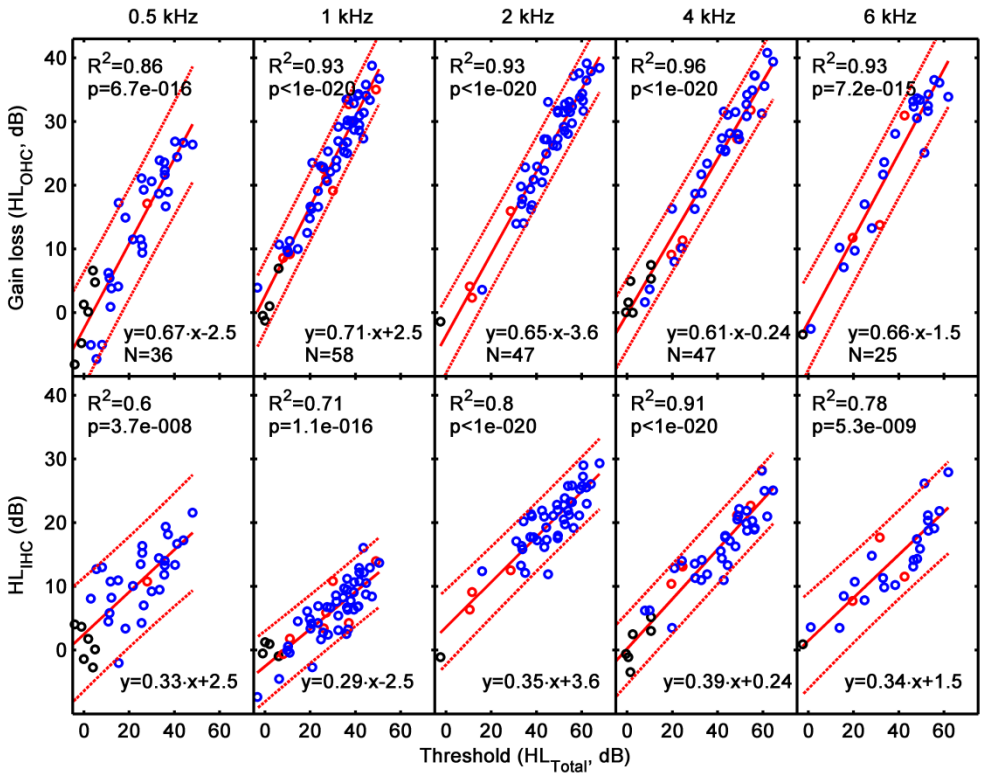

Figure 6. The contribution of HL_{OHC} (top) and HL_{IHC} (bottom) to HL_{TOTAL} assessed from the analysis of Type 1 I/O curves (i.e., from I/O curves with a CT). Each column is a for a different test frequency, as indicated by the column title. Results for the current HI listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted by black and red symbols, respectively. Continuous lines illustrate mean linear regression functions; dotted lines illustrate 5 and 95% confidence intervals of new individual observations. The insets show linear regression functions and related statistics.

The linear regression functions in **Figure 6** show that HL_{OHC} contributed between 61 and 70% to HL_{TOTAL}, and HL_{IHC} contributed the rest (30–39%). Interestingly, these percentages were approximately constant across test frequencies, as shown by the slopes of the regression lines. The individual variability of the contributions HL_{OHC} and HL_{IHC} can be assessed from the confidence limits for new single observations. The confidence intervals for HL_{OHC} and HL_{IHC} were around ±9 dB at 0.5 kHz and around ±6 dB over the range 1–6 kHz. In all cases, the confidence intervals were almost independent of the HL_{TOTAL}. Recall that these results were only for Type 1 I/O curves.

Figure 7 allows statistical judgment of the incidence of cases suffering from pure IHC loss, pure OHC loss, or mixed IHC/OHC loss. The figure illustrates absolute threshold (in dB HL) as a function of cochlear gain loss (HL_{OHC}) separately for each frequency. The vertical dotted red line (at HL_{OHC} = 0 dB) indicates the hypothetical location of cases whose hearing loss was exclusively due to IHC dysfunction (pure IHC loss). The blue diagonal line depicts the hypothetical location of cases whose hearing loss was exclusively due to cochlear gain loss (pure OHC loss). The blue-dotted diagonal lines show 5–95% confidence intervals for gain loss as calculated from the reference NH listeners (Lopez-Poveda and Johannesen, 2012). Note that the diagonal does not match with the condition HL_{TOTAL} = HL_{OHC}, as one might expect, because as explained by Lopez-Poveda and Johannesen (2012), their NH listeners did not have a mean hearing loss of 0 dB HL. The shaded area indicates the placement of cases whose hearing loss is due partly to cochlear gain loss (HL_{OHC}) plus an additional component (mixed OHC/IHC loss). The results from I/O curves with a CT are depicted as blue circles in the top panels of the figure. For completeness, also shown are the results for listeners with NH (black circles) and mild-to-moderate hearing loss (red circles) from our earlier study (Lopez-Poveda and Johannesen, 2012).

Figure 7(top) shows that pure OHC loss was rare and occurred mostly for low absolute thresholds (or, equivalently, small hearing losses). There were no cases of pure IHC loss, something not surprising considering that significant HL_{IHC} would probably make it impossible to measure a CT (Figure 1 in Lopez-Poveda and Johannesen, 2012) and **Figure 7**(top) only show results for cases with a CT. Most cases were in the shaded areas and thus were consistent with mixed IHC/OHC loss. The number of cases with mixed loss tended to increase with increasing absolute threshold (or hearing loss). Incidentally, the number of cases with mixed loss appeared somewhat larger at 2 kHz than at other frequencies. This may be somewhat artefactual due to our using the mean NH CT and absolute threshold at 4 kHz to estimate HL_{OHC} at 2 kHz. Any difference between the mean NH CTs at 2 and 4 kHz would bias the data horizontally and a difference between the mean NH absolute threshold at 2 and 4 kHz would bias the data vertically and thus might contribute to an apparent higher incidence of mixed IHC/OHC loss at 2 kHz.

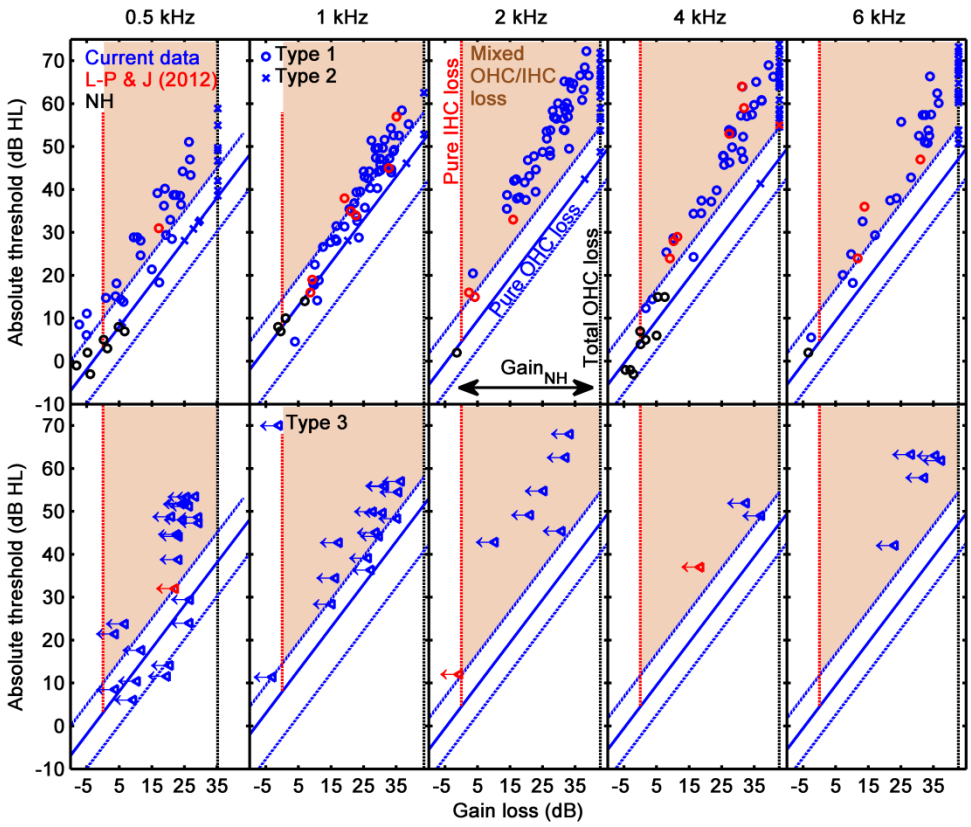

Figure 7. Absolute threshold as a function of cochlear mechanical gain loss (HL_{OHC}). Top: results for Type 1 (circles) and Type 2 (crosses) I/O curves. Bottom panels: results for Type 3 I/O curves (left-pointing triangles with arrows). Each column is for a different test frequency, as indicated by the column title. In each panel, the diagonal blue line and associated dotted lines indicate mean values and 5% confidence limits for pure OHC loss (HL_{TOTAL} = HL_{OHC}), and the vertical black, dotted line depicts the hypothetical location of cases with total cochlear gain loss, as inferred from the I/O curves of the reference, NH sample (black circles) (Johannesen and Lopez-Poveda, 2008). The red dotted lines depict the hypothetical location of cases with pure IHC loss (i.e., hearing loss with zero HL_{OHC}). The shaded areas indicate mixed OHC/IHC losses. Results for the current listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted as black and red symbols, respectively.

FROM LINEAR I/O CURVES

Linear I/O curves were assumed to be indicative of total gain loss. Hence, HL_{OHC} for these cases was set equal to the average cochlear gain for the NH reference group. The latter was estimated using Equation (2), and was equal to 35.2, 43.5,

42.7, 42.7, 42.7 dB at 0.5, 1, 2, 4, and 6 kHz. HL_{IHC} was then obtained using Equation (1).

Results for these cases are shown as blue crosses in the top panels of **Figure 7**. Clearly, the great majority of these cases were in the shaded area, hence were indicative of mixed OHC/IHC loss. In other words, for most of these cases, the hearing loss was greater than the maximum possible mechanical cochlear gain loss (the gain loss of NH listeners), hence $HL_{IHC} > 0$ dB.

FROM COMPRESSIVE I/O CURVES WITHOUT A COMPRESSION THRESHOLD

As explained above, I/O curves that were either compressive straight lines (with slopes <0.75 dB/dB; **Figure 5F**), or that showed an RLT but not a CT (as in **Figure 5H**) were assumed indicative of IHC dysfunction. This is because any gain reduction will only affect the low-level linear portion of the I/O curve and IHC dysfunction may increase the BM response at detection threshold above the knee-point of the I/O curve (Figure 1B of Lopez-Poveda and Johannesen, 2012). Lopez-Poveda and Johannesen (2012) argued that for these cases Equation (1) does not hold, and that it is reasonable to assume that the audiometric loss can be fully explained in terms of inefficient IHC transduction combined with residual compression (see their Figure 1D). Therefore, we assumed that for these cases HL_{TOTAL} was equal to HL_{IHC}.

This is not to say, however, that cochlear gain loss did not occur in these cases; we are saying that if cochlear gain loss did occur, it is unlikely that it contributed to the audiometric loss (see Figure 1D in Lopez-Poveda and Johannesen, 2012). Indeed, an estimate of (residual) gain was obtained as illustrated in **Figure 5F** or **Figure 5H** using Equation (2). Note that this gain estimate was almost certainly less than the actual residual gain because, due to IHC dysfunction, the measured compressive segment of the I/O was only a portion of the true compressive segment. Cochlear gain loss (HL_{OHC}) was estimated by subtracting the obtained gain estimate from the reference gain for NH listeners (see the previous section). The bottom panels of **Figure 7** illustrate residual gain for these cases. The left pointing arrows indicate that the actual HL_{OHC} was probably *smaller* than estimated, hence that symbols should be to the left of their position in the figure, and closer to the red-dotted line indicative of pure IHC loss. The figure reveals two important results. First,

most of these cases are indicative of mixed IHC and OHC dysfunction. Indeed, mixed dysfunction appears more frequent for these cases than for I/O curves with a CT (compare the placement of blue triangles and circles in the bottom and top panels of **Figure 7**). Second, for any given absolute threshold (or hearing loss), there were comparatively more cases with little gain loss (i.e., indicative of IHC dysfunction) at lower than at higher frequencies. In other words, low-frequency hearing loss is more likely related to IHC dysfunction than to cochlear gain loss.

Across Listener Variability of HL_{OHC}

Figure 6 suggests that HL_{OHC} accounted on average for 61–70% of HL_{TOTAL} but it also suggests that there was large across-listener variability. **Figure 8** illustrates this variability more clearly by showing the distribution of HL_{OHC} for three different ranges of HL_{TOTAL}: 15–35, 35–55, and 55–80 dB. Results are based on Type 1 and Type 2 I/O curves. At 2 kHz and above, HL_{OHC} tended to increase with increasing HL_{TOTAL}, while at 0.5 and 1 kHz it decreased slightly or remained approximately constant. The main result from this figure is, however, that for a given frequency and hearing-loss range, HL_{OHC} was broadly distributed across cases. For example, based on data for 25 subjects, at 4 kHz and for a hearing-loss range of 35–55 dB, HL_{OHC} accounted for between 55 and 100% of HL_{TOTAL}. [Note that the figure suggests that in a few cases with small losses, HL_{OHC} accounted for more than 100% of HL_{TOTAL}. These were cases whose CTs were lower than the mean CT for the reference, NH group (i.e., cases below the diagonal line in Figure 7)].

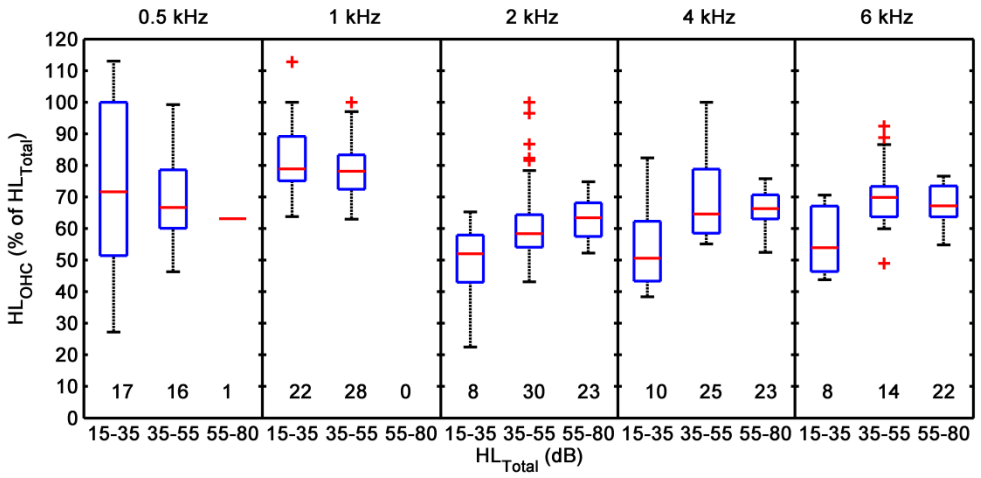

Figure 8. Across-listener variability in the proportion of HL_{TOTAL} explained by HL_{OHC}. Each box plot illustrates distribution percentiles: the bottom and top lines in each box depict the first and third quartiles of the distribution; the band inside the box is the second quartile (the median); the lower and upper whiskers' ends depict the 1 and 99% percentiles. Crosses (+) depict cases outside the latter percentiles. Each panel is for a different test frequency. In each panel, distributions are given for HL_{TOTAL} ranges of 15–35, 35–55, and 55–80 dB. The numbers below each box plot indicate the number of cases (sample size) included in each distribution. The figure includes data for Type 1 and Type 2 I/O curves from the present participants and from the participants in the study of Lopez-Poveda and Johannesen (2012).

PREVALENCE OF IHC AND OHC DYSFUNCTION

The previous analyses have focused mostly on the relative contribution of HL_{OHC} and HL_{IHC} to HL_{TOTAL}. The data may be alternatively analyzed with a focus on the type of hearing loss; that is, on how many data points fall in each of several regions depicted in **Figure 7**. To this end, Type 1 (CT present) and Type 2 (linear) I/O curves were split into two subcategories: "Pure OHC dysfunction," when the audiometric loss could be entirely explained as loss of cochlear gain, that is, when $HL_{TOTAL} \sim HL_{OHC}$ (points within the diagonal range in **Figure 7**); and "Mixed OHC/IHC dysfunction," when the audiometric loss exceeded the cochlear gain loss (i.e., when $HL_{IHC} > 0$; points in the shaded area of **Figure 7**). For the reasons explained above, for Type 3 I/O curves, the absence of a CT was taken as indicative that the audiometric loss could be explained entirely in terms of IHC dysfunction ($HL_{TOTAL} \sim HL_{IHC}$). As shown in the bottom panels of **Figure 7**, however, cochlear gain loss of uncertain extent

still occurred in a majority of these cases even though it probably did not contribute to the audiometric loss. Therefore, Type 3 I/O curves were also regarded as indicative of mixed OHC/IHC dysfunction.

The top part of **Table 4** gives the number of cases in each of these categories, and the bottom part of **Table 4** the corresponding percentages. Note that the number of cases of Type 3 I/O curves decreased with increasing frequency, suggestive that IHC dysfunction was more determinant to audiometric loss at low frequencies than cochlear gain loss. Note also that the percentage of cases of pure OHC loss decreased with increasing frequency, while the percentage of cases of mixed loss increased with increasing frequency, and that the two percentages add up to 100%. Mixed OHC/IHC loss was significantly more frequent than pure OHC at all frequencies. The bottom part of **Table 4** gives one additional percentage: "Total gain loss" refers to the total percentage of linear I/O curves, whether indicative of pure OHC dysfunction or mixed OHC/IHC dysfunction. The percentage of these cases increased with increasing frequency. Chi χ^2 tests were used to test if the above described frequency trends were statistically significant. The null hypothesis was that for each I/O curve type, the frequency distribution followed the distribution of the total number of cases (i.e., the distribution in the line labeled as "Total" in the table).

Table 4. Number of cases per I/O curve type and frequency (top) and percentage of cases per loss type (bottom). *p* indicates significance levels for chi-squared tests. The asterisk indicates that the statistical test was not reliable because the number of cases was insufficient.

		Frequency (kHz)					
I/O curve type	**Criterion**	**0.5**	**1**	**2**	**4**	**6**	***p***
Type 1 (CT present)	$HL_{TOTAL} \sim HL_{OHC}$	5	26	1	3	2	< 1e-6
	$HL_{IHC,}\ HL_{OHC} > 0$	24	28	45	35	22	0.082
Type 2 (Linear)	$HL_{TOTAL} \sim HL_{OHC}$	8	3	3	1	3	0.123*
	$HL_{IHC,}\ HL_{OHC} > 0$	5	1	14	22	19	1e-6
Type 3 (CT absent with compression)	$HL_{TOTAL} \sim HL_{IHC}$	25	15	7	3	5	3e-5
Total		67	73	70	64	51	
Loss type (%)	Total gain loss (linear I/O curve)	19.4	5.5	24.3	35.9	43.1	1.7e-4
	Pure OHC dysfun. ($HL_{TOTAL} \sim HL_{OHC}$)	19.4	39.7	5.7	6.3	9.8	1e-6
	Mixed OHC/IHC dysfun. ($HL_{OHC,}\ HL_{IHC} > 0$)	80.6	60.3	94.3	93.8	90.2	0.14

VERIFICATION AND EXTENSION OF MODEL ASSUMPTIONS

The present analysis was based on the hearing loss model of Plack et al. (2004) whereby OHC loss would reduce cochlear gain without significantly altering the amount of compression; that is, OHC loss would shift the low-level linear segment of the I/O curve without altering the slope of the compressive segment (Figure 7D of Plack et al., 2004). Their model was based on their observed lack of correlation between the compression exponent and absolute threshold accompanied by a strong negative correlation between gain and absolute threshold (their Figure 6). Their data were restricted to mild-to-moderate hearing losses and to a probe frequency of 4 kHz. Hence, one might object to the present analyses on the grounds that their model has not yet been corroborated for larger hearing losses or for the wider range of test frequencies used here. Our data, however, do support their model. **Figure 9** shows that the CT, a parameter of the I/O curve directly related with cochlear gain, is positively and highly significantly correlated with absolute threshold (**Figure 9**, bottom) while the average slope over the compressive segment of the I/O curve (i.e., over the input level range from the CT to the RLT) is uncorrelated with absolute threshold (**Figure 9**, top). This supports the results of Plack et al. (2004) at 4 kHz, extends their model to greater hearing losses and to a wider frequency range from 0.5 to 6 kHz, and supports the validity of our approach.

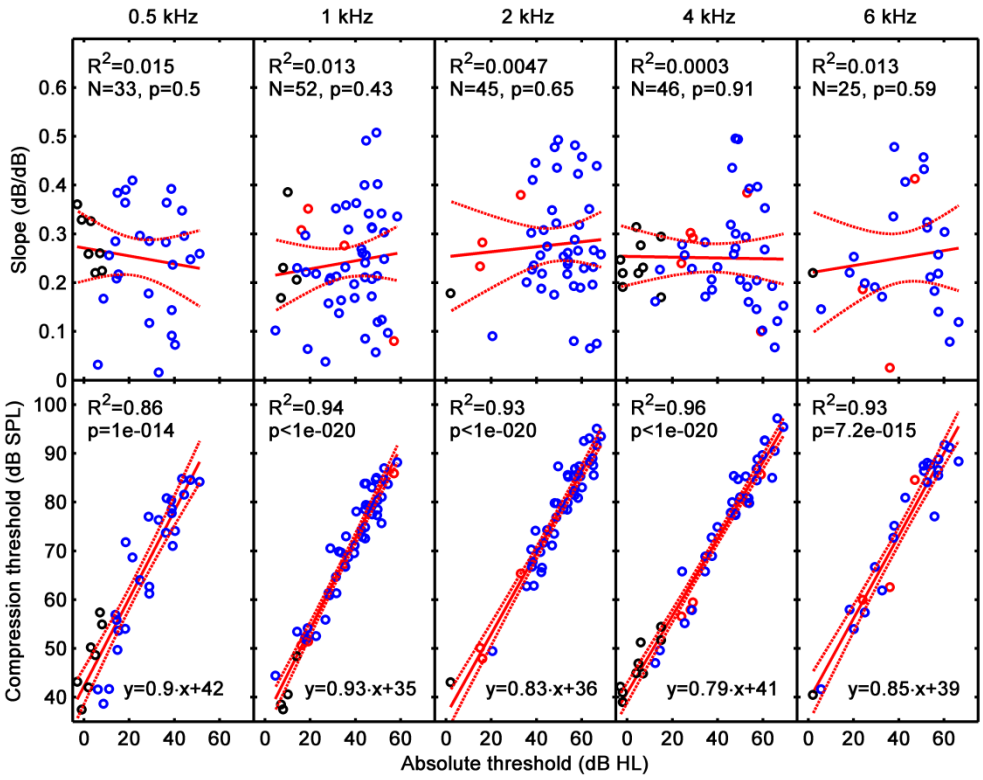

Figure 9. Correlation of average slope (i.e., the slope of the I/O over the compressive segment) (top) and compression threshold (bottom) with absolute threshold. Each column is for a different test frequency, as indicated by the column title. Results for the present listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted by black and red symbols, respectively. Continuous and dotted lines depict mean linear regression and 5–95% confidence intervals of the regression functions, respectively. The linear regression function and related statistics are shown in the insets.

4. FORWARD-MASKING RECOVERY AND THE ASSUMPTIONS OF THE TEMPORAL MASKING CURVE METHOD OF INFERRING COCHLEAR COMPRESSION[4]

INTRODUCTION

The TMC method used in Chapter 3 and elsewhere to infer cochlear I/O curves rests on two assumptions regarding the postmechanical rate of recovery from forward masking: (a) for a given probe frequency, it is independent of masker frequency; and (b) it is independent of probe frequency. Failure to meet these two assumptions, would question the method, the conclusions drawn in Chapter 3, and the conclusions drawn by numerous studies where this popular method has been applied (see the Introduction). The aim of the present chapter was to verify these two assumptions. Our approach was inspired by Stainsby and Moore (2006) but was carefully designed to overcome their methodological limitations.

APPROACH

For each of the 68 participants, we very carefully attempted to measure DPOAEs at four test frequencies (0.5, 1, 2, and 4 kHz) as follows. Over a wide

[4] A modified version of this chapter was published as: Pérez-González P, Johannesen PT, Lopez-Poveda EA. (2014). Forward-masking recovery and the assumptions of the temporal masking curve method of inferring cochlear compression. *Trends in Hearing* 19:1-14.

level range (recall that L_2 varied from 35 to 70 dB SPL in 5-dB steps; see Material and Methods), we searched combinations of primary levels that maximized DPOAE levels independently at each frequency, compared with Stainsby and Moore who used primaries with only a fixed level of 70 dB SPL each. In addition, we used longer measurement times of 30 sec at 500 Hz and 10 sec at higher frequencies compared with the 2 sec used by Stainsby and Moore. By including these improvements, we maximized the chance of detecting DPOAEs above the noise floor that might have otherwise be missed, particularly at low frequencies. In other words, the lack of DPOAEs as observed using our methods was a better indicator of *linear* cochlear responses than a lack of DPOAEs as observed using the methods of Stainsby and Moore.

From the 68 participants, we selected those who had (i) absolute thresholds equal to or higher than 40 dB HL (ANSI, 1996) at the TMC test frequencies, and (ii) absent DPOAEs for at least 29 of the 32 conditions (4 test frequencies x 8 primary levels) that were attempted. Only eight of the 68 participants met these two restrictive criteria (**Table 2**). Their DPOAEs are shown in **Table 5.** Our restrictive criteria made it likely that the eight selected participants had *linear* cochlear responses. In other words, our approach was similar to that of Stainsby and Moore (2006) but we overcame the limitations in their study by using a larger sample size ($N = 8$ vs. $N = 3$) and using improved DPOAE methods that made it more likely that the selected subjects had 'truly' linear cochlear responses.

Table 5. DPOAE levels (dB SPL) for the subset of participants (S#) with presumably linear cochlear responses. DPOAE levels are shown only for the participants, the test frequencies (Columns), and L_2 levels (Rows) for which DPOAEs were measurable.

	f_2 (kHz)							
	0.5		1		2		4	
L_2 (dB SPL)	S#	dB SPL	S#	dB SPL	S#	dB SPL	S#	dB SPL
70	S054	-1.5						
65	S199	-1.7	S116	-4.0	S199	3.9	S026	10.6
							S199	-0.3
60	S116	2.8						
	S121	7.5						
55	S054	-7.8	S012	-3.5				
	S142	1.8						
50			S142	-9.4				
45							S026	-6.0
40			S012	-5.6	S054	-14.1	S142	-6.3
					S121	-9.6		
35			S116	-5.2	S182	-14.1		

TMC ANALYSIS

For the eight selected participants, we analyzed their on-frequency TMCs at test frequencies of 0.5, 1, 2, 4, and 6 kHz as well as their linear reference TMCs seeking correlations of TMC slope with probe frequency and masker level.

As in many previous studies (e.g., Lopez-Poveda et al., 2003, 2005; Nelson and Schroder, 2004; Nelson et al., 2001; Plack et al., 2004; Stainsby and Moore, 2006), TMCs were fitted using a straight line:

$$L_{\mathrm{M}}(t)=L_0+b\cdot t, \tag{3}$$

where $L_{\mathrm{M}}(t)$ is the masker level (in dB SPL) at masker-probe time interval t (in ms), b is the TMC slope (dB/ms), and L_0 is the intercept masker level (in dB SPL) for a masker-probe time interval of 0 ms. Given that the selected participants presumably had linear cochlear responses, parameter b was taken as indicative of forward-masking recovery rate, and L_0 was used as indicative of the range of masker levels in a TMC.

DISTORTION PRODUCT OTOACOUSTIC EMISSIONS

Table 5 gives the DPOAE levels measured for each participant for each pair of test frequency, f_2, and primary level, L_2. Missing values indicate absent DPOAEs. DPOAEs were present for only 19 of the 256 possible cases (4 test frequencies × 8 primary levels × 8 participants). Furthermore, for no participant were DPOAEs present in more than 3 out of 32 conditions. The noise floor level was less than −4 dB SPL for all participants at 0.5 and 1 kHz, except for S121 at 500 Hz, for whom the noise floor was −1 dB SPL. The average noise floor level was −8.2 and −13.5 dB SPL at 0.5 and 1 kHz, respectively, and lower at higher frequencies. Altogether, these results suggest that the absence of DPOAEs for these participants is not due to high levels of noise. Therefore, we concluded the absence was due to their having linear (or almost linear) cochlear responses over the frequency range from 0.5 to 4 kHz. The accuracy of this conclusion will be discussed later.

TEMPORAL MASKING CURVES

Figure 10 shows experimental (symbols) and fitted (lines) TMCs. On-frequency and reference fitted TMCs are illustrated using continuous and dashed lines, respectively. Note that 46 TMCs were measured (38 on-frequency plus 8 reference TMCs) and that on-frequency TMCs are missing for S116 at 4 and 6 kHz (**Table 6**). For S116, probe thresholds were so high at 4 kHz that we anticipated masker levels would be higher than the maximum system output level. Hence, we did not attempt measuring on-frequency TMCs at 4 kHz. For S116, we tried measuring on-frequency TMCs at 6 kHz but masker levels exceeded the maximum system output. Except for one case, missing points in **Figure 10** are indicative that the corresponding masker levels would exceed the maximum system output level (105 dB SPL). The exception is the on-frequency TMC for S142 at 0.5 kHz. This TMC was nonmonotonic (i.e., masker levels decreased with increasing masker-probe time interval beyond 70 ms), probably because the subject had greater difficulty at keeping track of the probe for the longer masker-probe time intervals. We regarded the nonmonotonic trend as unrealistic and omitted the declining portion of the TMC.

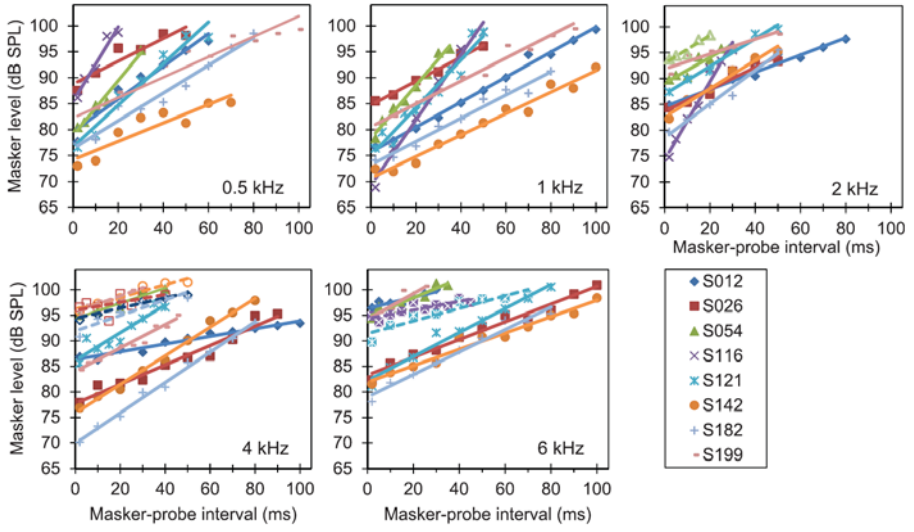

Figure 10. Experimental (symbols) and fitted (lines) TMCs. Each panel illustrates on-frequency TMCs (filled symbols, continuous lines) for a different probe frequency, as indicated by the numbers at the bottom-right corner of the panel. A panel also illustrates linear reference TMCs (dashed lines) if they were measured at the corresponding probe frequency.

Table 6. Linear regression parameters and goodness-of-fit for each subject (S#) and TMC. Each line is for a different on-frequency or linear-reference (LR) TMC. RMS is the root-mean-square error in decibels; R2 is the proportion of variance explained by the linear regression model. Empty cells indicate that the corresponding TMC was not available (see main text).

		Linear regression model (Eq. 3)				
S#	kHz	L_0 (dB SPL)	*b* (dB/ms)	R^2	RMS (dB)	Num. points
S012	0.5	79.6	0.32	0.95	1.40	7
S026	0.5	88.8	0.22	0.86	1.45	6
S054	0.5	78.9	0.53	0.98	0.77	5
S116	0.5	85.4	0.72	0.94	1.13	5
S121	0.5	76.7	0.40	0.95	1.73	7
S142	0.5	74.2	0.18	0.83	1.80	8
S182	0.5	76.4	0.27	0.97	1.29	9
S199	0.5	82.3	0.20	0.89	2.18	11
S012	1	75.7	0.24	0.99	0.67	11
S026	1	84.7	0.23	0.99	0.41	6
S054	1	78.3	0.51	0.98	0.75	8
S116	1	69.3	0.63	0.98	1.29	6
S121	1	75.0	0.46	0.94	1.76	11
S142	1	70.7	0.21	0.97	1.07	11
S182	1	73.2	0.22	0.97	1.00	9
S199	1	80.5	0.22	0.97	1.02	10
S012	2	84.6	0.17	0.97	0.70	9
S026	2	83.7	0.21	0.94	0.88	6
S054	2	89.1	0.25	0.91	0.75	7
S116	2	74.2	0.76	0.97	1.24	7
S121	2	87.0	0.27	0.98	0.70	6
S142	2	82.6	0.27	0.98	0.70	6
S182	2	78.6	0.33	0.98	0.78	6
S199	2	91.9	0.14	0.90	0.78	6
S012	4	86.3	0.08	0.96	0.49	11
S026	4	77.7	0.19	0.96	1.16	10
S054	4	94.4	0.15	0.91	0.65	5
S116	4					
S121	4	86.1	0.27	0.86	1.39	9
S142	4	75.8	0.28	0.99	0.66	9
S182	4	69.9	0.30	0.99	0.63	9
S199	4	84.0	0.23	0.96	0.64	10
S012	6	96.3	0.11	0.82	0.49	7
S026	6	83.3	0.17	0.97	0.88	11
S054	6	94.7	0.19	0.91	0.65	8
S116	6					
S121	6	82.2	0.24	0.97	0.97	9
S142	6	81.9	0.16	0.96	0.97	11
S182	6	79.0	0.22	0.97	0.95	9
S199	6	94.2	0.25	0.80	1.00	6
S012	LR-4	94.4	0.10	0.92	0.49	6
S026	LR-4	96.0	0.08	0.29	1.44	8
S054	LR-2	92.9	0.27	0.92	0.51	5
S116	LR-6	94.4	0.08	0.74	0.69	10
S121	LR-6	91.4	0.12	0.87	1.07	8
S142	LR-4	96.0	0.13	0.93	0.56	6
S182	LR-4	92.0	0.15	0.88	0.93	6
S199	LR-4	95.5	0.16	0.91	0.49	7

Table 6 gives the parameters and goodness-of-fit statistics of the straight line fits to the TMCs (RMS errors, and proportion of variance explained, R^2). The variance explained by the fit was ≥90% for 36 of the 46 measured TMCs, between 80% and 90% for eight TMCs, and 74% and 29% for the remaining two TMCs. The RMS error was always less than 2.2 dB, with a mean value of 0.96 dB. These statistics justify the use of a linear regression model (Equation 3) to analyze the present TMCs.

Forward-Masking Recovery as a Function of Probe Frequency and TMC Intercept Level

The middle panels of **Figure 11** and **Figure 12** show the slope of on-frequency TMCs (i.e., parameter b in Equation 3) as a function of probe frequency expressed as $\log_{10}$(Hz); the rightmost panels show TMC slope as a function of TMC intercept level (i.e., parameter L_0 in Equation 3). The leftmost panels in the two figures illustrate masker absolute thresholds and TMC intercept levels as a function of frequency. Each row of each figure shows results for an individual participant, as indicated in the leftmost panels of each figure. For some participants, TMC slope decreased with increasing frequency and with increasing L_0, while for other participants TMC slope remained approximately constant across frequencies and L_0. Linear regression functions were fitted to the trends in **Figure 11** and **Figure 12**. These are shown as straight lines together with their corresponding equations and proportion of explained variance (R^2). Note that a low value of R^2 does not necessarily imply a poor linear regression fit; indeed, low R^2 values also occur when TMC slope remains constant across frequencies or intercept levels.

Figure 13 shows the slopes of the linear regression fits for each participant. Different symbols illustrate the slope of the linear regression trends for frequency (triangles) and L_0 (circles). Negative and positive values indicate that TMC slope decreased and increased with increasing frequency or L_0, respectively. For five participants (S026, S116, S142, S182, and S199), TMC slope barely changed across frequencies or TMC intercept levels. For the remaining three participants (S012, S054, and S121), however, TMC slope decreased with increasing frequency and with increasing TMC intercept level. Interestingly, for the latter participants, TMC slope co-varied with L_0 and with frequency, an aspect that will be further investigated later.

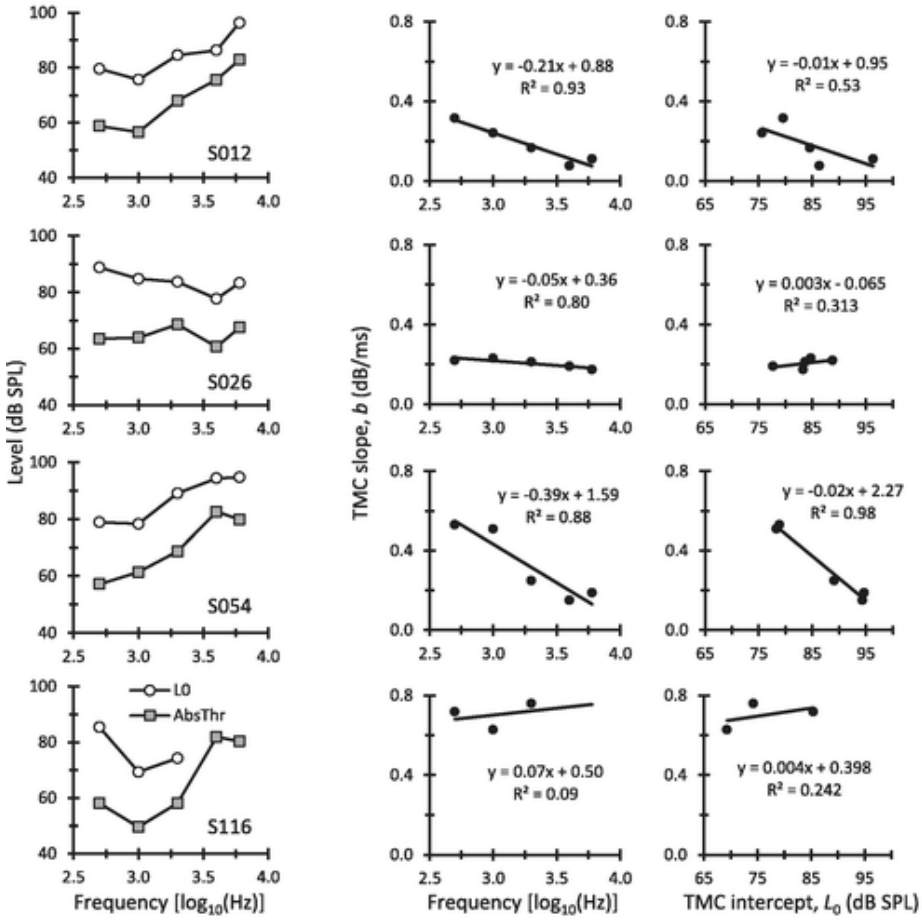

Figure 11. On-frequency TMC characteristics for four participants (S012, S026, S054, and S116). Left: Masker absolute thresholds (gray squares) and TMC intercept levels (L_0, open circles). Middle: TMC slope, *b*, as a function of frequency. Right: TMC slope, *b*, as a function of intercept level, L_0. Each row is for a different participant, as indicated in the bottom-right corner of the left panels. Straight lines and equations in the middle and right panels illustrate linear regression fits together with their corresponding equations and proportion of predicted variance (R^2).

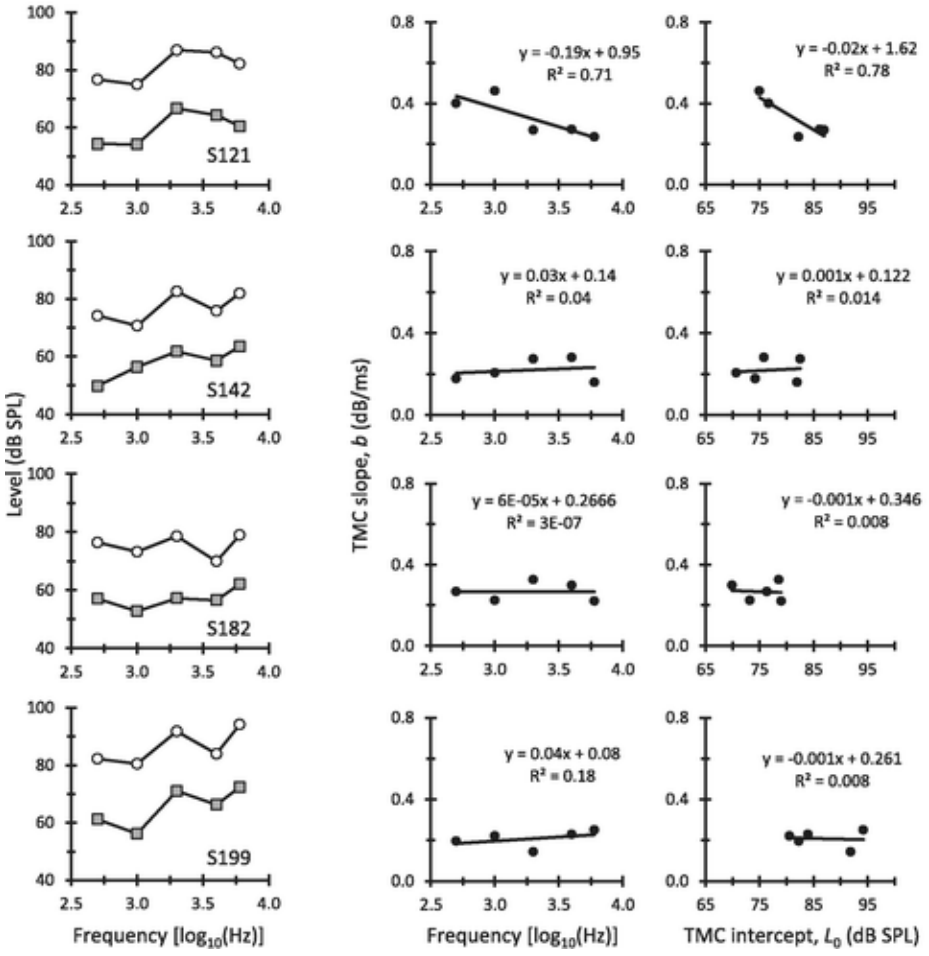

Figure 12. As Figure 11 but for four other participants (S121, S142, S182 and S199).

The filled symbols in **Figure 13** show mean slopes of the linear regression trends across participants. On average, TMC slope decreased slightly with increasing frequency (mean = −0.08, $SD = 0.16$ dB/ms/$\log_{10}$(Hz)) indicating that on-frequency TMCs were on average about 10% shallower at 6000 than at 500 Hz. Mean TMC slope also decreased slightly with increasing L_0 (mean = −0.005, $SD = 0.0097$ dB/ms/dB) indicating that TMCs with $L_0 = 95$ dB SPL were on average about 10% shallower than those with $L_0 = 75$ dB SPL. Given the rather large variability across participants, however, the mean linear regression slopes were not statistically different from zero. In other words, mean TMC slope decreased slightly with increasing frequency and intercept

level, across the probe frequency range (500–6000 Hz) and intercept level range (69–96 dB SPL) tested, but the trends were not significant.

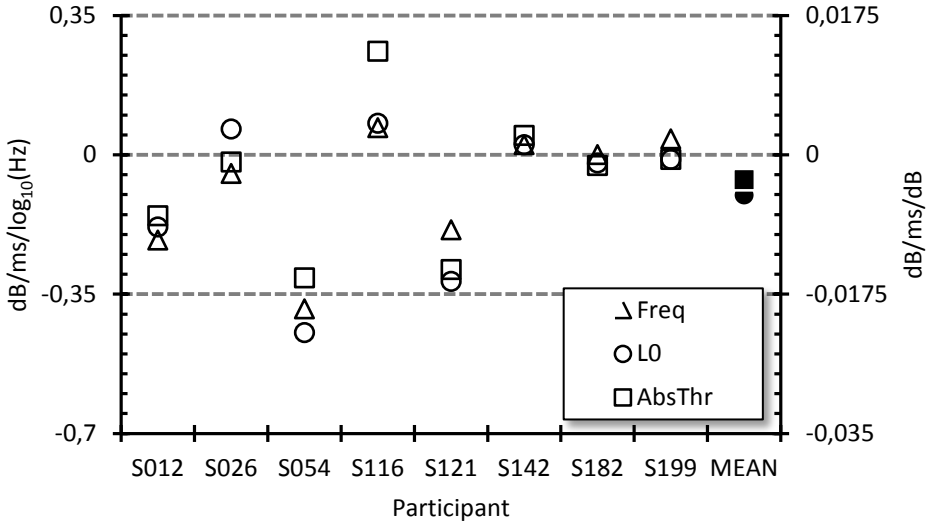

Figure 13. Trends of on-frequency TMC slope as a function of frequency or level for each participant or the mean. Each point depicts the slope of the linear regression lines in Figures 2 and 3. In other words, positive/negative values indicate that TMC slope increases/decreases with increasing frequency (left ordinate) or level (right ordinate).

POSSIBLE FREQUENCY-LEVEL INTERACTIONS ON FORWARD-MASKING RECOVERY

As shown in **Figure 13**, TMC slope co-varied with frequency and with TMC intercept level. Probe frequency and intercept level were closely related with each other: Intercept level was higher at higher frequencies, particularly for those participants with sloping audiograms (left panels in **Figure 11** and **Figure 12**). An attempt was made to disentangle which of these two factors (probe frequency or intercept level) had a stronger influence on TMC slope. Our approach was based on the idea that if the main factor were level, then for a given probe frequency TMC slope should be negatively correlated with intercept level; however, if the main factor were frequency, then for TMCs with comparable intercept levels TMC slope should be negatively correlated with

probe frequency. A third possibility could be that TMC slope concomitantly decreased with increasing probe frequency *and* intercept level.

Figure 14 illustrates the results of this analysis. The left panels show TMC slope against intercept level separately for each of the five frequencies tested. Note that the different points in a given panel correspond to different participants. TMC slope tended to be negatively correlated with level at frequencies of 1, 2, and 4 kHz. Despite the trends, however, the correlation was statistically significant only at 2 kHz (two-tailed t test, $N = 8$; $r = -.794$, $p = .0327$). The right panels in **Figure 14** show TMC slope against probe frequency (expressed as $\log_{10}$(Hz)) for TMCs with intercept levels around approximately 76 (**Figure 14F**), 80 (**Figure 14G**), 85 (**Figure 14H**), and 89 dB SPL (**Figure 14I**), respectively. Slope also tended to be negatively correlated with frequency for intercept levels of 80, 85, and 89 dB SPL, but not for 76 dB SPL. Despite the trends, the correlations were not statistically significant at any of the four intercept levels.

In summary, the present data suggest that the rate of forward-masking recovery decreased with increasing level at frequencies of 1 to 4 kHz. They also suggest that the rate of forward-masking recovery decreased with increasing frequency, at least for TMCs that involved masker levels ≥80 dB SPL. Overall, however, the trends were not statistically significant possibly due to the small sample size.

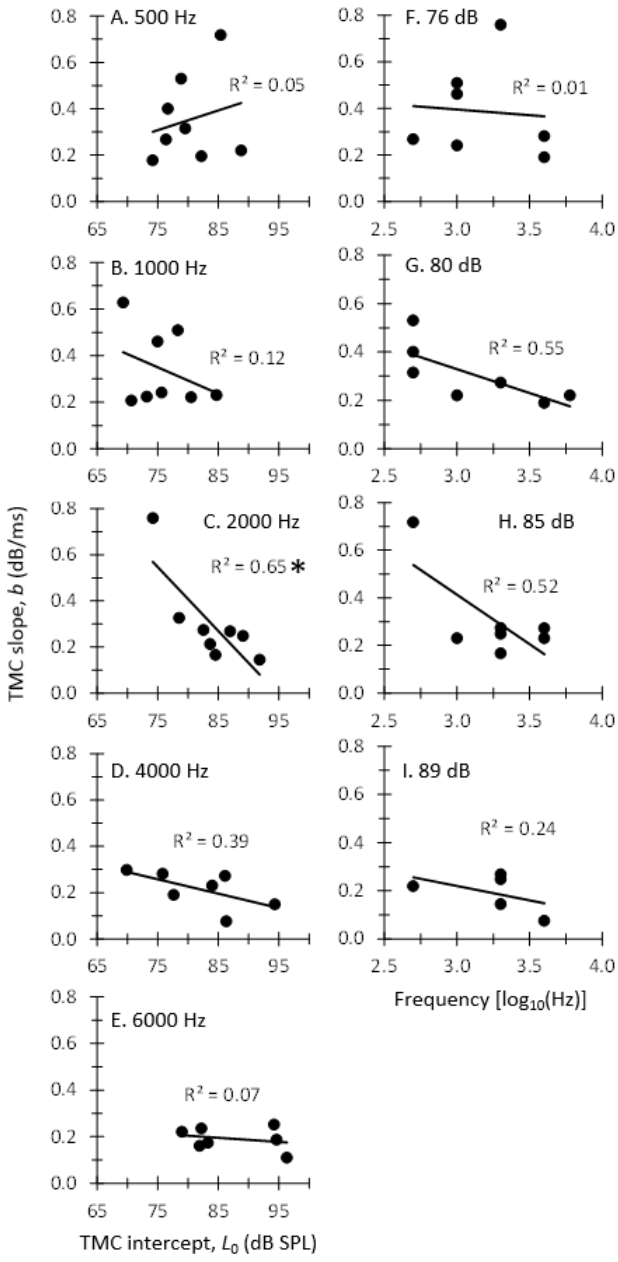

Figure 14. Left: On-frequency TMC slope as a function of intercept level. Each panel is for a different probe frequency, as indicated at the top of the panel. Right: On-frequency TMC slope as a function of frequency. Each panel is for a different intercept level, as indicated at the top of the panel. In each panel, different points are for different participants ($N = 8$). Missing points indicate that the corresponding TMC could not be measured. An asterisk (*) indicates a statistically significant correlation (two-tailed t test, $p < .05$).

To further assess the effect of level on forward-masking recovery while minimizing the potentially concomitant effect of frequency, we compared the slope of reference and on-frequency TMCs measured at the same probe frequency. If forward-masking recovery were independent of level, on-frequency and reference TMCs should have comparable slopes. The relevant data are shown in **Figure 15**. Note that only seven of the eight possible pairs of reference and on-frequency TMCs (**Table 2**) were available because the on-frequency TMC was missing for S116 at 6 kHz. In all cases, reference TMCs had higher intercept levels than corresponding on-frequency TMCs. For four of the seven participants (S026, S121, S142, and S182), reference TMCs had shallower slopes than their corresponding on-frequency TMCs. For the remaining three participants (S012, S054, and S199), the slope of the reference TMC was comparable with or slightly greater than that of the corresponding on-frequency TMC. On average, reference TMCs had shallower slopes than on-frequency TMCs (0.15 vs. 0.22 dB/ms), but the difference was not statistically significant (two-tailed *t* test, $N = 7$, $p = .0851$).

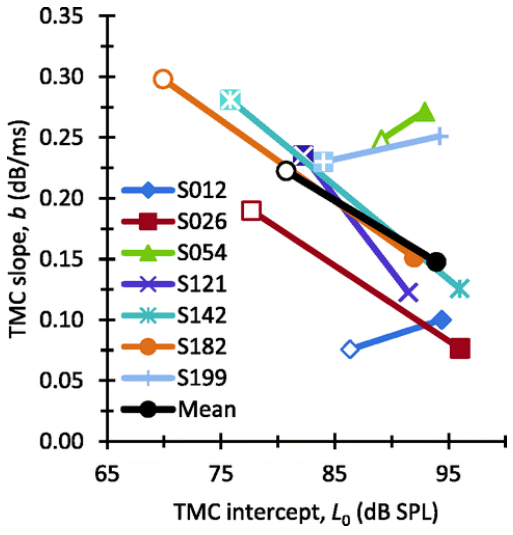

Figure 15. Slope of on-frequency (left symbols) and reference (right symbols) TMCs as a function of TMC intercept level. Each pair of data points is for a different participant.

5. THE INFLUENCE OF COCHLEAR MECHANICAL DYSFUNCTION ON THE INTELLIGIBILITY OF AUDIBLE SPEECH IN NOISE FOR HEARING-IMPAIRED LISTENERS[5]

INTRODUCTION

The present chapter was aimed at assessing the relative importance of cochlear mechanical dysfunction for understanding audible speech in noisy environments by HI listeners. In Chapter 3, we reported behaviorally inferred estimates of cochlear mechanical gain loss (HL_{OHC}), inner hair cell loss (HL_{IHC}), and residual compression (i.e., the slope of the I/O curve over its compressive segment or BMCE) for 68 HI listeners. Those estimates were used in the present study as indicators of cochlear mechanical dysfunction and the participants from that study were invited back into the laboratory to assess their ability to understand audible speech in various types of noise.

Recall that speech-in-noise intelligibility was assessed using the speech reception threshold (SRT), defined as the speech-to-noise ratio (SNR) required to correctly recognize 50% of the sentences that listeners were presented with in a noise background (e.g., Peters et al., 1998). When measuring SRTs, stimuli were linearly amplified in a frequency-specific manner to minimize the effect of

[5] Portions of this chapter were published in: Johannesen PT, Pérez-González P, Kalluri S, Blanco JL, Lopez-Poveda EA. (2016). The influence of cochlear mechanical dysfunction, temporal processing deficits, and age on the intelligibility of audible speech in noise by hearing-impaired listeners. *Trends in Hearing* 20:1-14.

reduced audibility on intelligibility. SRTs were measured for two types of maskers: steady, speech-shaped noise (SSN) and time-reversed two-talker masker (R2TM). The latter masker was used because it has the same temporal and spectral properties as forward speech and was thus expected to have the same energetic masking properties as speech but without semantic information that may contribute to informational masking (e.g., Hornsby and Ricketts, 2007).

Speech Reception Thresholds

For most listeners, SRT_{SSN} values were in the range −5 to 1 dB SNR (**Figure 16**), thus in line with values reported by earlier studies for SSN maskers (George, Festen, and Houtgast, 2006; Gregan et al., 2013; Peters et al., 1998). SRT_{R2TM} values were in the range −2 to 5 dB SNR and generally higher than SRT_{SSN} values (**Figure 16**). This trend and range of values are consistent with those reported elsewhere for HI listeners for a R2TM (e.g., Festen and Plomp, 1990 reported SRT_{R2TM} values from −4 to 2 dB SNR). The present SRT_{R2TM} values were about 3, 5, and 5 dB higher than the SRTs for interrupted or modulated noise backgrounds reported by George et al. (2006), Peters et al. (1998), and Gregan et al. (2013), respectively. The fact that SRTs differ for different types of fluctuating maskers is consistent with previous studies (e.g., Festen and Plomp, 1990).

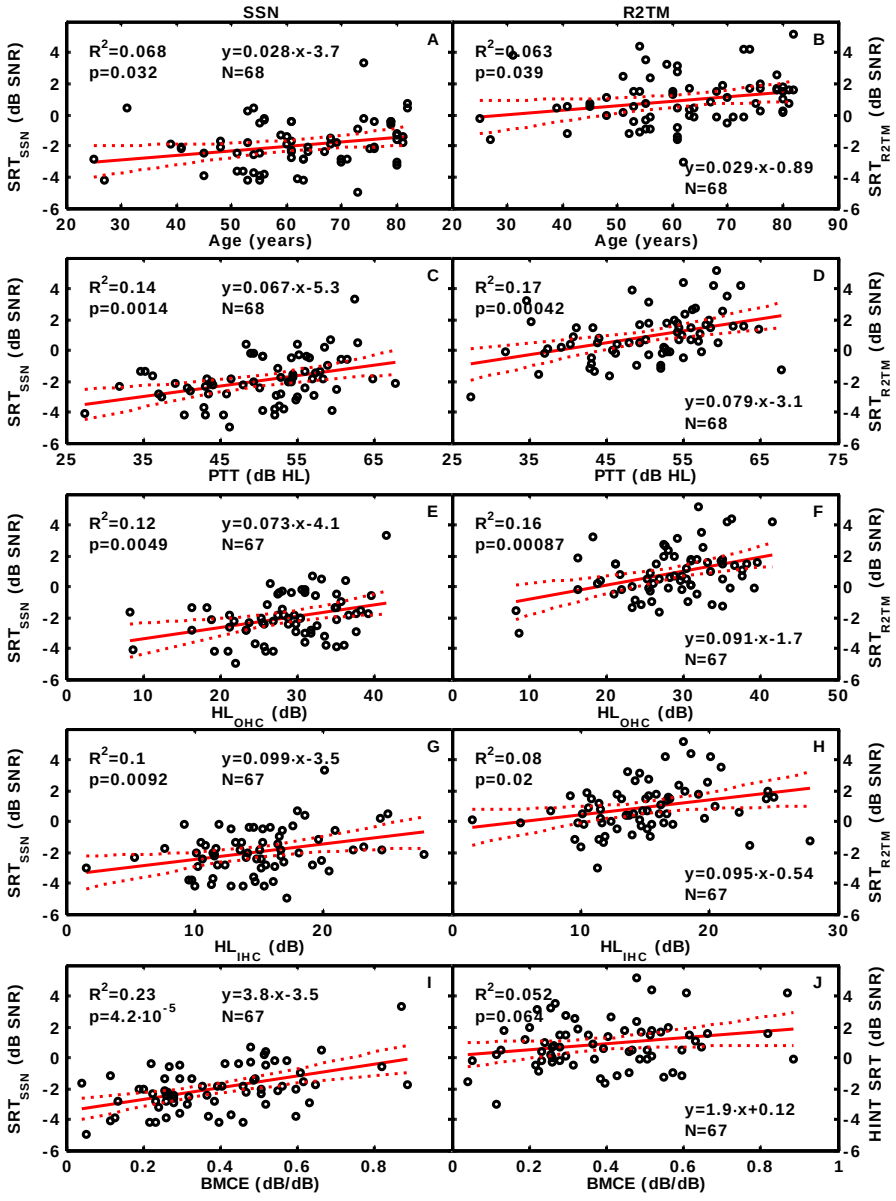

Figure 16. Aided speech reception thresholds for SSN (left column) and R2TM (right column) against across-frequency SII-weighted predictor variables. Each row is for a different predictor (age, PTT, HL_{OHC}, HL_{IHC} and BMCE) as indicated in the abscissa of each panel. Solid lines depict linear regression lines; dashed lines depict the 5 and 95% confidence interval of the regression line. The upper left inset in each panel informs of the proportion of variance of aided HINT SRTs (R^2) explained by the different predictors and the probability (p) for the value to occur by chance. The lower inset presents the regression equation and the number of cases (N). *Note*. SRT = speech reception threshold; SSN = speech-shaped noise; R2TM = time-reversed two-talker masker; SII = speech-intelligibility index; HL_{OHC}: contribution of cochlear gain loss to the audiometric loss; HL_{IHC}: contribution of inner hair cell dysfunction to the audiometry loss; BMCE = basilar-membrane compression exponent; HINT = hearing-in-noise test.

PAIRWISE PEARSON CORRELATIONS

Table 7 shows squared Pearson correlation coefficients (R^2 values) for pairs of variables. HL_{OHC} and HL_{IHC} were significantly correlated with PTT but were uncorrelated with each other. This supports one of our hypotheses (and the idea put forward elsewhere) that listeners with similar audiometric losses can suffer from different degrees of mechanical cochlear gain loss (e.g., Johannesen et al., 2014; Lopez-Poveda and Johannesen, 2012; Lopez-Poveda, Johannesen, and Merchán, 2009; Moore and Glasberg, 1997; Plack, Drga, and Lopez-Poveda, 2004).

Table 7. Squared pairwise Pearson correlations (R^2) and significance levels (p) between potential predictors and aided SRTs for SSN and R2TM. The p-values in the diagonal indicate the probability for a non-Gaussian distribution of the corresponding variable. Statistical significance ($p < 0.05$) is indicated with bold font.

		Age	PTT	HL_{OHC}	HL_{IHC}	BMCE	SRT_{SSN}	SRT_{R2TM}
Age (years)	R^2	-	0.01	0.02	0.00	0.02	**0.07**	**0.06**
	p	0.40	0.48	0.28	0.62	0.22	**0.032**	**0.039**
PTT (dB HL)	R^2	-	-	**0.63**	**0.30**	**0.15**	**0.14**	**0.17**
	p	-	0.088	**$8.9\cdot10^{-16}$**	**$1.4\cdot10^{-6}$**	**$1.0\cdot10^{-3}$**	**$1.4\cdot10^{-3}$**	**$4.2\cdot10^{-4}$**
HL_{OHC} (dB)	R^2	-	-	-	0.01	**0.39**	**0.12**	**0.16**
	p	-	-	0.25	0.50	**$1.5\cdot10^{-8}$**	**$4.9\cdot10^{-3}$**	**$8.7\cdot10^{-4}$**
HL_{IHC} (dB)	R^2	-	-	-	**-**	0.00	**0.10**	**0.08**
	p	-	-	-	**0.031**	0.76	**$9.2\cdot10^{-3}$**	**0.020**
BMCE (dB/dB)	R^2	-	-	-	-	**-**	**0.23**	0.05
	p	-	-	-	-	**0.043**	**$4.2\cdot10^{-5}$**	0.064
SRT_{SSN} (dB SNR)	R^2	-	-	-	-	-	-	**0.51**
	p	-	-	-	-	-	0.17	**$1.1\cdot10^{-11}$**
SRT_{R2TM} (dB SNR)	R^2	-	-	-	-	-	-	-
	p	-	-	-	-	-	-	0.31

BMCE was positively correlated with PTT and HL_{OHC}, indicating that the greater the audiometric loss or the loss of cochlear gain, the more linear (greater BMCE) the cochlear input/output curves. The positive correlation between BMCE and PTT appears inconsistent with earlier studies that reported no correlation between those two variables (Plack et al., 2004). Indeed, in Chapter

3 (top panels in **Figure 9**) we have reported no correlation between BMCE and audiometric loss based on the same data used to compute the correlations in **Table 7**. Differences in the data analyses might explain this discrepancy. First, the results in Chapter 3 or those reported by Plack et al. (2014) were based on frequency-by-frequency correlation analyses, whereas the correlation in **Table 7** is based on across-frequency SII-weighted averages (see Material and Methods). Second, BMCE was set here to 1 dB/dB whenever the audiometric loss was so high that a corresponding input/output curve could not be measured, something that possibly biased and increased the correlation slightly.

POTENTIAL PREDICTORS OF SPEECH-IN-NOISE INTELLIGIBILITY

Table 7 shows that all of the independent variables used in the present study were significantly correlated with SRT_{SSN} and SRT_{R2TM}, except for BMCE which was significantly correlated with SRT_{SSN} only. Therefore, virtually all of them could in principle be related to the measured SRTs. **Figure 16** shows scatter plots of SRT_{SSN} (left) and SRT_{R2TM} (right) against each of the six predictor variables (one variable per row), together with linear regression functions (fitted by least squares) and corresponding statistics. The plots suggest a linear relationship between each of the predictors and the aided SRTs. PTT explained slightly more SRT_{R2TM} variance ($R^2 = 0.17$) than SRT_{SSN} variance ($R^2 = 0.14$; compare **Figure 16C** and **Figure 16D**. This trend and values are consistent with those reported by Peters et al. (1998), who found R^2 values in the range of 0.07 to 0.11 for SSN and 0.11 to 0.25 for fluctuating maskers, although they did not specifically use R2TMs (see their Table IV).

Figure 16 suggests that PTT, HL_{OHC}, and HL_{IHC} had only a small influence on aided SRTs, as the largest amount of variance explained by any of these three predictors for either of the two SRTs was 17%; this was the variance in SRT_{R2TM} predicted by PTT (**Figure 16D**). For both SRT_{SSN} and SRT_{R2TM}, HL_{OHC} and HL_{IHC} predicted less variance than PTT, which suggests that specific knowledge about the proportion of the PTT that is due to cochlear mechanical gain loss (HL_{OHC}) or other uncertain factors (HL_{IHC}) does not provide much more information than the PTT alone about aided speech-in-noise intelligibility deficits.

BMCE predicted 23% of SRT_{SSN} variance (**Figure 16I**) but was *not* a significant predictor of SRT_{R2TM} (**Figure 16J**). This suggests that residual cochlear compression could be more important for understanding speech in steady than in fluctuating backgrounds.

STEPWISE MLR MODELS

Stepwise MLR models for SRT_{SSN} and SRT_{R2TM} are shown in **Table 8.** The model for aided SRT_{SSN} includes only those predictors whose contribution to the predicted variance was statistically significant. We note that we have included age as a predictor in the SRT_{R2TM} model because its contribution just missed statistical significance (p = 0.053). For each model, the predictors' priority order was established according to how much the corresponding predictor contributed to the predicted variance (higher priority was given to larger contributions).

Table 8. Stepwise MLR models of aided SRT_{SSN} and SRT_{R2TM}. Columns indicate the predictor's priority order and name, the regression coefficient, the *t*-value and corresponding probability for a significant contribution (*p*), and the accumulated proportion of total variance explained (Accum. R^2), respectively. The priority order reflects how much the corresponding predictor contributed to the predicted variance (higher priority is given to larger contributions). The accumulated R^2 is the predicted variance adjusted for the number of variables included in the regression model.

Priority	Predictor	Coefficient	*t*-value	*p*	Accum. R^2
		SRT_{SSN}			
n/a	Intercept	–7.7	–8.0	4.1×10^{-11}	-
1	BMCE	3.46	4.5	3.2×10^{-5}	0.22
2	HL_{IHC}	0.104	3.4	1.0×10^{-3}	0.32
3	Age	0.031	2.9	5.8×10^{-3}	0.39
		SRT_{R2TM}			
n/a	Intercept	–4.45	–3.5	8.9×10^{-4}	-
1	PTT	0.076	3.6	6.0×10^{-4}	0.195
2	Age	0.025	1.97	0.0536	0.26

The top part of **Table 8** shows that, in the MLR model for aided SRT_{SSN}, the most significant predictor was cochlear compression (BMCE), which explained 22% of the SRT_{SSN} variance, followed by HL_{IHC} and age, which explained 10% and 7% more of the predicted variance, respectively. The model predicted a

total of 39% of the SRT_{SSN} variance. Including PTT or HL_{OHC} as additional predictors did not increase the variance predicted by the model. Also, despite the correlation between HL_{OHC} and BMCE ($R^2 = 0.39$, **Table 7**), these two variables could not be interchanged in the MLR model. In other words, HL_{OHC} alone explained less variance that BMCE alone. Indeed, BMCE remained as a significant predictor of SRT_{SSN} when HL_{OHC} was included as the first predictor in the stepwise approach but HL_{OHC} became a non-significant predictor as soon as BMCE was included in the model.

The MLR model for aided SRT_{R2TM} was strikingly different from the model for SRT_{SSN} (compare the top and bottom parts of **Table 8**). The most significant predictor of SRT_{R2TM} was PPT, which explained 19.5% of the SRT_{R2TM} variance, followed by age, which explained 6.5% more of the variance. Altogether, the model accounted for 26% of the SRT_{R2TM} variance. Neither HL_{OHC} or BMCE, the two indicators of cochlear mechanical dysfunction, was found to be a significant predictor of SRT_{R2TM}. HL_{IHC} did not increase the variance predicted by this model.

6. DISCUSSION

BEHAVIORAL ESTIMATES OF THE CONTRIBUTION OF INNER AND OUTER HAIR CELL DYSFUNCTION TO INDIVIDUALIZED AUDIOMETRIC LOSS

One aim of the present thesis was to assess to what extent the audiometric loss is due to a reduction in cochlear mechanical gain (i.e., OHC dysfunction), and/or to an additional component, referred here to as IHC dysfunction. A second aim was to investigate the frequency distribution of the two potential contributions. A third aim was to investigate the degree of variability of the two contributions across listeners. Our approach was based on the analysis of behaviorally inferred cochlear I/O curves proposed by Lopez-Poveda and Johannesen (2012).

Regarding the first and second aims, results for Type 1 I/O curves (i.e., for curves with a CT) suggest that on average IHC and OHC dysfunction contribute 30–40 and 60–70% to the audiometric loss, respectively, and that these percentages hold approximately constant across the frequency range from 500 Hz to 6 kHz (**Figure 6**). Regarding the third aim, results suggest that the proportion of the audiometric loss attributed to cochlear gain loss can vary largely across listeners with similar hearing losses, without a clear frequency pattern (**Figure 8**). Cases for which audiometric thresholds could be explained exclusively in terms of IHC dysfunction (Type 3 I/O curves) or in terms of cochlear gain loss (points in the diagonal region of **Figure 7**) were comparatively more numerous at low than at high frequencies (**Table 4**). The large majority of cases, however, were consistent with mixed OHC/IHC dysfunction, even though in some of these cases (Type 3 I/O curves) cochlear

gain loss was unlikely to contribute to the audiometric loss (**Table 4**). Total cochlear gain loss (i.e., linear I/O curves), occurred more frequently at high frequencies than at low frequencies (**Table 4**).

POTENTIAL METHODOLOGICAL SOURCES OF BIAS

On the accuracy of the TMC method for estimating I/O curves

In inferring I/O curves from TMCs, the assumption has been made that the post-mechanical rate of recovery from forward masking is independent of masker frequency and level (Nelson et al., 2001). Evidence exists, however, that for NH listeners the recovery rate is twice as fast for masker levels below around 83 dB SPL than for higher masker levels (Wojtczak and Oxenham, 2009). This level effect, however, does not occur for HI listeners (Wojtczak and Oxenham, 2010). There also exists evidence that the recovery rate might be slower at low (≤1 kHz) than at high probe frequencies (Stainsby and Moore, 2006), although this evidence is controversial (Lopez-Poveda and Alves-Pinto, 2008). Lopez-Poveda and Johannesen (2012) discussed that if these assumptions did not hold, Type 1 I/O curves (i.e., curves with a CT) would lead to larger HL_{IHC} and smaller HL_{OHC}. In the present context, this means that if the assumptions were not valid, the contribution of HL_{IHC} to the total hearing loss might be higher than reported in **Figure 6**.

However, based on the analysis of TMCs for HI listeners with presumably linear BM responses described in Chapter 4, we can conclude that forward-masking recovery is independent of probe frequency and of masker level, hence that it is reasonable to use a TMC for a high-frequency probe and a low-frequency masker as a linear reference to infer cochlear compression at lower frequencies. In other words, the results from the analysis reported in Chapter 4 support the estimates of cochlear mechanical dysfunction reported in Chapter 3 (see also the Discussion below).

Ambiguity of linear I/O curves

Linear I/O curves have been assumed indicative of total cochlear gain loss. This assumption may be inaccurate sometimes. Assuming that cochlear I/O curves become linear at high input levels (something still controversial, Robles and Ruggero, 2001, pp. 1308–1309), for cases with substantial IHC dysfunction, the

mechanical cochlear response at the probe detection threshold might be so much higher with respect to NH that only the high-level linear segment of the I/O curve can be measured (e.g., Figure 1D of Lopez-Poveda and Johannesen, 2012). Hence, linear I/O curves at high input levels may indicate two different things: total cochlear gain loss or substantial IHC dysfunction. It is not possible to distinguish between these two cases. Therefore, some of the cases presently classified as "total cochlear gain loss" (or total OHC dysfunction) may actually reflect substantial IHC dysfunction.

An arbitrary slope criterion of 0.75 dB/dB has been used to separate Type 2 from Type 3 I/O curves. A sensitivity analysis was done to test to what extent results depended on the slope criterion value and we found that only five out of the 325 I/O curves would change type if the slope criterion were varied from 0.6 to 1 dB/dB. Therefore, I/O curve classification seems rather insensitive to slope criterion within these limits.

The impact of using a mean linear-reference TMC for some cases

A linear reference TMC could not be measured for eight participants (four of them from the study of Lopez-Poveda and Johannesen, 2012) because their hearing losses at the linear reference probe frequencies (**Table 1**) were so high that masker levels would have exceeded the maximum output level of our system. I/O curves for these cases were inferred using a mean linear reference TMC from all other subjects (see Chapter 2. Material and Methods). It is unlikely that this methodological difference affected the main results. First, CTs inferred using the mean linear reference TMC were within 5 dB of corresponding estimates inferred using the variant TMC method of Lopez-Poveda and Alves-Pinto (2008), a method that does not require a linear reference TMC (results not shown). Second, the number of I/O curves inferred using a mean linear reference TMC was only a very small fraction of the total number of I/O curves used in the present study.

Cochlear gain for NH listeners and total OHC loss

Linear I/O curves were regarded as indicative of total cochlear gain loss (**Figure 4**, and **Figure 5**). For these cases, HL_{OHC} was set equal to the mean cochlear gain of the reference, NH group. If the latter were inaccurate, this could have affected the present estimates of HL_{OHC} (i.e., the number and

position of blue crosses in **Figure 7**). Gain for the NH group was calculated as described in Chapter 3 (section 'I/O Curve Analyses and Taxonomy') and one might argue that this method underestimated gain for those NH I/O curves with absent CT or RLT; that is, for I/O cures that were still compressive at the lowest or the highest input levels in the I/O curve. The present NH gain values at high frequencies, however, compare well with previously reported values inferred using different psychoacoustical methods and with values inferred from direct BM recordings. For example, at 4 kHz, mean gain was 42.7 dB hence comparable to the value (43.5 dB) reported by Plack et al. (2004). Plack et al. estimated gain as the difference between the masker levels of the linear-reference and on-frequency TMCs for the shortest gap, while gain was defined here as the sensitivity difference for low and high input levels (see Ruggero et al., 1997 for a discussion of different gain definitions). Gain for the present NH group would have been 48.9 dB had it been calculated using the definition of Plack et al. (2004), hence slightly higher than the value of Plack et al. The present NH gain compares well also with the value (35 dB at 6 kHz) that would be obtained from the I/O curves in Figure 2 of Oxenham and Plack (1997) that were inferred using a different psychoacoustical method known as growth of forward masking. Also, the present NH gain values at 4 kHz are within the value range suggested by direct basal BM recordings (range = 19–62 dB; median = 40 dB; mean = 38 dB; **Table 1** of Robles and Ruggero, 2001). Altogether, this suggests that the present high-frequency NH gain values were reasonable.

Direct BM recording in animals suggest that cochlear gain is less for apical than for basal BM regions although it is possible that the difference is partly due to damage of apical cochlear mechanics during experimental recordings. For example, the change of chinchilla BM sensitivity at the characteristic frequency between low and high input levels is 10–20 dB at 500–800 Hz compared to 50 dB at 8–9 kHz (Tables 2, 3 in Robles and Ruggero, 2001). Previous psychoacoustical reports in humans using other methods and assumptions also suggest less gain at low frequencies but do not provide quantitative estimates (Plack et al., 2008). Gain estimates for the present NH group were 35.2 dB at 500 Hz and 42.7 dB at 4 kHz. The frequency trend in the present results is thus qualitatively consistent with direct BM observations, and quantitative differences might be due to differences in cochlear tonotopic mappings across

species. If, however, the post-mechanical rate of recovery from forward masking were after all faster at lower frequencies (see the previous sections and Chapter 4), then cochlear gain would be smaller than reported here and the pattern of results would become more consistent with the animal data.

In summary, the NH gain values used here to quantify HL_{OHC} for cases of total OHC loss (linear I/O curves) seem reasonable at high frequencies but are less certain at low frequencies.

Incidentally, it is noteworthy that the present NH gain increased from 35.2 dB at 500 Hz to 43.5 dB at 1 kHz (unpaired, equal variance, *t*-test, $p = 0.014$) and then gain remained constant at higher frequencies (42.7 dB at 4 kHz). This pattern differed slightly from that reported by Johannesen and Lopez-Poveda, (2008), from where some of the present NH data were taken. Indeed, in that study, gain increased gradually with increasing frequency from 37 dB at 500 Hz to 55 dB at 4 kHz (see their Figure 11A). This discrepancy is almost certainly due to methodological differences. First, the two studies used different definitions of gain; Johannesen and Lopez-Poveda (2008) calculated gain as the difference between the RLT and CT. Second, the present NH data combined data from the 10 participants that took part in the study of Johannesen and Lopez-Poveda (2008) plus data for five more NH participants from Lopez-Poveda and Johannesen (2009); the latter contributed data particularly at 0.5 and 1 kHz. Third, Johannesen and Lopez-Poveda (2008) fitted their I/O curves with a third-order polynomial, which "forces" an RLT when a CT is present because the slopes of a third-order polynomial are identical below and above its inflection point. Indeed, fewer of the I/O curves from the study of Johannesen and Lopez-Poveda (2008) retained an RLT when they were re-analyzed using the present fitting approach.

The influence of conductive hearing loss on the results

Participants were controlled for conductive hearing loss. Nonetheless, their air-bone gaps could have differed by ≤15 dB at one frequency and/or ≤10 dB at any other frequency (see Chapter 2. Material and Methods). Small conductive losses might have increased probe absolute threshold and hence TMC masker levels by an amount equal to the conductive loss at the corresponding probe frequencies. The influence on the inferred I/O curve would be an upward

vertical shift of the I/O curve equal to the conductive loss at the frequency of the linear reference probe and a rightward horizontal shift equal to the conductive loss at the frequency of the on-frequency masker. The CT would be affected only by the horizontal shift. Therefore, conductive loss at the particular frequency might lead to an overestimate of HL_{OHC} at that frequency. Pearson's correlation between HL_{OHC} and air-bone gap was significant only at 1 kHz and indicated decreasing HL_{OHC} for increasing air-bone gap (results not shown). The direction of the effect was therefore opposite to the presumed effect of conductive hearing loss on HL_{OHC} and hence we concluded that conductive loss was unlikely to affect mean HL_{OHC} estimates in **Figure 6**.

The potential influence of dead regions on the results

A "dead region" is "a region in the cochlea where the IHCs and/or neurons are functioning so poorly that a tone which produces peak BM vibration in that region is detected via an adjacent region where the IHCs and/or neurons are functioning more efficiently" (p. 272 in Moore, 2007). In principle, dead regions could affect TMC measures as the probe presented in a dead region would be detected at a cochlear place removed from the probe place: e.g., at a place where the on-frequency masker might be subject to a compression regime different from compression at the normal probe place. For example, if the 4-kHz cochlear region was dead, a 4-kHz probe might be detected at the 2-kHz cochlear region where a 1.6-kHz (off-frequency) masker, which is typically regarded as a linear-reference condition, might be actually subject to significant compression.

Dead regions occur almost always for hearing losses above ~60 dB HL (Table 1 in Vinay and Moore, 2007) and the present listeners were roughly selected to have hearing losses <80 dB HL to be able to measure TMCs for a majority of test frequencies (**Figure 1**). Despite this, TMCs could not be measured for the higher losses. Of the 325 measured I/O curves, the number that may have been affected by dead regions can be roughly estimated from the data in Table 1 of Vinay and Moore (2007) (note that their data goes to 4 kHz only and we have assumed that the incidence of dead regions is identical at 4 and 6 kHz). Our analysis revealed that the expected incidence of dead regions was one, two and two at 2, 4, and 6 kHz, respectively. These numbers are so low that they are unlikely to have biased the reported HL_{OHC} and HL_{IHC}.

COMPARISON WITH EARLIER STUDIES

Based on our analysis of Type 1 I/O curves, we have shown that HL_{OHC} is on average 60–70% of HL_{TOTAL} across the frequency range from 0.5 to 6 kHz. This number is roughly consistent with that reported by earlier studies for more restricted frequency ranges, mostly at 4 kHz (Plack et al., 2004; Lopez-Poveda and Johannesen, 2012). It is, however, slightly lower than the 80–90% value reported elsewhere based on loudness models (Moore and Glasberg, 1997). Jürgens et al. (2011) showed that the two approaches (loudness model and TMCs) should give similar results. Therefore, the reason for this difference is uncertain.

We have also shown that even though the percentage of cases for which HL_{IHC} accounts entirely for HL_{TOTAL} (the percentage of Type 3 I/O curves) or the percentage of cases for which $HL_{OHC} \sim HL_{TOTAL}$ (the percentage of pure OHC dysfunction) are small, they are both larger for frequencies ≤1 kHz and decrease with increasing frequency (**Table 4**). To the best of our knowledge, these trends have not been reported explicitly before, possibly due to the use of small sample sizes in earlier studies, but are not without precedent. For example, Moore and Glasberg (1997) used a model of loudness growth to estimate HL_{IHC} and found that it increased with decreasing frequencies for three listeners. Likewise, Jepsen and Dau (2011) reported greater HL_{IHC} at lower frequencies for a few subjects, although their average results were still consistent with the common notion that the most typical functional deficit is the loss of mechanical gain in the cochlear base.

An important distinction between the present and earlier analyses is that here, HL_{IHC} and HL_{OHC} were not always regarded as mutually exclusive, additive contributions to HL_{TOTAL}. Instead, the possibility has been contemplated that Equation (1) does not hold for cases where IHC dysfunction is so significant that it makes it impossible to measure a CT. In these cases, it was assumed that HL_{TOTAL} may be explained fully in terms of HL_{IHC} even though concomitant cochlear gain loss did probably occurred (**Figure 7**, bottom).

ON THE VALIDITY OF THE TMC METHOD FOR INFERRING COCHLEAR INPUT/OUTPUT CURVES

Another specific aim of the present thesis was to verify the assumptions of the psychoacoustical TMC method for inferring cochlear mechanical I/O curves in humans. To accomplish this goal, we have investigated forward-masking recovery in a subset of eight HI listeners carefully selected to have absent or nearly absent DPOAEs over the range of primary L_2 levels from 35 to 70 dB SPL and over the range of primary f_2 frequencies from 500 to 4000 Hz (**Table 5**). The main findings were:

1. For most cases, forward-masking recovery appeared constant across frequencies and levels; for some cases, however, forward-masking recovery decreased with increasing frequency and with increasing level (**Figure 11** and **Figure 12**).
2. For those cases in which forward-masking recovery decreased with increasing frequency, forward-masking recovery also decreased with increasing level (**Figure 13**).
3. On average, however, forward-masking recovery did not change significantly across the range of probe frequencies (500–6000 Hz) or levels (70–100 dB SPL) tested.
4. For some individuals, forward-masking recovery measured using a fixed high-frequency probe was slower for low off-frequency maskers than for on-frequency maskers, while for others forward-masking recovery was comparable for on- and off-frequency maskers (**Figure 15**).
5. On average, however, forward-masking recovery was not significantly different for on- and off-frequency maskers.

LIMITATIONS OF THE PRESENT DATA

Assuming that the absence of DPOAEs for levels below 70 dB SPL is indicative of linear cochlear responses, the present results would suggest that forward-masking recovery is frequency- and level-independent on average and for a majority of individuals but not for all individuals. One might argue, however, that the absence of DPOAEs below 70 dB SPL does not necessarily imply linear

responses at the higher levels involved in the present TMCs (70–100 dB SPL, **Figure 10**). In other words, one might argue that the present TMCs could still be affected by compression. We could not rule this possibility out experimentally because the distortion generated by our DPOAE measurement system was too high at levels L_2 >70 dB SPL to reliably assess the presence or absence of cochlear-generated DPOAEs at those levels. (We note that this limitation is common to most DPOAE measurements systems; see, e.g., Dorn et al., 2001.) In primates, however, cochlear gain, defined as the cochlear sensitivity at the CF pre-mortem or post-mortem, is about 40 dB at 6.5 to 8 kHz (see Table 1 of Robles and Ruggero, 2001). The subset of participants used to verify the assumptions of the TMC method in Chapter 4 had hearing losses of at least 40 dB and typically greater at all test frequencies (**Figure 11** and **Figure 12**). Therefore, it is not unreasonable to assume that cochlear responses were linear for a majority of those participants and conditions.

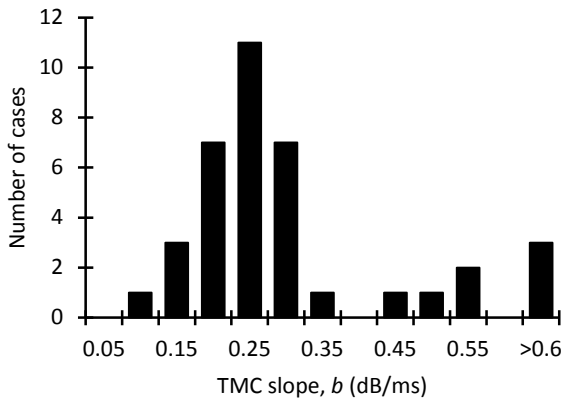

Figure 17. Histogram of on-frequency TMC slopes for the subset of participants with presumably linear cochlear responses used in Chapter 4. Note that the total number of cases is 46 (8 participants × 6 frequencies minus two TMCs that could not be measured for S116,

Table 6).

On the other hand, residual compression would lead to abnormally steep TMCs (Nelson et al., 2001). **Figure 17** shows a histogram of the present on-frequency TMC slopes. The figure clearly suggests two groups of TMCs: a normally distributed group with slopes ≤0.35 dB/ms and a group with higher slopes. It is tempting to speculate that the former group (with shallower slopes) possibly corresponds to TMCs unaffected by compression while the latter group (with steeper slopes) corresponds to TMCs that might be affected by residual compression. The latter group includes the steeper TMCs for participants S054, S116, and S121. These three participants had *sloping* audiograms; that is, greater losses at high than at low frequencies (left panels in **Figure 11** and **Figure 12**). Coincidentally, S054 and S121 are two of three cases for whom TMC slopes decreased with increasing frequency (S012, S054, and S121). If the present data were reanalyzed omitting slopes greater than 0.35 dB/ms, there would remain only one case (S012) for whom TMC slope would still change with frequency or level; for all other cases, TMC slope would be approximately constant across frequencies and levels. Therefore, it is tempting to conclude that TMC slope decreased with increasing frequency or level for some of the participants used in the analysis of Chapter 4 because they had residual compression and that in the absence of compression forward-masking recovery would be constant across frequencies and levels.

We have carried over the assumption from seminal reports that the TMC slope depends simultaneously on the amount of BM compression affecting the masker *and* on the rate of recovery from the internal (post-BM) masker effect (Nelson et al., 2001). Recent physiological, psychophysical, and modeling studies have shown or suggested sources of post-BM nonlinearity in the cochlea on responses that provide the input to the auditory nerve. For example, a recent study has shown that the motion of the reticular lamina shows more compression than the corresponding BM motion (Chen et al., 2011), indicating that the motion of the inner hair cell (IHC) stereocilia is not directly coupled to BM motion as is commonly thought (Guinan, 2012). In addition, Lopez-Poveda et al. (2005) noted that reference TMCs are shallower for some HI than for NH listeners and argued that this could be due to frequency-unspecific compression in the IHCs that is present in NH listeners but reduced or absent in HI listeners. This idea that IHC nonlinearities could be steepening the TMC

slope has been later supported by model simulations of IHC potentials (Lopez-Poveda and Eustaquio-Martin, 2006) and by other psychoacoustical studies (Plack and Arifianto, 2010). This recent evidence suggests that in addition to BM compression, the slope of a TMC may also be affected (steepened) by compression added by the reticular lamina or the IHC. In the present context, this implies that even if the present TMCs were unaffected by BM compression, they might still be affected by post-BM compression. In that case, the present analysis would still be correct if the post-BM compression were comparable across all the conditions tested here, something that is admittedly uncertain.

Of course, the TMC method was designed to infer BM compression specifically. Because it consists of comparing the slopes of two TMCs measured with different frequencies and because there is no evidence (to our knowledge) that post-BM compression is frequency selective, post-BM compression effects on individual TMCs would be cancelled in the comparison and hence the TMC method may still be useful for its purpose.

RELATIONSHIP WITH EARLIER STUDIES

Using an approach similar to the approach conducted in Chapter 4, Stainsby and Moore (2006) concluded that forward-masking recovery was negatively correlated with frequency. The present study uses a larger sample selected with more rigorous DPOAE criteria and a different analysis. The present results suggest that the trends reported by Stainsby and Moore could be due to their participants having residual compression at low frequencies.

IMPLICATIONS FOR ESTIMATING COMPRESSION FROM TMCS

In inferring peripheral cochlear compression from TMCs, it is assumed that the post-mechanical (or 'compression free') rate of recovery from the masker effect is independent of probe frequency and of masker level (Lopez-Poveda et al., 2003; Nelson et al., 2001). The mean results reported in Chapter 4 support the assumptions of the TMC method. This is not to say, however, that it would be accurate to infer cochlear compression from comparisons of on-frequency and reference TMC slopes in all cases. Efferent effects might affect forward-masking recovery in NH listeners or in HI listeners with residual OHC function (Jennings, Strickland, and Heinz, 2009; Wojtczak and Oxenham, 2009;

Wojtczak and Oxenham, 2010; Yasin et al., 2013). Therefore, that post-mechanical forward-masking recovery is generally frequency- and level-independent for hearing-impaired listeners with absent compression does not imply that compression estimates inferred with the standard TMC method are accurate. Wojtczak and Oxenham (2009) showed that for NH listeners, forward-masking recovery is slower for levels above than below 83 dB SPL. They reasoned that the TMC method can overestimate compression by approximately a factor of two when reference TMCs involve levels above 83 dB SPL (i.e., in those cases, the actual compression exponent could be half of the inferred value). Wojtczak and Oxenham argued that this was possibly due to high-level off-frequency masker activating the MEMR.

The results in Chapter 4 suggest that something similar may also happen for HI listeners. Reference TMCs had shallower slopes than on-frequency TMCs measured with the same probe frequency (**Figure 15**). One explanation for this result might be that despite our precautions, the subset of participants used in our analysis still had residual compression at high frequencies despite our efforts to use participants with linear cochlear responses. On the other hand, the reference TMCs for those participants always involved values higher than 90 to 95 dB SPL (their L_0 is illustrated by the rightmost points in the **Figure 15**), hence comparable with the threshold levels of activation of the MEMR for the present participants (shown in **Table 2**). Indeed, the actual activation threshold of the MEMR can be 8 to 14 dB lower than estimated with clinical methods similar to the one employed here (Feeney, Keefe, and Marryott, 2003; Neumann, Uppenkamp, and Kollmeier, 1996). The MEMR can be elicited by sounds with a duration of 116 ms (Keefe, Fitzpatrick, Liu, Sanford, and Gorga, 2010), which is approximately half the duration of the present maskers. The MEMR hinders the transmission of frequencies between 300 and 1000 Hz and has no significant effect on the transmission of frequencies higher than 2000 Hz but *facilitates* the transmission of frequencies between 1000 and 2000 Hz (see the top panels in Figure 1 of Feeney et al., 2003 and in Figure 2 of Feeney, Keefe, and Sanford, 2004). The maskers used to measure the reference TMCs were long enough that the MEMR could be active during the course of the masker and had frequencies (800–2000 Hz) within the range of the facilitating effect of MEMR. Therefore, it is conceivable that MEMR facilitated the transmission of the reference maskers, thereby reducing the masker level at

the probe masked threshold. The MEMR would have a much lesser effect for corresponding on-frequency TMCs because the involved masker frequencies were higher than 2000 kHz, where the MEMR effect is negligible. Therefore, an alternative explanation for the shallower slopes of reference TMCs could be that forward-masking recovery did depend on masker level possibly due to the activation of the MEMR. If the latter explanation were correct, the data in **Figure 15** would indicate that compression inferred from comparisons of on-frequency and reference TMCs can be twice as much as the actual compression for HI listeners whose reference TMCs involve masker levels above the individual threshold of activation of the MEMR.

THE INFLUENCE OF COCHLEAR MECHANICAL DYSFUNCTION ON SPEECH-IN-NOISE INTELLIGIBILITY

The main aim of the present thesis was to assess the relative importance of cochlear mechanical dysfunction for the ability of HI listeners to understand individually amplified speech in SSN (SRT_{SSN}) and R2TM (SRT_{R2TM}) backgrounds. To this end, the main findings were:

1. For the present sample of HI listeners, age, PTT, and BMCE were virtually uncorrelated with each other (**Table 7**) and yet they were significant predictors of SRTs in noisy backgrounds (**Table 8**).
2. Residual cochlear compression (BMCE) was the most important single predictor of SRT_{SSN}, while PPT was the most important single predictor of SRT_{R2TM} (**Figure 16**, and **Table 8**).
3. Cochlear mechanical gain loss (HL_{OHC}) was correlated with SRT_{SSN} and SRT_{R2TM} (**Table 7**) but did not improve the MLR models of SRT_{SSN} or SRT_{R2TM} once the previously mentioned predictors were included in the models.
4. Age was a significant predictor of SRT_{SSN} and SRT_{R2TM}, and it was virtually independent of BMCE (**Table 7**).

The absence of a correlation between age and PTT in the present sample of HI listeners was surprising, given the well-established relationship between those two variables (reviewed by Gordon-Salant, Frisina, Popper, and Fay, 2010). One possible explanation is that our participants were required to be hearing-

aid candidates (something necessary for an aspect of the study not reported here) while having mild-to-moderate audiometric losses in the frequency range from 0.5 to 6 kHz, something necessary to infer HL_{OHC} estimates using behavioral masking methods (Chapter 3). Thus, it is possible that their hearing losses spanned a narrower range than would be observed across the same age span in a random sample.

The finding that PTT and BMCE were correlated with speech-in-noise intelligibility was expected (**Table 7**) for the reasons reviewed in the Introduction. A significant, though incidental aspect of the present study was, however, that for the present group of HI listeners those factors were uncorrelated or barely correlated with each other (**Table 7**) and yet they all affected intelligibility in different proportions for the two types of maskers (**Table 8**).

Of the two indicators used here to characterize cochlear mechanical dysfunction, cochlear gain loss (HL_{OHC}) was correlated with speech intelligibility in the two maskers tested (SSN and a R2TM), while residual compression (BMCE) was correlated with speech intelligibility in SSN only. The two indicators (HL_{OHC} and BMCE) were correlated with each other (**Table 7**). However, HL_{OHC} did not remain as a significant predictor of intelligibility for either of the two maskers when other variables were included in the MLR model, while BMCE was the most significant predictor of intelligibility only for SSN (**Table 8**). The present estimates of HL_{OHC} and BMCE are indirect and based on numerous assumptions (see Chapter 3 and Chapter 4). Assuming nonetheless that these estimates are reasonable, the present findings suggest that cochlear mechanical gain loss (HL_{OHC}) and residual compression (BMCE) are not equivalent predictors of the impact of cochlear mechanical dysfunction on intelligibility in SSN. This further suggests that residual compression might be more significant than cochlear gain loss, perhaps because the impact of HL_{OHC} on intelligibility may be compensated with linear amplification but the impact of BMCE may not.

The importance of compression for intelligibility in SSN appears inconsistent with the findings reported in some studies. For example, Noordhoek, Houtgast, and Festen (2001) found little influence of residual compression on the intelligibility of narrow-band speech centered on 1 kHz. Similarly, Summers,

Makashay, Theodoroff, and Leek (2013) reported that compression was not clearly associated with understanding intense speech (at a fixed level of 92 dB SPL) in steady noise. This inconsistency may be partly due to methodological differences across studies. First, Summers et al. assessed intelligibility using the percentage of sentences identified correctly for a fixed SNR rather than the SRT (in dB SNR). Second, and perhaps most importantly, although Summers et al. inferred compression from TMCs, as we did, they did not take into account important precautions that are necessary to infer accurate compression estimates using the TMC method. As explained in the Introduction, the TMC method is based on the assumption that cochlear compression may be inferred from comparisons of the slopes of TMCs unaffected by compression (linear references) with those of TMCs affected by compression. Summers et al. used different linear reference TMCs for different test frequencies and their linear references were TMCs for a masker frequency equal to 0.55 times the probe frequency. It has been shown that this almost certainly underestimates compression, particularly at lower frequencies (e.g., Lopez-Poveda and Alves-Pinto, 2008; Lopez-Poveda, Plack, and Meddis, 2003; see also Chapter 4). As a result, Summers et al. almost certainly underestimated compression, particularly for their NH listeners, something that might have contributed to hiding differences in compression across listeners with different audiometric thresholds.

For the present sample of HI listeners, BMCE was the most significant predictor of aided speech intelligibility in SSN, while PPT was the most significant predictor of aided intelligibility in a R2TM (**Table 8**). Hopkins and Moore (2011) investigated the effects of age and cochlear hearing loss on sensitivity to temporal fine structure (TFS), frequency selectivity, and speech reception in noise for a sample of NH and HI listeners. They reported that once absolute threshold was partialled out, TFS sensitivity was the only significant predictor of speech intelligibility in amplitude-modulated noise while auditory filter bandwidth was the only significant predictor of intelligibility in steady SSN (see their Table IV). Although not reported here, temporal processing abilities as indexed by frequency-modulation detection thresholds, was the most

significant predictor of intelligibility in a R2TM for the present participants[6] (see Johannesen et al., 2014). The present results combined with those of Johannesen et al. (2014) appear broadly consistent with those of Hopkins and Moore considering that auditory filter bandwidth is a psychoacoustical correlate of cochlear frequency selectivity (e.g., Evans, 2001; Shera, Guinan, and Oxenham, 2002) and thus an indicator of cochlear dysfunction.

Of course, peripheral compression (BMCE) and auditory filter bandwidth are both indirect and different behavioral indicators of cochlear dysfunction but are related. A behavioral study has shown that the auditory filter bandwidth increases as the compression decreases (Moore, Vickers, Plack, and Oxenham, 1999) and physiological studies have shown that OHC dysfunction reduces both cochlear frequency selectivity and compression (Ruggero et al., 1996). In the light of this evidence, the mechanism behind intelligibility in SSN for the present HI listeners might be poorer spectral separation of the speech cues due to increased filter bandwidth (Moore, 2007). It seems puzzling, however, that the same mechanism is not at least slightly involved in the intelligibility of speech in modulated noise (Hopkins and Moore, 2011) or R2TMs (present results).

The finding that age remained as a significant predictor of intelligibility after the effects of BMCE on SRT_{SSN} and of PPT on SRT_{R2TM} were partialled out suggests that age *per se* affects intelligibility in noise. This result is consistent with that of Füllgrabe, Moore, and Stone (2015), who showed that for audiometrically matched young and old listeners, age was a significant contributor for intelligibility in various types of maskers also after the effect of TFS sensitivity was accounted for.

[6] The importance of temporal processing skills for intelligibility was investigated in parallel to the work presented here and for the same set of HI listeners, and the results are reported in Johannesen et al. (2014).

7. CONCLUSIONS

1. For hearing-impaired listeners with cochlear input/output curves showing a compression threshold, inner hair cell and outer hair cell dysfunction contribute on average to 30–40 and 60–70% to the total audiometric loss, and these contributions are approximately constant across the frequency range from 0.5 to 6 kHz.
2. The individual variability of the relative contributions of inner hair cell and outer hair cell dysfunction to the audiometric loss is, however, large, particularly at low frequencies or for mild-to-moderate hearing losses.
3. The large majority of hearing-impaired listeners suffer from mixed inner hair cell and outer hair cell dysfunction, even though in some cases with presumably substantial inner hair cell dysfunction, any concomitant outer hair cell dysfunction does not contribute to the audiometric loss.
4. The percentage of cases for which the audiometric loss can be explained exclusively in terms of cochlear gain loss or of inefficient inner hair cell processes (i.e., cases of pure outer hair cell or inner hair cell dysfunction, respectively) is higher at frequencies ≤1 kHz and decreases gradually with increasing frequency.
5. The percentage of cases suffering from total cochlear gain loss (i.e., cases showing linear input/output curves) increases gradually with increasing frequency.
6. On the basis of the analysis of temporal masking curves for hearing-impaired listeners with presumably linear basilar membrane responses, we conclude that forward-masking recovery is independent of probe frequency and of masker level, hence that it is reasonable to

use a linear reference temporal masking curve for a high-frequency probe to infer cochlear compression at lower frequencies.

7. Linear reference temporal masking curves can be sometimes shallower than corresponding on-frequency temporal masking curves for identical probe frequencies. The reason is uncertain. It might occur when the masker used to measure the reference temporal masking curve is of sufficient duration and intensity to activate the middle-ear muscle reflex. Whatever the reason, basilar membrane compression could be overestimated in these cases by as much as a factor of two.
8. Estimated outer hair cell dysfunction (cochlear gain loss) is unrelated to the ability to understand audible speech in steady-state noise.
9. Residual cochlear compression is related to speech understanding in speech-shaped steady noise but not in a time-reversed two-talker masker.
10. Age per se reduces the intelligibility of speech in any of the two maskers tested here, regardless of absolute thresholds or cochlear mechanical dysfunction.

8. REFERENCES

AAO-HNS. (1993). American Academy of Otolaryngology – Head and Neck Surgery. *Bulletin* 16–17.

ANSI. (1996). S3.6 Specification for Audiometers. New York, NY: American National Standards Institute.

ANSI. (1997). S3.5 methods for calculation of the speech intelligibility index. New York, NY.

Bacon SP, Fay RR, Popper, AN. (2004). Compression: From Cochlea to Cochlear Implants. New York, NY: Springer-Verlag.

Baer T, Moore BCJ. (1994). Effects of spectral smearing on the intelligibility of sentences in the presence of interfering speech. *Journal of the Acoustical Society of America,* 95, 2277–2280.

Brown GJ, Ferry RT, Meddis R. (2010). A computer model of auditory efferent suppression: Implications for the recognition of speech in noise. *Journal of the Acoustical Society of America*, 127, 943–954.

Byrne D, Dillon H, Tran K, Arlinger S, Wilbraham K, Cox R, Ludvidsen C. (1994). An international comparison of long-term average speech spectra. *Journal of the Acoustical Society of America*, 96, 2108–2120.

Byrne D, Dillon H. (1986). The national acoustic laboratories' (NAL) new procedure for selecting the gain and frequency response of a hearing aid. *Ear and Hearing*, 7, 257–265.

Chen F, Zha D, Fridberger A, Zheng J, Choudhury N, Jacques SL, Wang RK, Shi X, Nuttall AL. (2011). A differentially amplified motion in the ear for near-threshold sound detection. *Nature Neuroscience*, 14, 770–774.

Chen GD, Fechter LD. (2003). The relationship between noise-induced hearing loss and hair cell loss in rats. *Hear. Res*. 177, 81–90.

Deng L, Geisler CD, Greenberg S. (1987). Responses of auditory-nerve fibers to multiple-tone complexes. *Journal of the Acoustical Society of America,* 82, 1989–2000.

Dorn PA, Konrad-Martin D, Neely ST, Keefe DH, Cyr E, Gorga MP. (2001). Distortion product otoacoustic emission input/output functions in normal-hearing and hearing-impaired human ears. *The Journal of the Acoustical Society of America*, 110, 3119–3131.

Eisenberg LS, Dirks DD, Takayanagi S, Martinez AS. (1998). Subjective judgements of clarity and intelligibility for filtered stimuli with equivalent speech intelligibility index predictions. *Journal of Speech, Language, and Hearing Research*, 41, 327–339.

Evans EF. (2001). Latest comparison between physiological and behavioral frequency selectivity. In A. J. M. Houtsma, A. Kohlraush, V. F. Prijs, R. Schoonhoven, and J. Breebaart (Eds.), *Physiological and psychophysical bases of auditory function* (pp. 382–387). Maastricht, The Netherlands: Shaker.

Feeney MP, Keefe DH, Marryott LP. (2003). Contralateral acoustic reflex thresholds for tonal activators using wideband energy reflectance and admittance. *Journal of Speech, Language, and Hearing Research*, 46, 128–136.

Feeney MP, Keefe DH, Sanford CA. (2004). Wideband reflectance measures of the ipsilateral acoustic stapedius reflex threshold. *Ear and Hearing*, 25, 421–430.

Festen JM, Plomp R. (1983). Relations between auditory functions in impaired hearing. *Journal of the Acoustical Society of America*, 73, 652–662.

Festen JM, Plomp R. (1990). Effects of fluctuating noise and interfering speech on the speech-reception threshold for impaired and normal hearing. *Journal of the Acoustical Society of America*, 88, 1725–1736.

Fletcher H, Galt R. (1950). Perception of speech and its relation to telephony. *Journal of the Acoustical Society of America*, 22, 89–151.

Füllgrabe C, Moore BCJ, Stone MA. (2015). Age group differences in speech identification despite matched audiometrically normal hearing: contributions from auditory temporal processing and cognition. *Frontiers in Aging Neuroscience*, 6, 347.

George EL, Festen JM, Houtgast T. (2006). Factors affecting masking release for speech in modulated noise for normal-hearing and hearing-impaired listeners. *Journal of the Acoustical Society of America*, 120, 2295–2311.

Gordon-Salant S, Frisina RD, Popper AN, Fay RR. (2010). The aging auditory system. New York, NY: Springer.

Goodman A. (1965). Reference zero levels for pure-tone audiometer. *ASHA*, 7, 262-263.

Gregan MJ, Nelson PB, Oxenham AJ. (2013). Behavioral measures of cochlear compression and temporal resolution as predictors of speech masking release in hearing-impaired listeners. *Journal of the Acoustical Society of America*, 134, 2895–2912.

Guinan JJ. (2010). Cochlear efferent innervation and function. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 18, 447–453.

Guinan JJ. (2012). How are inner hair cells stimulated? Evidence for multiple mechanical drives. *Hearing Research*, 292, 35–50.

Hopkins K, Moore BCJ. (2009). The contribution of temporal fine structure to the intelligibility of speech in steady and modulated noise. *Journal of the Acoustical Society of America*, 125, 442–446.

Hopkins K, Moore BCJ. (2010). The importance of temporal fine structure information in speech at different spectral regions for normal-hearing and hearing-impaired subjects. *Journal of the Acoustical Society of America*, 127, 1595–1608.

Hopkins K, Moore BCJ. (2011). The effects of age and cochlear hearing loss on temporal fine structure sensitivity, frequency selectivity, and speech reception in noise. *Journal of the Acoustical Society of America*, 130, 334–349.

Hornsby BWY, Ricketts TA. (2007). Directional benefit in the presence of speech and speech like maskers. *Journal of the American Academy of Audiology*, 18, 5–16.

Huarte A. (2008). The Castilian Spanish hearing in noise test. *International Journal of Audiology*, 47, 369–370.

Humes LE. (2002). Factors underlying the speech-recognition performance of elderly hearing-aid wearers. *Journal of the Acoustical Society of America*, 112, 1112–1132.

Jennings SG, Strickland EA, Heinz MG. (2009). Precursor effects on behavioral estimates of frequency selectivity and gain in forward masking. *Journal of the Acoustical Society of America*, 125, 2172–2181.

Jepsen ML, Dau T. (2011). Characterizing auditory processing and perception in individual listeners with sensorineural hearing loss. *J. Acoust. Soc. Am*. 129, 262–281.

Johannesen PT, Lopez-Poveda EA. (2008). Cochlear nonlinearity in normal-hearing subjects as inferred psychophysically and from distortion-product otoacoustic emissions. *Journal of the Acoustical Society of America*, 124, 2149–2163.

Johannesen PT, Pérez-González P, Lopez-Poveda EA. (2014). Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Frontiers in Neuroscience*, 8, 214.

Jürgens T, Kollmeier B, Brand T, Ewert SD. (2011). Assessment of auditory nonlinearity for listeners with different hearing losses using temporal masking and categorical loudness scaling. *Hearing Research*, 280, 177–191.

Keefe DH, Fitzpatrick D, Liu YW, Sanford CA, Gorga MP. (2010). Wideband acoustic-reflex test in a test battery to predict middle-ear dysfunction. *Hearing Research*, 263, 52–65.

Kim SH, Frisina RD, Frisina DR. (2006). Effects of age on speech understanding in normal hearing listeners: Relationship between the auditory efferent system and speech intelligibility in noise. *Speech Communication*, 48, 855–862.

Levitt H. (1971). Transformed up-down methods in psychoacoustics. *Journal of the Acoustical Society of America*, 49(Suppl. 2): 467–477.

Löhler J, Akcicek B, Wollenberg B, Schönweiler R, Verges L, Langer Ch, Machate U, Noppeney R, Schultz K, Kleeberg J, Junge-Hülsing B, Walther LE, Schlattmann P, Ernst A. (2015). *Eur Arch Otorhinolaryngol.* Sep; 272(9): 2135-42.

Lopez-Poveda EA, Alves-Pinto A. (2008). A variant temporal-masking-curve method for inferring peripheral auditory compression. *Journal of the Acoustical Society of America,* 123, 1544–1554.

Lopez-Poveda EA, Eustaquio-Martin A. (2006). A biophysical model of the inner hair cell: The contribution of potassium currents to peripheral auditory compression. *Journal of the Association for Research in Otolaryngology*, 7, 218–235.

Lopez-Poveda EA, Johannesen PT, Merchán MA. (2009). Estimation of the degree of inner and outer hair cell dysfunction from distortion product

otoacoustic emission input/output functions. *Audiological Medicine*, 7, 22–28.

Lopez-Poveda EA, Johannesen PT. (2009). Otoacoustic emission theories and behavioral estimates of human basilar membrane motion are mutually consistent. *Journal of the Association for Research in Otolaryngology*, 10, 511–523.

Lopez-Poveda EA, Johannesen PT. (2012). Behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Journal of the Association for Research in Otolaryngology*, 13, 485–504.

Lopez-Poveda EA, Plack CJ, Meddis R, Blanco JL. (2005). Cochlear compression in listeners with moderate sensorineural hearing loss. *Hearing Research*, 205, 172–183.

Lopez-Poveda EA, Plack CJ, Meddis R. (2003). Cochlear nonlinearity between 500 and 8000 Hz in listeners with normal hearing. *Journal of the Acoustical Society of America*, 113, 951–960.

Lopez-Poveda EA. (2014). Why do I hear but not understand? Stochastic undersampling as a model of degraded neural encoding of speech. *Frontiers in Neuroscience*, 8, 348.

MacLeod A, Summerfield QA. (1990). Procedure for measuring auditory and audio–visual speech-reception thresholds for sentences in noise: Rationale, evaluation, and recommendations for use. British *Journal of Audiology*, 24, 29–43.

Moore BCJ, Glasberg BR. (1997). A model of loudness perception applied to cochlear hearing loss. *Auditory Neuroscience*, 3, 289–311.

Moore BCJ, Sek A. (1996). Detection of frequency modulation at low modulation rates: Evidence for a mechanism based on phase locking. *Journal of the Acoustical Society of America*, 100, 2320–2331.

Moore BCJ, Vickers DA, Plack CJ, Oxenham AJ. (1999). Inter-relationship between different psychoacoustic measures assumed to be related to the cochlear active mechanism. *Journal of the Acoustical Society of America*, 106, 2761–2778.

Moore BCJ. (2007). Cochlear hearing loss. Chichester, England: John Wiley & Sons, Ltd.

Neely ST, Johnson TA, Gorga MP. (2005). Distortion-product otoacoustic emission measured with continuously varying stimulus level. *Journal of the Acoustical Society of America*, 117, 1248–1259.

Nelson DA, Schroder AC, Wojtczak M. (2001). A new procedure for measuring peripheral compression in normal hearing and hearing-impaired listeners. *Journal of the Acoustical Society of America*, 110, 2045–2064.

Nelson DA, Schroder AC. (2004). Peripheral compression as a function of stimulus level and frequency region in normal-hearing listeners. *Journal of the Acoustical Society of America*, 115, 2221–2233.

Neumann J, Uppenkamp S, Kollmeier B. (1996). Detection of the acoustic reflex below 80 dB HL. *Audiol Neurootol*, 1, 359–369.

Nilsson M, Soli SD, Sullivan JA. (1994). Development of the hearing in noise test for the measurement of speech reception thresholds in quiet and in noise. *Journal of the Acoustical Society of America*, 95, 1085–1099.

Noordhoek IM, Houtgast T, Festen JM. (2001). Relations between intelligibility of narrow-band speech and auditory functions, both in the 1-kHz frequency region. *Journal of the Acoustical Society of America*, 109, 1197–1212.

Oxenham AJ, Bacon SP. (2004). Psychophysical manifestations of compression: Normal-hearing listeners. In S. P. Bacon, R. R. Fay, and A. N. Popper (Eds.), Compression: From cochlea to cochlear implants (pp. 62–106). New York, NY: Springer.

Oxenham AJ, Plack CJ. (1997). A behavioral measure of basilar-membrane nonlinearity in listeners with normal and impaired hearing. *Journal of the Acoustical Society of America*, 101, 3666–3675.

Pavlovic CV, Studebaker GA. (1984). An evaluation of some assumptions underlying the articulation index. *Journal of the Acoustical Society of America*, 75, 1606–1612.

Peters RW, Moore BCJ, Baer T. (1998). Speech reception thresholds in noise with and without spectral and temporal dips for hearing-impaired and normally hearing people. *Journal of the Acoustical Society of America*, 103, 577–587.

Plack CJ, Arifianto D. (2010). On- and off-frequency compression estimated using a new version of the additivity of forward masking technique. *Journal of the Acoustical Society of America*, 128, 771–786.

Plack CJ, Drga V, Lopez-Poveda EA. (2004). Inferred basilar-membrane response functions for listeners with mild to moderate sensorineural hearing loss. *Journal of the Acoustical Society of America*, 115, 1684–1695.

Plack CJ, O'Hanlon CG. (2003). Forward masking additivity and auditory compression at low and high frequencies. *Journal of the Association for Research in Otolaryngology*, 4, 405–415.

Plack CJ, Oxenham AJ, Simonson AM, O'Hanlon CG, Drga V, Arifianto D. (2008). Estimates of compression at low and high frequencies using masking additivity in normal and impaired ears. *Journal of the Acoustical Society of America*, 123, 4321–4330.

Plack CJ, Oxenham AJ. (2000). Basilar-membrane nonlinearity estimated by pulsation threshold. *Journal of the Acoustical Society of America*, 107, 501–507.

Plomp R, Mimpen AM. (1979). Speech-reception threshold for sentences as a function of age and noise level. *Journal of the Acoustical Society of America*, 66(5), 1333-42.

Rhebergen KS, Versfeld NJ, Dreschler WA. (2006). Extended speech intelligibility index for the prediction of the speech reception threshold in fluctuating noise. *Journal of the Acoustical Society of America*, 120, 3988–3997.

Rhebergen KS, Versfeld NJ, Dreschler WA. (2009). The dynamic range of speech, compression, and its effect on the speech reception threshold in stationary and interrupted noise. *Journal of the Acoustical Society of America*, 126, 3236–3245.

Robles L, Ruggero MA. (2001). Mechanics of the mammalian cochlea. *Physiological Reviews*, 81, 1305–1352.

Ruggero MA, Rich NC, Robles L, Recio A. (1996). The effects of acoustic trauma, other cochlear injury and death on basilar-membrane responses to sound. In A. Axelson, H. Borchgrevink, P. -A. Hellstro¨ m, D. Henderson, R. P. Hamernik, and R. J. Salvi (Eds.), Scientific basis of noise-induced hearing loss (pp. 23–35). New York, NY: Medical Publishers.

Schoepflin JR. (2012). Back to basics: Speech audiometry. AudiologyOnline. http://www.audiologyonline.com/articles/back-to-basics-speech-audiometry-6828.

Scollie SD. (2008). Children's speech recognition scores: The speech intelligibility index and proficiency factors for age and hearing level. *Ear and Hearing*, 29, 543–556.

Shera CA, Guinan JJ, Oxenham AJ. (2002). Revised estimates of human cochlear tuning from otoacoustic and behavioral measurements. *Proceedings of the National Academy of Science*, 99, 3318–3323.

Stainsby TH, Moore BC. (2006). Temporal masking curves for hearing-impaired listeners. *Hearing Research*, 218, 98–111.

Studebaker GA, McDaniel DM, Sherbecoe RL. (1995). Evaluating relative speech recognition performance using the proficiency factor and rationalized arcsine differences. *Journal of the American Academy of Audiology*, 6, 173–182.

Summers V, Makashay MJ, Theodoroff SM, Leek MR. (2013). Suprathreshold auditory processing and speech perception in noise: Hearing-impaired and normal-hearing listeners. *Journal of the American Academy of Audiology*, 24, 274–292.

ter Keurs M, Festen JM, Plomp R. (1992). Effect of spectral envelope smearing on speech reception. I. *Journal of the Acoustical Society of America*, 91, 2872–2880.

Theil H, Goldberger AS. (1961). On pure and mixed statistical estimation in economics. *International Economic Review*, 2, 65–78.

Vinay, Moore BC. (2007). Prevalence of dead regions in subjects with sensorineural hearing loss. *Ear Hear*. 28, 231–241.

Watson CS, Gengel RW. (1969). Signal duration and signal frequency in relation to auditory sensitivity. *Journal of the Acoustical Society of America*, 46, 989–997.

Wojtczak M, Oxenham AJ. (2009). Pitfalls in behavioral estimates of basilar-membrane compression in humans. *Journal of the Acoustical Society of America*, 125, 270–281.

Wojtczak M, Oxenham AJ. (2010). Recovery from on and off-frequency forward masking in listeners with normal and impaired hearing. *Journal of the Acoustical Society of America*, 128, 247–256.

Woods WS, Kalluri S, Pentony S, Nooraei N. (2013). Predicting the effect of hearing loss and audibility on amplified speech reception in a multi-talker listening scenario. *Journal of the Acoustical Society of America*, 133, 4268–4278.

World Health Organization. (2017). Deafness and hearing loss. http://www.who.int/mediacentre/factsheets/fs300.

Yasin I, Drga V, Plack CJ. (2013). Estimating peripheral gain and compression using fixed-duration masking curves. *Journal of the Acoustical Society of America*, 133, 4145–4155.

Young ED. (2008). Neural representation of spectral and temporal information in speech. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 363, 923–945.

PUBLICATIONS AND CONFERENCE COMMUNICATIONS RESULTING FROM THIS THESIS

PEER-REVIEWED PAPERS

Johannesen PT, **Pérez-González P**, Lopez-Poveda EA. (**2014**). Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Front Neurosci*. **8**:214.

Pérez-González P, Johannesen PT, Lopez-Poveda EA. (**2014**). Forward-masking recovery and the assumptions of the temporal masking curve method of inferring cochlear compression. *Trends Hear*. **19**:1-14.

Johannesen PT, **Pérez-González P**, Kalluri S, Blanco JL, Lopez-Poveda EA. (**2016**). The influence of cochlear mechanical dysfunction, temporal processing deficits, and age on the intelligibility of audible speech in noise by hearing-impaired listeners. *Trends Hear*. **20**:1-14.

OTHER PAPERS

Pérez-González P, Gorospe JM, Lopez-Poveda EA. (**2013**). A Castilian Spanish digit triplet identification test for assessing speech intelligibility in quiet and in noise. *Revista de Acústica* **45**:13-24.

Pérez-González P, Lopez-Poveda EA. (**2013**) Level-dependent effects on speech intelligibility. POMA-Proc. Meetings on Acoustics 19, 050065.

Johannesen PT, **Pérez-González P**, Kalluri S, Blanco JL, Lopez-Poveda EA. (**2016**). "Predictors of supra-threshold speech-in-noise intelligibility by hearing-impaired listeners," in Proc. ISAAR 2015: Individual Hearing Loss: Characterization, Modelling, Compensation Strategies, Aug. 2015, Nyborg, Denmark. Edited by Santurette S, Dau T, Dalsgaard JC, Tranebjaerg L, and Andersen T. ISBN: 978-87-990013-5-4. The Danavox Jubilee Foundation, 2015.

CONFERENCE COMMUNICATIONS

Pérez–González P, Lopez–Poveda EA. "Level–dependent effects on speech intelligibility". International Congress on Acoustics, 2–7 June **2013**, Montreal, Canada. Psychological and Physiological Acoustics. Session 2pPPb: Speech. Attention, and impairment (Poster Session).

Johannesen PT, **Pérez–González P**, Lopez–Poveda EA. "Otoacoustic Emission and Behavioral Estimates of the Contribution of Inner and Outer Hair Cell Dysfunction to Audiometric Loss" 37 MidWinter Meeting of the Association for Research in Otolaryngology (22–26 February **2014**, San Diego, California, USA). Podium: Otoacoustic Emissions. PD–074.

Pérez–González P, Johannesen PT, Lopez–Poveda EA. "A test of the assumptions of the temporal masking curve method of assessing cochlear nonlinearity". 37 MidWinter Meeting of the Association for Research in Otolaryngology (22–26 February **2014**, San Diego, California, USA). Poster Session: Psychoacoustics I. PS–144.

Johannesen PT, **Pérez-González P**, Kalluri S, Blanco JL, Lopez-Poveda EA. (**2015**). Predictors of supra-threshold speech-in-noise intelligibility by hearing-impaired listeners. Int. Symp. Auditory & Audiol. Res. (ISAAR 2015) 26-28 August **2015**, Nyborg (Denmark).

Relationship between Cochlear Mechanical Dysfunction and Speech-In-Noise Intelligibility for Hearing-Impaired Listeners

APPENDIX A

REPRINTS OF PUBLISHED ARTICLES

Patricia Pérez González

Instituto de Neurociencias de Castilla y León

Universidad de Salamanca

Julio 2017

frontiers in
NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 23 July 2014
doi: 10.3389/fnins.2014.00214

Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss

Peter T. Johannesen[1,2], Patricia Pérez-González[1,2] and Enrique A. Lopez-Poveda[1,2,3]*

[1] Auditory Computation and Psychoacoustics, Instituto de Neurociencias de Castilla y León, University of Salamanca, Salamanca, Spain
[2] Grupo de Audiología, Instituto de Investigación Biomédica de Salamanca, University of Salamanca, Salamanca, Spain
[3] Departamento de Cirugía, Facultad de Medicina, Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain

Edited by:
Monica Munoz-Lopez, University of Castilla-La Mancha, Spain

Reviewed by:
Chris Plack, The University of Manchester, UK
Tim Juergens, Universität Oldenburg, Germany

***Correspondence:**
Enrique A. Lopez-Poveda, Instituto de Neurociencias de Castilla y León, Universidad de Salamanca, Calle Pintor Fernando Gallego 1, 37007 Salamanca, Spain
e-mail: ealopezpoveda@usal.es

Identifying the multiple contributors to the audiometric loss of a hearing impaired (HI) listener at a particular frequency is becoming gradually more useful as new treatments are developed. Here, we infer the contribution of inner (IHC) and outer hair cell (OHC) dysfunction to the total audiometric loss in a sample of 68 hearing aid candidates with mild-to-severe sensorineural hearing loss, and for test frequencies of 0.5, 1, 2, 4, and 6 kHz. It was assumed that the audiometric loss (HL_{TOTAL}) at each test frequency was due to a combination of cochlear gain loss, or OHC dysfunction (HL_{OHC}), and inefficient IHC processes (HL_{IHC}), all of them in decibels. HL_{OHC} and HL_{IHC} were estimated from cochlear I/O curves inferred psychoacoustically using the temporal masking curve (TMC) method. 325 I/O curves were measured and 59% of them showed a compression threshold (CT). The analysis of these I/O curves suggests that (1) HL_{OHC} and HL_{IHC} account on average for 60–70 and 30–40% of HL_{TOTAL}, respectively; (2) these percentages are roughly constant across frequencies; (3) across-listener variability is large; (4) residual cochlear gain is negatively correlated with hearing loss while residual compression is not correlated with hearing loss. Altogether, the present results support the conclusions from earlier studies and extend them to a wider range of test frequencies and hearing-loss ranges. Twenty-four percent of I/O curves were linear and suggested total cochlear gain loss. The number of linear I/O curves increased gradually with increasing frequency. The remaining 17% I/O curves suggested audiometric losses due mostly to IHC dysfunction and were more frequent at low (≤1 kHz) than at high frequencies. It is argued that in a majority of listeners, hearing loss is due to a common mechanism that concomitantly alters IHC and OHC function and that IHC processes may be more labile in the apex than in the base.

Keywords: cochlear non-linearity, auditory masking, hearing aid, cochlear damage, hearing loss, hearing impairment

INTRODUCTION

Cochlear hearing loss occurs when absolute hearing thresholds for pure tones are higher than normal without signs of middle-ear or auditory neural pathology (Moore, 2007). In the healthy cochlea, inner hair cells (IHCs) transduce mechanical basilar membrane (BM) vibrations into nerve signals, while outer hair cells (OHCs) amplify BM responses to low-level sounds and are thus responsible for our high auditory sensitivity (Bacon et al., 2004). A reduction in the number of OHCs or lesions to the OHCs or associated structures can reduce the cochlear gain to low level sounds and hence cause an audiometric loss. Similarly, a reduction in IHC count or lesions to the IHCs or their associated structures can increase the BM excitation required for detecting a signal, which may also cause an audiometric loss (Moore, 2007). Although it is not generally possible to establish a one-to-one correspondence between audiometric loss and the degree of physical IHC/OHC loss or injury (Chen and Fechter, 2003; Lopez-Poveda and Johannesen, 2012), it is reasonable to assume that the audiometric loss may be due to combined loss or dysfunction of IHCs and OHCs. Indeed, some authors have assumed that the audiometric loss (HL_{TOTAL}) for a given test frequency may be conveniently expressed as the sum of two contributions: one associated with cochlear mechanical gain loss, or OHC dysfunction (HL_{OHC}), and one associated with inefficient IHC transduction, or IHC dysfunction (HL_{IHC}), where HL_{TOTAL}, HL_{IHC} and HL_{OHC} are all in decibels (dB) (Moore and Glasberg, 1997; Plack et al., 2004; Moore, 2007; Jepsen and Dau, 2011; Lopez-Poveda and Johannesen, 2012). The aim of the present study was to assess HL_{OHC} and HL_{IHC} over the frequency range from 500 Hz to 6 kHz in a large sample of listeners with mild-to-severe sensorineural hearing loss.

The prevailing view is that OHCs are generally more labile than IHCs and that IHCs and OHCs in the basal region of the cochlea are damaged first and to a greater extent than cells in the

apical region (reviewed by Møller, 2000). The relative degree of physical IHC/OHC loss or dysfunction and the location of the dysfunction, however, almost certainly depend on the cause and magnitude of the lesion. Noise-induced hearing loss is associated mostly with loss of basal OHCs (Chen and Fechter, 2003). In human, temporal bone studies of noise-induced hearing loss report increased cell death in basal BM locations and fewer surviving OHCs than IHCs (McGill and Schuknecht, 1976). On the other hand, acoustic trauma damages IHC and OHC stereocilia to similar degrees, which suggests that noise-induced hearing loss probably has a substantial contribution from IHC dysfunction (Liberman and Dodds, 1984). The cochlear location of the dysfunction almost certainly depends on the noise spectrum.

Some ototoxic drugs also cause a hearing loss. In this case, the degree of physical IHC and OHC damage depends on the drug employed. Aminoglycosides cause mostly OHC dysfunction and basal OHCs are first affected and more affected than apical OHCs (van Ruijven et al., 2004; Selimoglu, 2007; Pickles, 2008). Carboplatin, by contrast, does not reduce otoacoustic emission levels (Trautwein et al., 1996) or the sharpness of neural response tuning curves (Wang et al., 1997), which suggests that carboplatin hardly affects cochlear mechanics and affects mostly IHCs or their related structures. Furthermore, carboplatin raises the tips of neural tuning curves comparably at all frequencies (Wang et al., 1997), which indicates that its effect on IHCs is comparable along the cochlear length. In humans, histological studies of aminoglycoside-induced hearing loss report increased cell death in basal BM location and fewer surviving OHCs than IHCs (Huizing and de Groot, 1987).

Sensorineural hearing loss, however, need not always be caused by reduced counts or injury to hair cells or their associated structures. Metabolic presbycusis, for example, a form of age-related hearing loss (Schmiedt et al., 2002), causes a reduction of the endocochlear potential that can simultaneously reduce the cochlear mechanical gain (Saremi and Stenfelt, 2013) *and* the IHC response (Meddis et al., 2010; Panda et al., 2014) Functionally, this can manifest as a simultaneous dysfunction of IHCs and OHCs. Computer simulation studies suggest that whatever the mechanism, a reduction of the endocochlear potential always raises absolute thresholds more at high than at low frequencies (Meddis et al., 2010; Saremi and Stenfelt, 2013; Panda et al., 2014), which probably explains the association between aging and gradually sloping high-frequency losses. Likewise, aspirin, an ototoxic agent that impairs OHC function, broadens psychoacoustical tuning curves, reduces two-tone suppression, and linearizes growth-of-masking functions slightly more at 3 kHz than at 750 Hz, which can be explained in terms of greater involvement of labile cochlear non-linear processes in basal than in apical cochlear regions (Hicks and Bacon, 1999). In summary, it would be erroneous to conclude that the typically greater high-frequency losses are always due to comparatively greater loss or injury of basal than apical IHCs and/or OHCs.

Regardless of its actual cause, sensorineural hearing loss is typically treated with hearing aids. In programming a hearing aid, the assumption is made that HL_{TOTAL} is partly due to cochlear mechanical gain loss (akin to HL_{OHC}) and partly due to other factors (akin to HL_{IHC}). Individual across-frequency estimates of HL_{OHC} and HL_{IHC} would be highly useful to optimize individualized treatment with hearing aids (Muller and Janssen, 2004; Mills, 2006). Estimation of HL_{OHC} and HL_{IHC} is, however, hard because it can only be done using indirect methods. For this reason, large-scale studies are rare. Using a loudness model, Moore and Glasberg (1997) concluded that HL_{OHC} and HL_{IHC} account on average for 80 and 20% of HL_{TOTAL}, respectively, but reported that for a few listeners the loss attributable to OHC damage appears to be less than 50%. Plack et al. (2004) used the temporal masking curve (TMC) method (Nelson et al., 2001) to infer I/O curves at 4 kHz and estimated that HL_{OHC} contributes 65% of HL_{TOTAL}. Also based on TMC data, Jepsen and Dau (2011) used a computer auditory model to estimate HL_{IHC} and HL_{OHC} at 1 and 4 kHz in 10 hearing impaired (HI) listeners. Their results were broadly consistent with the common view that HL_{OHC} is greater and more frequent than HL_{IHC}, but they also reported some cases with substantial HL_{IHC} at low frequencies. Jürgens et al. (2011) concluded that at 4 kHz cochlear gain loss (or HL_{OHC}) was proportional to HL_{TOTAL} but 10–15 dB lower (p. 189). More recently, we have proposed a more refined method for estimating HL_{OHC} and HL_{IHC} from the analysis of TMC-based input/output (I/O) curves. We concluded that HL_{OHC} and HL_{IHC} account on average for 60 and 40% of HL_{TOTAL} with large variability across cases; indeed, percentages were sometimes reversed (Lopez-Poveda and Johannesen, 2012). Our conclusions were based on 26 I/O curves (most of them for a test frequency of 4 kHz) from 18 listeners with mild-to-moderate sensorineural hearing losses and are awaiting confirmation and extension to other frequencies and broader range of hearing losses.

The main aim of the present study was to assess HL_{IHC} and HL_{OHC} from behaviorally inferred I/O curves for a large sample of hearing aid candidates ($N = 68$) and for test frequencies of 0.5, 1, 2, 4, and 6 kHz. A second objective was to investigate to what extent HL_{IHC} and HL_{OHC} vary across test frequencies to examine potential structure-function correlations; that is, to examine the potential correspondence between HL_{OHC} and HL_{IHC} with existing evidence regarding physical loss or injury and/or dysfunction of OHCs and IHCs and their distribution across frequency. A third objective was to investigate the degree of variability of HL_{OHC} and HL_{IHC} across listeners. We used virtually the same approach as in our recent study (Lopez-Poveda and Johannesen, 2012). The present work, however, extends our previous study in several important aspects: first, HL_{OHC} and HL_{IHC} estimates in our previous study were restricted to I/O curves that showed a "knee-point" or a compression threshold (CT), whereas the present analysis is extended to all I/O curves; second, the present study is for a much larger subject sample and for a wider range of frequencies; third, the present study included participants with hearing losses from mild to severe, hence more representative of the hearing-aid candidate population.

METHODS

APPROACH AND ASSUMPTIONS

Our approach was virtually identical to that of Lopez-Poveda and Johannesen (2012). The details can be found in that publication and for conciseness only a summary is provided here. After Moore and Glasberg (1997), we assumed that the total audiometric loss

may be split into two contributions: one pertaining to a reduction of mechanical cochlear gain due to OHC dysfunction and a remaining component, which, for convenience, will be assumed due to inefficient IHC processes, or IHC dysfunction:

$$HL_{TOTAL} = HL_{OHC} + HL_{IHC}, \quad (1)$$

where HL_{TOTAL}, HL_{OHC}, and HL_{IHC} are all in dB. In what follows, HL_{OHC} and HL_{IHC} will be referred to as "OHC loss" and "IHC loss," respectively, and should be interpreted as contribution to audiometric loss (in dB) rather than as anatomical lesions or reduced cell counts.

We further assumed that HL_{OHC} can be found using the OHC dysfunction model of Plack et al. (2004). In this model, a cochlear mechanical input/output (I/O) curve is modeled by a function consisting of a linear segment (slope ~1 dB/dB) at low input levels, followed by a compressive segment at mid-level inputs (slope < 1 dB/dB), eventually followed by another linear segment at high input levels. The breakpoint between the low-level linear segment and the compressive segment is referred to as the CT and the breakpoint between the mid-level compressive segment and the high-level linear segment is referred to as the return-to-linearity threshold (RLT). OHC dysfunction causes a loss of low-level cochlear gain and is modeled as a horizontal shift of the low-level linear segment of the I/O curve toward higher input levels without affecting the slope of the compressive segment (Plack et al., 2004). An assumption of our approach is that HL_{OHC} can be found by comparing the CT of a given hearing-impaired (HI) listener with a reference CT for normal hearing (NH) listeners (Lopez-Poveda and Johannesen, 2012). When an HL_{OHC} estimate is available, then HL_{IHC} can be estimated using Equation (1) as the difference between HL_{OHC} and HL_{TOTAL}. For a sufficiently large OHC dysfunction, all the cochlear gain is lost, the I/O curve becomes linear (absent CT) and HL_{OHC} is assumed to be equal to the NH gain.

IHC dysfunction is assumed to increase the BM excitation needed for signal detection at threshold. When estimating the I/O curve with a psychophysical approach, only the part of the I/O curve that is above the cochlear mechanical excitation required for detection can be measured. For a large increase in BM excitation, a CT may be absent and only a part of the compressive portion of the I/O curve is available. Therefore, the absence of a CT with presence of a compressive segment in the I/O curve is assumed as indicative of substantial HL_{IHC}. For these cases, it is assumed that Equation (1) does not hold and that $HL_{TOTAL} \sim HL_{IHC}$. In other words, it is assumed that even though HL_{OHC} may occur, it does not contribute to the audiometric hearing loss (for a full explanation, see Figure 1D in Lopez-Poveda and Johannesen, 2012 and its related text).

Estimation of HL_{IHC} and HL_{OHC} as outlined above requires access to cochlear I/O curves. We assumed that I/O curves can be inferred behaviorally using the TMC method of Nelson et al. (2001). Briefly, this method consists of measuring the levels of a pure tone forward masker required to just mask a following fixed low-level probe tone as a function of the masker-probe time gap. Two TMCs are measured to infer an I/O curve: one for a condition where the masker is processed linearly by the BM (linear reference); and one for a condition where the masker and the probe tones are equal in frequency (on-frequency). It is assumed that the slope of the linear-reference TMC reflects the post-mechanical rate of recovery from forward masking while the slope of the on-frequency TMC reflects both BM compression on the masker *and* the post-mechanical rate of recovery from forward masking. Under the assumption that the post-mechanical rate of recovery is independent of masker level and frequency, a cochlear I/O curve can be inferred by plotting the masker levels of the linear reference TMC as a function of the masker levels for the on-frequency TMC for paired time gaps (Nelson et al., 2001). Lopez-Poveda et al. (2003) proposed to use a common linear-reference TMC for a high-frequency probe and a low-frequency masker to infer I/O curves for all probe frequencies on the assumption that the recovery from forward masking is also independent of the probe frequency.

PARTICIPANTS

A total of 68 listeners (43 males) with symmetrical sensorineural hearing loss participated in the study. Their ages ranged from 25 to 82 years (median = 61 years). Air conduction absolute thresholds were measured using a clinical audiometer (Interacoustics AD229e) at the typical audiometric frequencies (0.125, 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz) (ANSI, 1996). Bone conduction thresholds were measured at 0.5, 1, 2, 3, and 4 kHz. Air and bone conduction thresholds were also measured at 0.75 and 1.5 kHz for a large subset of subjects. A hearing loss was regarded as sensorineural when tympanometry was normal and air-bone gaps were smaller than or equal to 15 dB at one frequency and smaller than or equal to 10 dB at any other frequency. Participants were recruited for a large-scale bilateral hearing-aid outcome study. Therefore, they were additionally required to be hearing-aid candidates (as judged by an experienced audiologist) and to have symmetrical bilateral loss. A hearing loss was regarded as symmetrical when the mean air conduction thresholds at 0.5, 1, and 2 kHz differed by less than 15 dB between the two ears, and the mean difference at 3, 4, and 6 kHz was less than 30 dB (AAO-HNS, 1993). For the current purpose, each participant was tested in one ear. The ear was selected to maximize the number of test frequencies for which TMCs could be obtained. For the majority of cases, this meant selecting the ear with better thresholds in the 2–6 kHz frequency range (30 left ears, 38 right ears). **Figure 1** gives an idea of the distribution of hearing losses (see below).

The data from our previous related study was also included in the present analysis (Lopez-Poveda and Johannesen, 2012). This included reference data for 15 NH listeners and data for 18 listeners with mild-to-moderate sensorineural hearing loss. Results for these groups will be clearly identified below.

All procedures were approved by the human experimentation ethical review board of the University of Salamanca. Subjects gave their signed informed consent prior to their inclusion in the study.

TMC STIMULI AND PROCEDURE

Stimuli and procedure were similar to those of Lopez-Poveda and Johannesen (2012). On-frequency TMCs were measured for

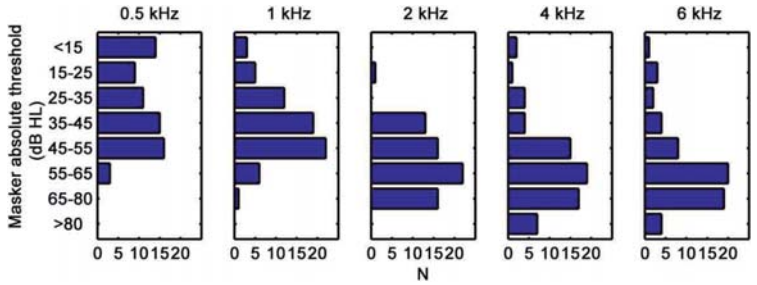

FIGURE 1 | Distributions of corrected masker absolute thresholds, in dB HL (see text for details). Each panel is for a different test frequency, as indicated at the top.

probe frequencies (f_P) of 0.5, 1, 2, 4, and 6 kHz. Maskers and probes were sinusoids. The duration of the maskers was 210 ms including 5-ms cosine-squared onset and offset ramps. Probes had durations of 10 ms, including 5-ms cosine-squared onset and offset ramps with no steady state portion, except for the 500-Hz probe, whose duration was 30 ms with 15-ms ramps and no steady state portion. The level of the probes was fixed at 10 dB above the individual absolute threshold for the probe. Masker-probe time gaps, defined as the period from masker offset to probe onset, ranged from 5 to 100 ms in 10-ms steps with an additional gap of 2 ms. Masker levels sometimes reached the maximum permitted sound level output (105 dB SPL) after a few time gaps. If the number of measured data points was insufficient for curve fitting (see below), masker levels were measured for additional intermediate gaps (e.g., 5, 15, 25 ms). In a few cases, masker levels were atypically low for a time gap of 100 ms. In these cases, masker levels were measured for additional gaps in the range 110–140 ms.

A single linear reference TMC was measured for each listener and it was used to infer I/O curves for all other probe frequencies (Lopez-Poveda et al., 2003). The linear reference TMC was for a probe frequency of 2, 4, or 6 kHz and for a masker frequency equal to $0.4f_p$ or $0.5f_p$. The selection of linear reference condition depended on the listener's hearing loss at the linear-reference probe frequency and on the maximum permitted sound level output (105 dB SPL). Following the indications of earlier studies, (Lopez-Poveda et al., 2003; Lopez-Poveda and Alves-Pinto, 2008), the linear reference conditions were sought in the order of priority shown in **Table 1**.

Stimuli were generated digitally in Matlab and output via an RME Fireface 400 sound card (sampling frequency of 44100 Hz, 24-bit resolution) and delivered to the listeners through Sennheiser HD-580 headphones. Sound pressure levels (SPL) were calibrated by placing the headphones on a KEMAR equipped with a Zwislocki DB-100 artificial ear connected to a sound level meter. Calibration was performed at 1 kHz only and the obtained sensitivity was used at all other frequencies.

Masker levels at threshold were measured using a two-interval, two-alternative, forced-choice adaptive procedure with feedback. The inter-stimulus interval was 500 ms. The initial masker level was set sufficiently low that the listener always could hear both the masker and the probe. Masker level was then changed according to a two-up, one-down adaptive procedure to estimate the 71% point on the psychometric function (Levitt, 1971). An initial step size of 6 dB was applied, which was decreased to 2 dB after three reversals. The adaptive procedure continued until a total of 12 reversals in masker level were measured. Threshold was calculated as the mean masker level at the last 10 reversals. A measurement was discarded if the standard deviation of the last 10 reversals exceeded 6 dB. Three threshold estimates were obtained in this way and their mean was taken as the threshold. If the standard deviation of these three measurements exceeded 6 dB, one or more additional threshold estimates were obtained and included in the mean. Measurements were made in a double-wall sound attenuating booth. Listeners were given at least 2 h of training on the TMC task before data collection began.

Table 1 | Prioritized linear-reference TMC conditions and number of cases (*N*) where each condition applied (see also red curves in Figure 2).

Priority order	①	②	③	④	⑤	⑥
Probe (kHz)	4	4	6	6	2	2
Masker (kHz)	1.6	2	2.4	3	0.8	1
N	34	6	4	4	9	6

Note that these numbers add up to 63 rather than to the total number of participants (N = 68). This is because a linear reference TMC could not be measured for four participants, and the data from one additional participant who performed inconsistently during the task were excluded from the analysis.

Absolute thresholds for the probes and maskers were measured using a similar procedure except that the adaptive procedure was one-up, two-down.

TMC and absolute threshold measurements took between 12 and 15 h per participant in total and were distributed in several (1- or 2-h) sessions on several days.

TMC FITTING

Linear-reference and on-frequency TMCs were fitted before they were used to infer I/O curves. Linear reference TMCs were fitted with a double exponential function with four parameters (Lopez-Poveda and Johannesen, 2012); on-frequency TMCs were fitted

with a function consisting of the double exponential function fitted to the linear reference TMC plus a second-order Boltzmann function with six parameters (Lopez-Poveda and Johannesen, 2012). When fitting the on-frequency TMC, the parameters of the double exponential function were held fixed and only the parameters of the second-order Boltzmann function were allowed to vary. When the number of data points in a TMC was equal or fewer than the number of parameters of the double exponential or the second-order Boltzmann function, single exponential (two parameters) and first-order (four parameters) Boltzmann functions were used instead. A full justification of this approach can be found elsewhere (Lopez-Poveda and Johannesen, 2012). The goodness-of-fit was assessed using the root-mean-square (RMS) error between measured and fitted TMCs. RMS errors were less than 2 dB for all linear reference TMCs, and less than 4 dB for on-frequency TMCs, except for three cases for which RMS errors were less than 6 dB.

INFERENCE OF I/O CURVES

I/O curves were inferred for each participant by plotting the masker levels of his/her linear reference TMC against the masker levels for the on-frequency TMCs paired according to time gaps (Nelson et al., 2001). For any given participant, a common linear reference condition was used to infer I/O curves at all test frequencies (Lopez-Poveda et al., 2003). A linear reference TMC could not be found for four participants because their hearing loss was too high at the linear-reference probe frequencies (**Table 1**). In these four cases, an average linear reference (mean across all other participants for the condition $f_P = 4$ kHz and $f_m = 1.6$ kHz) was used to infer I/O curves. This average linear reference TMC was also used for reanalysis of four cases from our previous study (Lopez-Poveda and Johannesen, 2012) that did not have linear reference for the same reason.

RESULTS

HEARING LOSS DISTRIBUTIONS

Absolute thresholds for the maskers were used to assess hearing losses. Masker duration was shorter for the present participants (200 ms) than for the NH reference group or the HI listeners used in our previous study (300 ms in Lopez-Poveda and Johannesen, 2012). Because absolute threshold depends on signal duration, this difference in masker duration could have introduced a small difference in threshold for the participants in each study. Given that HL_{TOTAL} was defined as the difference between masker thresholds of the HI and NH listeners, an attempt was made to correct the present masker thresholds for the influence of duration on absolute thresholds by adding the difference between NH absolute thresholds for pure tone durations of 300 and 200 ms to the masker thresholds of the present HI subjects (Watson and Gengel, 1969). Corrections were smaller than 1 dB at all frequencies. **Figure 1** shows the corrected absolute thresholds for the present participants; thresholds for the HI participants from our previous study are omitted in **Figure 1** but can be found in the original reference. Clearly, on average, participants had high-frequency losses typical of presbycusis but the range of hearing losses at each frequency was quite variable.

TEMPORAL MASKING CURVES

Figure 2 shows fitted linear-reference and on-frequency TMCs for 67 participants; one participant performed inconsistently during the TMC task and her data were excluded from further analysis. Measured TMCs are omitted in **Figure 2** to avoid clutter. Each column is for a different test frequency as indicated by column title, and each row is for a hearing-loss range as indicated by the text on the right-most ordinate. Both linear-reference (red curves) and on-frequency TMCs (black curves) had characteristics similar in most aspects to those published in earlier reports (Nelson et al., 2001; Plack et al., 2004; Lopez-Poveda et al., 2005; Jepsen and Dau, 2011; Lopez-Poveda and Johannesen, 2012). The on-frequency masker levels for the shortest time gap (2 ms) decreased with decreasing frequency and on-frequency and linear-reference TMCs were less parallel (i.e., on-frequency TMCs were steeper than linear-reference TMCs) at lower than at higher frequencies. Both these aspects are consistent with listeners having less hearing loss (**Figure 1**) and presumably less gain loss and more compression at low than at high frequencies.

Lopez-Poveda and Alves-Pinto (2008) argued that an ideal linear-reference TMC for inferring I/O curves would be for $f_p = 4$ kHz and $f_m = 1.6$ kHz on the grounds that the slope of such a TMC would be unlikely affected by cochlear compression and would reflect only the post-mechanical rate of recovery from forward masking. As explained above, the hearing loss of some listeners was so large at 4 kHz that it was not possible to measure this preferred linear-reference TMC and alternative linear references were measured instead (**Table 1**). Before using these linear references to infer I/O curves, we verified that their slopes were statistically comparable to the slopes of the preferred linear reference. To do it, we calculated the mean slope of all measured linear reference TMCs across all available time gaps (red curves in **Figure 2**), and compared the mean slope of the preferred linear reference condition (denoted as priority ① in **Table 1**) with the mean slope for every other condition (denoted as priority orders ② to ⑥ in **Table 1**) using a Student's *t*-test. The tests confirmed that all linear references had statistically equivalent slopes ($p > 0.05$). The difference for conditions ① and ⑤ was close to being significant ($p = 0.055$) but did not reach significance. Therefore, we concluded that all linear-reference TMCs had statistically comparable slopes and that it was reasonable to use them to infer I/O curves.

I/O CURVES INFERRED FROM TMCs

Figure 3 shows the I/O curves inferred from the TMCs of **Figure 2**. Dotted lines depict linearity with no gain (input level = output level). The large majority of I/O curves had shapes typical of HI subjects: they often had a linear segment at low input levels followed by a compressive segment at mid input levels, followed sometimes by another linear segment at high input levels. Other I/O curves were best described by an almost straight line with either a compressive slope or with a slope close to linearity. Few I/O curves showed unusual characteristics. For example, their RLTs were surprisingly low (50–70 dB SPL), particularly at low frequencies. Also, some I/O curves were almost flat (e.g., at 1 kHz for hearing loss below 15 dB HL). The latter occurs because their corresponding linear reference TMCs were very shallow. Overall, I/O curves extended to lower input levels at low than

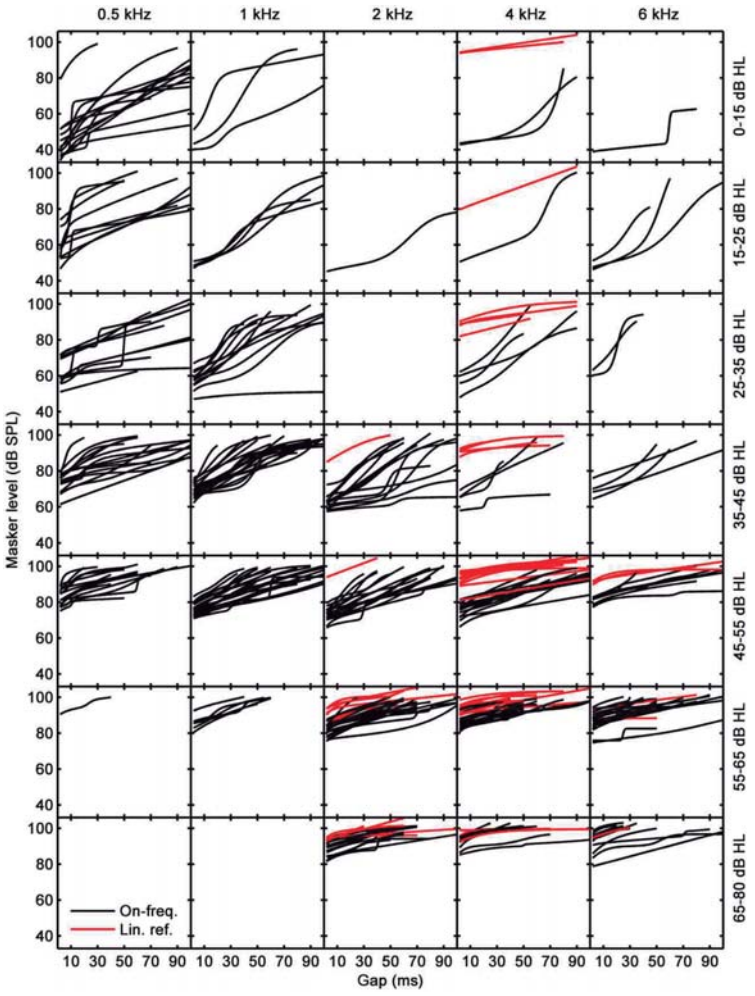

FIGURE 2 | Fitted linear-reference (red curves) and on-frequency TMCs (black curves). Each column corresponds to a different test frequency as indicated by the column title and each row to different a hearing-loss range, as indicated by the text on the right-most ordinate.

at high frequencies, a reasonable result considering that on average participants had greater hearing losses for high than for low frequencies (**Figure 1**).

I/O CURVE ANALYSES AND TAXONOMY

Lopez-Poveda and Johannesen (2012) argued that HL_{OHC} and HL_{IHC} may be reliably obtained from an I/O curve only if the I/O curve in question shows a CT. They nonetheless hinted that the shape of the I/O curves may be indicative of the type and extent of HL_{OHC} or HL_{IHC} (see their Figure 1 and related text). Here, each I/O curve was analyzed in search for HL_{OHC} and HL_{IHC} using their reasoning and following the logic outlined in **Figure 4**.

A CT was first sought for each I/O curve. Lopez-Poveda and Johannesen (2012) arbitrarily defined the CT as the input level where the I/O curve reached a slope of 0.5 dB/dB from a higher value at lower input levels (**Figure 5B**). To take into account the experimental TMC variability on the CT estimate, rather than inferring the CT from the mean I/O curve, they simulated 100 I/O curves for each condition using a Monte-Carlo approach and used the median CT of those simulations in their subsequent analysis. They regarded the obtained CT as unreliable when it was the lowest input level in the mean I/O curve or if the mean I/O curve slope did not reach the criterion value of 0.5 dB/dB, something infrequent in their data (see Lopez-Poveda and Johannesen,

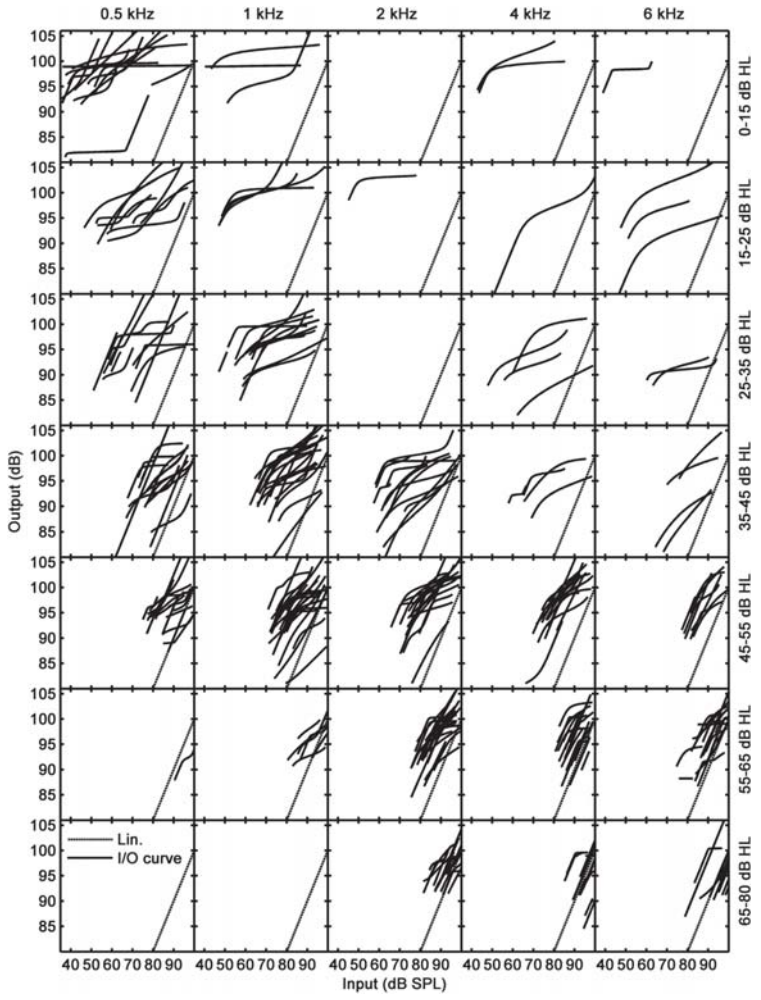

FIGURE 3 | Inferred I/O curves. Columns and rows are as in **Figure 2**.

2012). Here, we first tried to apply their same criteria but found many instances where the resulting CTs were unreliable. To maximize the number of I/O curves with valid CTs, we opted to apply slightly different criteria: (1) that 60% of the Monte-Carlo simulated I/O curves showed a valid CT; *and* (2) that the residual cochlear gain of the mean I/O curve (estimated as described below) was greater than zero. The median CT of the Monte-Carlo simulated I/O curves was taken as the final CT.

A large proportion of I/O curves showed a CT (**Table 2**). Many other I/O curves, however, were best described as straight lines with varying slopes (as depicted in **Figure 5D** or **Figure 5F**) or showed a compressive segment and an RLT but no CT (as shown in **Figure 5H**). The distinction between these cases was made based on residual gain and mean slope using the logic depicted in **Figure 4**.

Gain was defined here as the difference in sensitivity for low and high input levels, as illustrated in the right panels of **Figure 5**. That is, gain was defined as the horizontal distance between intersects with the abscissa of two lines with slopes 1 dB/dB that passed through the end points of the I/O curve. Of course, if the measured I/O curve were only a segment of the actual underlying I/O curve, as would happen for instance for straight-line I/O curves like those shown in **Figure 5D** or **Figure 5F**, this gain estimate would be smaller than the actual residual gain. Actually, insofar as an I/O curve is inferred from an on-frequency and a linear-reference TMC (compare the left and right panels of

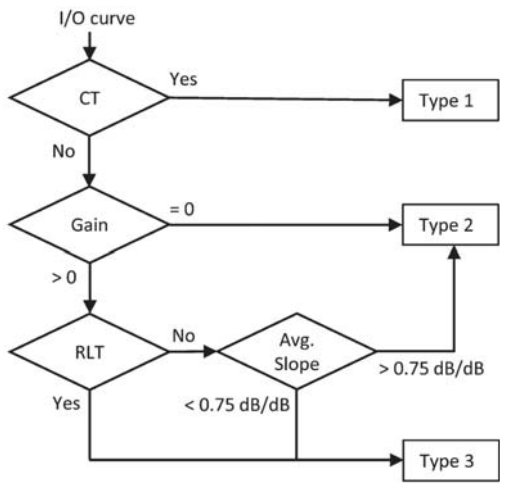

FIGURE 4 | Flow-diagram and logic used to classify each I/O curve into one of three categories: Type 1 = I/O curve with a compression threshold; Type 2 = Linear I/O curve; Type 3 = I/O curve with residual compression but no compression threshold.

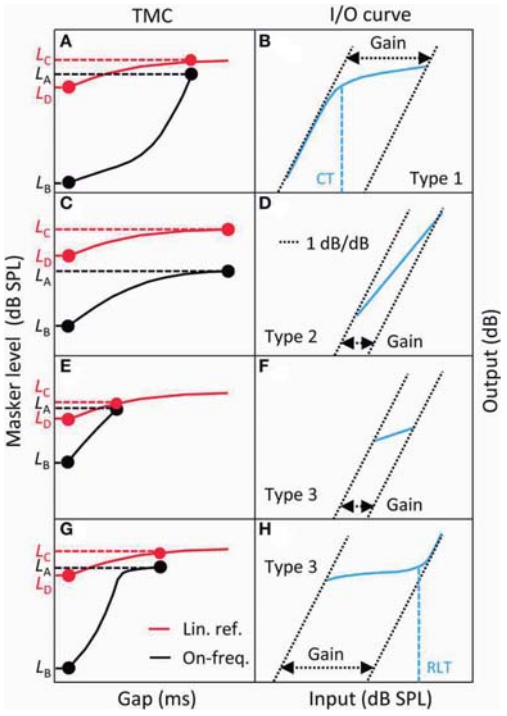

FIGURE 5 | A taxonomy of I/O curves (blue line, right panels) and their corresponding TMCs (left panels). Left: linear-reference (red curves) and on-frequency (black curves) TMCs. Right: corresponding, inferred I/O curves. **(A,B)** for Type 1 I/O curves. **(C,D)** for Type 2 I/O curves. **(E,F)** for Type 3 I/O curves with little residual gain. **(G,H)** for Type 3 I/O curves with large residual gain. CT, compression threshold; RLT, return-to-linearity threshold. See main text for details.

Figure 5), gain for all types of I/O curves was directly obtained from the corresponding TMCs as follows:

$$gain = (L_A - L_B) - (L_C - L_D) \quad (2)$$

where L_A, L_B, L_C, and L_D were defined as in **Figure 5**.

If gain was not significantly different from zero[1], then the I/O curve was regarded as linear, hence indicative of total gain loss. If, however, gain was greater than zero, we tried to find an RLT[2] in the I/O curve (as shown in **Figure 5H**). If absent, the I/O curve was regarded as linear when its average slope was steeper than an arbitrary value of 0.75 dB/dB. This criterion prevented cases with small amounts of residual gain and a moderate degree of compression from being erroneously classified as total gain loss; that is, it served to distinguish cases like that shown in **Figure 5F**, almost certainly indicative of significant IHC dysfunction, from cases like that shown in **Figure 5D**, almost certainly indicative of total gain loss. If, however, a RLT was present or if the average slope of the I/O curve was <0.75 dB/dB, then we assumed that compression was present and that the I/O curve was indicative of significant IHC dysfunction.

Table 2 shows the number of I/O curves in each of the three categories (Type 1: CT present; Type 2: linear; Type 3: CT absent with compression). The proportion of linear I/O curves was greater at and above 2 kHz than at lower frequencies. The proportion of Type 3 I/O curves was greater at lower than at higher frequencies. In a few cases, the hearing loss was so high (above ~70 dB HL) that measuring the TMC needed to infer an I/O curve would have required masker levels beyond the maximum sound pressure output of our system. These cases, classified

Table 2 | Number of I/O curves according to their shapes.

Frequency (kHz)	0.5	1	2	4	6
Type 1 (CT present)	29	54	46	38	24
Type 2 (Linear)	13	4	17	23	22
Type 3 (CT absent with compression)	25	15	7	3	5
Too-high loss	3	2	2	12	20
Total	70	75	72	76	71

The table includes the present data plus data from (Lopez-Poveda and Johannesen, 2012).

[1]Because each TMC was measured at least three times, we could assess the variance in L_A, L_B, L_C, and L_D, hence the gain variance (Equation 2). A Student's *t*-test was then used to verify if the mean gain estimate was statistically greater than zero at the 5% significance level.

[2]The return-to-linearity (RLT) was defined as the input level at which the slope of the I/O curve reached an arbitrary value of 0.5 dB/dB from a lower value at lower input levels. It was obtained using the same method and criteria that were used to obtain the CT.

as "too-high loss" in **Table 2**, increased slightly in number with increasing frequency.

Once classified, different I/O curves types were analyzed in search of HL_{OHC} and HL_{IHC}. Type 1 I/O curves were analyzed as suggested by Lopez-Poveda and Johannesen (2012); Type 2 and Type 3 I/O curves were analyzed differently, as described below.

HL_{OHC} AND HL_{IHC} ESTIMATES FROM I/O CURVES

From I/O curves with a compression threshold

For I/O curves with a CT (Type 1), HL_{OHC} was calculated as the difference between the CT and the mean CT for the reference NH group multiplied by (1–*c*) (Equation 2 in Lopez-Poveda and Johannesen, 2012), where *c* is the mean compression exponent over the compressive segment of the NH I/O curves. HL_{IHC} was obtained as HL_{TOTAL}–HL_{OHC} (Equation 1). This procedure required having mean reference CT and *c* values for NH listeners at each of the test frequencies (0.5, 1, 2, 4, and 6 kHz). Lopez-Poveda and Johannesen (2012) provided reference data for 0.5, 1, and 4 kHz but, to the best of our knowledge, reference data are still lacking at 2 and 6 kHz. For this reason, in the current analysis, the reference values at 4 kHz were used to infer HL_{OHC} and HL_{IHC} also at 2 and 6 kHz. The impact of this approximation on the results is discussed below.

Figure 6 illustrates HL_{OHC} (top) and HL_{IHC} (bottom) as a function of HL_{TOTAL}. Note that HL_{TOTAL} is defined here as the difference between a participant's absolute threshold for the masker and the mean absolute masker threshold of the reference NH group (the latter was not 0 dB HL as noted by Lopez-Poveda and Johannesen, 2012). Each column illustrates results for a different test frequency, as indicated at the top of each column. The lower insets in each panel show corresponding linear-regression functions and the number of data points (N) used in the regression; the upper insets show regression statistics, where R^2 is the proportion of variance explained by the regression line, and the *p*-value is the probability of the relationship between the two variables occurring by chance. Red dashed lines depict 95% confidence intervals for a new observation rather than the confidence intervals of the regression lines.

The linear regression functions in **Figure 6** show that HL_{OHC} contributed between 61 and 70% to HL_{TOTAL}, and HL_{IHC} contributed the rest (30–39%). Interestingly, these percentages were approximately constant across test frequencies, as shown by the slopes of the regression lines. The individual variability of the contributions HL_{OHC} and HL_{IHC} can be assessed from the confidence limits for new single observations. The confidence intervals for HL_{OHC} and HL_{IHC} were around ±9 dB at 0.5 kHz and around ±6 dB over the range 1–6 kHz. In all cases, the confidence

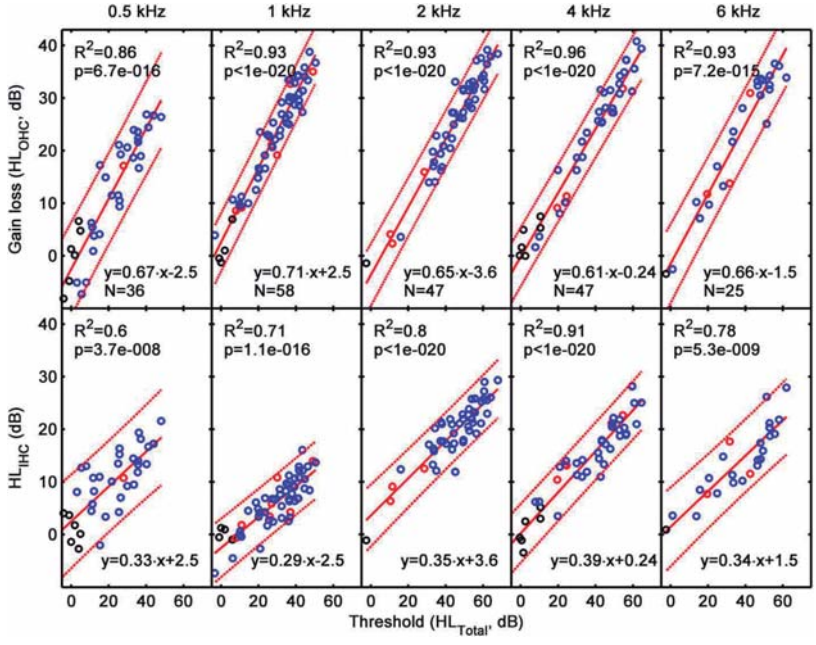

FIGURE 6 | The contribution of HL_{OHC} (top) and HL_{IHC} (bottom) to HL_{TOTAL} assessed from the analysis of Type 1 I/O curves (i.e., from I/O curves with CT present). Each column is a for a different test frequency, as indicated by the column title. Results for the current hearing-impaired listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted by black and red symbols, respectively. Continuous lines illustrate mean linear regression functions; dotted lines illustrate 5 and 95% confidence intervals of new individual observations. The insets show linear regression functions and related statistics.

intervals were almost independent of the HL_{TOTAL}. Recall that these results were only for Type 1 I/O curves.

Figure 7 allows statistical judgment of the incidence of cases suffering from pure IHC loss, pure OHC loss, or mixed IHC/OHC loss. The figure illustrates absolute threshold (in dB HL) as a function of cochlear gain loss (HL_{OHC}) separately for each frequency. The vertical dotted red line (at $HL_{OHC} = 0$ dB) indicates the hypothetical location of cases whose hearing loss was exclusively due to IHC dysfunction (pure IHC loss). The blue diagonal line depicts the hypothetical location of cases whose hearing loss was exclusively due to cochlear gain loss (pure OHC loss). The blue-dotted diagonal lines show 5–95% confidence intervals for gain loss as calculated from the reference NH listeners (Lopez-Poveda and Johannesen, 2012). Note that the diagonal does not match with the condition $HL_{TOTAL} = HL_{OHC}$, as one might expect, because as explained by Lopez-Poveda and Johannesen (2012), their NH listeners did not have a mean hearing loss of 0 dB HL. The shaded area indicates the placement of cases whose hearing loss is due partly to cochlear gain loss (HL_{OHC}) plus an additional component (mixed OHC/IHC loss). The results from I/O curves with a CT are depicted as blue circles in the top panels of the figure. For completeness, also shown are the results for listeners with NH (black circles) and mild-to-moderate hearing loss (red circles) from our earlier study (Lopez-Poveda and Johannesen, 2012).

Figure 7(top) shows that pure OHC loss was rare and occurred mostly for low absolute thresholds (or, equivalently, small hearing losses). There were no cases of pure IHC loss, something not surprising considering that significant HL_{IHC} would probably make it impossible to measure a CT (Figure 1 in Lopez-Poveda and Johannesen, 2012) and **Figure 7**(top) only show results for cases with a CT. Most cases were in the shaded areas and thus were consistent with mixed IHC/OHC loss. The number of cases with mixed loss tended to increase with increasing absolute threshold (or hearing loss). Incidentally, the number of cases with mixed loss appeared somewhat larger at 2 kHz than at other frequencies. This may be somewhat artifactual due to our using the mean NH CT and absolute threshold at 4 kHz to estimate HL_{OHC} at 2 kHz. Any difference between the mean NH CTs at 2 and 4 kHz would bias the data horizontally and a difference between the mean NH absolute threshold at 2 and 4 kHz would bias the data vertically

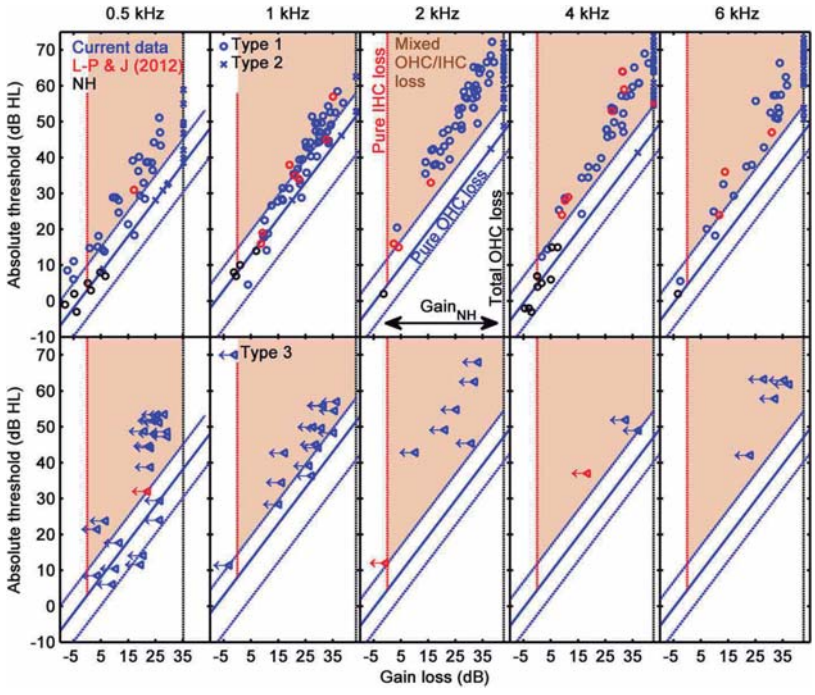

FIGURE 7 | Absolute threshold as a function of gain loss. Top: results for Type 1 (circles) and Type 2 (crosses) I/O curves. **Bottom panels:** results for Type 3 I/O curves (left-pointing triangles with arrows). Each column is for a different test frequency, as indicated by the column title. In each panel, the diagonal blue line and associated dotted lines indicate mean values and 5% confidence limits for pure OHC loss ($HL_{TOTAL} = HL_{OHC}$), and the vertical black, dotted line depicts the hypothetical location of cases with total cochlear gain loss, as inferred from the I/O curves of the reference, NH sample (black circles) (Johannesen and Lopez-Poveda, 2008). The red dotted lines depict the hypothetical location of cases with pure IHC loss (i.e., hearing loss with zero HL_{OHC}). The shaded areas indicate mixed OHC/IHC losses. Results for the current listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted as black and red symbols, respectively.

and thus might contribute to an apparent higher incidence of mixed IHC/OHC loss at 2 kHz.

From linear I/O curves

Linear I/O curves were assumed to be indicative of total gain loss. Hence, HL_{OHC} for these cases was set equal to the average cochlear gain for the NH reference group. The latter was estimated using Equation (2), and was equal to 35.2, 43.5, 42.7, 42.7, 42.7 dB at 0.5, 1, 2, 4, and 6 kHz. HL_{IHC} was then obtained using Equation (1).

Results for these cases are shown as blue crosses in the top panels of **Figure 7**. Clearly, the great majority of these cases were in the shaded area, hence were indicative of mixed OHC/IHC loss. In other words, for most of these cases, hearing loss was greater than the maximum possible mechanical cochlear gain loss (the gain loss of NH listeners), hence $HL_{IHC} > 0$ dB.

From compressive I/O curves without a compression threshold

As explained above, I/O curves that were either compressive straight lines (with slopes <0.75 dB/dB; **Figure 5F**), or that showed an RLT but not a CT (as in **Figure 5H**) were assumed indicative of IHC dysfunction. This is because any gain reduction will only affect the low-level linear portion of the I/O curve and IHC dysfunction may increase the BM response at detection threshold above the knee-point of the I/O curve (Figure 1B of Lopez-Poveda and Johannesen, 2012). Lopez-Poveda and Johannesen (2012) argued that for these cases Equation (1) does not hold, and that it is reasonable to assume that the audiometric loss can be fully explained in terms of inefficient IHC transduction combined with residual compression (see their Figure 1D). Therefore, we assumed that for these cases HL_{TOTAL} was equal to HL_{IHC}.

This is not to say, however, that cochlear gain loss did not occur in these cases; we are saying that if cochlear gain loss did occur, it is unlikely that it contributed to the audiometric loss (see Figure 1D in Lopez-Poveda and Johannesen, 2012). Indeed, an estimate of (residual) gain was obtained as illustrated in **Figure 5F** or **Figure 5H** using Equation (2). Note that this gain estimate was almost certainly less than the actual residual gain because, due to IHC dysfunction, the measured compressive segment of the I/O was only a portion of the true compressive segment. Cochlear gain loss (HL_{OHC}) was estimated by subtracting the obtained gain estimate from the reference gain for NH listeners (see the previous section). The bottom panels of **Figure 7** illustrate residual gain for these cases. The left pointing arrows indicate that the actual HL_{OHC} was probably *smaller* than estimated, hence that symbols should be to the left of their position in the figure, and closer to the red-dotted line indicative of pure IHC loss. The figure reveals two important results: first, that most of these cases are indicative of mixed IHC and OHC dysfunction (indeed, mixed dysfunction appears more frequent for these cases than for I/O curves with a CT; compare the placement of blue triangles and circles in the bottom and top panels of **Figure 7**); and second, that for any given absolute threshold (or hearing loss), there were comparatively more cases with little gain loss (i.e., indicative of IHC dysfunction) at lower than at higher frequencies. In other words, low-frequency hearing loss is more likely related to IHC dysfunction than to cochlear gain loss.

ACROSS LISTENER VARIABILITY OF HL_{OHC}

Figure 6 suggests that HL_{OHC} accounted on average for 61–70% of HL_{TOTAL} but it also suggests that there was large across-listener variability. **Figure 8** illustrates this variability more clearly by showing the distribution of HL_{OHC} for three different ranges of HL_{TOTAL}: 15–35, 35–55, and 55–80 dB. Results are based on Type 1 and Type 2 I/O curves. At 2 kHz and above, HL_{OHC} tended to increase with increasing HL_{TOTAL}, while at 0.5 and 1 kHz it decreased slightly or remained approximately constant. The main

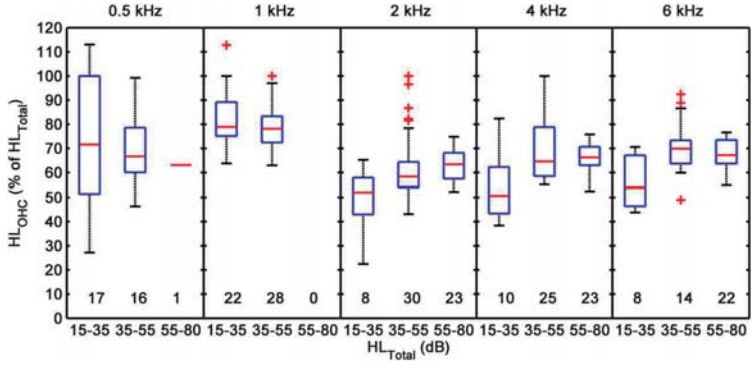

FIGURE 8 | Across-listener variability in the proportion of HL_{TOTAL} explained by HL_{OHC}. Each box plot illustrates distribution percentiles: the bottom and top lines in each box depict the first and third quartiles of the distribution; the band inside the box is the second quartile (the median); the lower and upper whiskers' ends depict the 1 and 99% percentiles. Crosses (+) depict cases outside the latter percentiles. Each panel is for a different test frequency. In each panel, distributions are given for HL_{TOTAL} ranges of 15–35, 35–55, and 55–80 dB. The numbers below each box plot indicate the number of cases (sample size) included in each distribution. The figure includes data for Type 1 and Type 2 I/O curves from the present participants and from the participants in our previous study.

result from this figure is, however, that for a given frequency and hearing-loss range, HL_{OHC} was broadly distributed across cases. For example, based on data for 25 subjects, at 4 kHz and for a hearing-loss range of 35–55 dB, HL_{OHC} accounted for between 55 and 100% of HL_{TOTAL}. [Note that the figure suggests that in a few cases with small losses, HL_{OHC} accounted for more than 100% of HL_{TOTAL}. These were cases whose CTs were lower than the mean CT for the reference, NH group (i.e., cases below the diagonal line in **Figure 7**)].

PREVALENCE OF IHC AND OHC DYSFUNCTION

The previous analyses have focused mostly on the relative contribution of HL_{OHC} and HL_{IHC} to HL_{TOTAL}. The data may be alternatively analyzed with a focus on the type of hearing loss; that is, on how many data points fall in each of several regions depicted in **Figure 7**. To this end, Type 1 (CT present) and Type 2 (linear) I/O curves were split into two subcategories: "Pure OHC dysfunction," when the audiometric loss could be entirely explained as loss of cochlear gain, that is, when $HL_{TOTAL} \sim HL_{OHC}$ (points within the diagonal range in **Figure 7**); and "Mixed OHC/IHC dysfunction," when the audiometric loss exceeded the cochlear gain loss (i.e., when $HL_{IHC} > 0$; points in the shaded area of **Figure 7**). For the reasons explained above, for Type 3 I/O curves, the absence of a CT was taken as indicative that the audiometric loss could be explained entirely in terms of IHC dysfunction ($HL_{TOTAL} \sim HL_{IHC}$). As shown in the bottom panels of **Figure 7**, however, cochlear gain loss of uncertain extent still occurred in a majority of these cases even though it probably did not contribute to the audiometric loss. Therefore, Type 3 I/O curves were also regarded as indicative of mixed OHC/IHC dysfunction.

The top part of **Table 3** gives the number of cases in each of these categories, and the bottom part of **Table 3** the corresponding percentages. Note that the number of cases of Type 3 I/O curves decreased with increasing frequency, suggestive that IHC dysfunction was more determinant to audiometric loss at low frequencies than cochlear gain loss. Note also that the percentage of cases of pure OHC loss decreased with increasing frequency, while the percentage of cases of mixed loss increased with increasing frequency, and that the two percentages add up to 100%. Mixed OHC/IHC loss was significantly more frequent than pure OHC at all frequencies. The bottom part of **Table 3** gives one additional percentage: "Total gain loss" refers to the total percentage of linear I/O curves, whether indicative of pure OHC dysfunction or mixed OHC/IHC dysfunction. The percentage of these cases increased with increasing frequency. Chi χ^2 tests were used to test if the above described frequency trends were statistically significant. The null hypothesis was that for each I/O curve type, the frequency distribution followed the distribution of the total number of cases (i.e., the distribution in the line labeled as "Total" in the table).

VERIFICATION AND EXTENSION OF MODEL ASSUMPTIONS

The present analysis was based on the hearing loss model of Plack et al. (2004) whereby OHC loss would reduce cochlear gain without significantly altering the amount of compression; that is, OHC loss would shift the low-level linear segment of the I/O curve without altering the slope of the compressive segment (Figure 7D of Plack et al., 2004). Their model was based on their observed lack of correlation between the compression exponent and absolute threshold accompanied by a strong negative correlation between gain and absolute threshold (their Figure 6). Their data was restricted to mild-to-moderate hearing losses and to a probe frequency of 4 kHz. Hence, one might object to the present analyses on the grounds that their model has not yet been corroborated for larger hearing losses or for the wider range of test frequencies used here. Our data, however, do support their model. **Figure 9** shows that the CT, a parameter of the I/O curve directly related with cochlear gain, is positively and highly significantly

Table 3 | Number of cases per I/O curve type and frequency (top) and percentage of cases per loss type (bottom).

		Frequency (kHz)					
I/O curve type	**Criterion**	**0.5**	**1**	**2**	**4**	**6**	***p***
Type 1 (CT present)	$HL_{TOTAL} \sim HL_{OHC}$	5	26	1	3	2	<1e–6
	$HL_{IHC}, HL_{OHC} > 0$	24	28	45	35	22	0.082
Type 2 (Linear)	$HL_{TOTAL} \sim HL_{OHC}$	8	3	3	1	3	0.123*
	$HL_{IHC}, HL_{OHC} > 0$	5	1	14	22	19	1e–6
Type 3 (CT absent with compression)	$HL_{TOTAL} \sim HL_{IHC}$	25	15	7	3	5	3e–5
Total		67	73	70	64	51	
Loss type (%)	Total gain loss (linear I/O curve)	19.4	5.5	24.3	35.9	43.1	1.7e–4
	Pure OHC dysfun. ($HL_{TOTAL} \sim HL_{OHC}$)	19.4	39.7	5.7	6.3	9.8	1e–6
	Mixed OHC/IHC dysfun. ($HL_{OHC}, HL_{IHC} > 0$)	80.6	60.3	94.3	93.8	90.2	0.14

p indicates significance levels for chi-squared tests. The asterisk indicates that the statistical test was not reliable because the number of cases was insufficient.

correlated with absolute threshold (**Figure 9**, bottom) while the average slope over the compressive segment of the I/O curve (i.e., over the input level range from the CT to the RLT) is uncorrelated with absolute threshold (**Figure 9**, top). This supports the results of Plack et al. (2004) at 4 kHz, extends their model to greater hearing losses and to a wider frequency range from 0.5 to 6 kHz, and supports the validity of our approach.

DISCUSSION

The aim of the current study was threefold: (1) to assess to what extent the audiometric loss is due to a reduction in cochlear gain (or OHC dysfunction), and/or to an additional component, referred here to as IHC dysfunction; (2) to investigate the frequency distribution of the two potential contributions; and (3) to investigate the degree of variability of the two contributions across listeners. Our approach was based on the analysis of behaviorally inferred cochlear I/O curves, as we proposed elsewhere (Lopez-Poveda and Johannesen, 2012).

Regarding the first and second aims, results for Type 1 I/O curves (i.e., for curves with a CT) suggest that on average IHC and OHC dysfunction contribute 30–40 and 60–70% to the audiometric loss, respectively, and that these percentages hold approximately constant across the frequency range from 500 Hz to 6 kHz (**Figure 6**). Regarding the third aim, results suggest that the proportion of the audiometric loss attributed to cochlear gain loss can vary largely across listeners with similar hearing losses, without a clear frequency pattern (**Figure 8**). Cases for which audiometric thresholds could be explained exclusively in terms of IHC dysfunction (Type 3 I/O curves) or in terms of cochlear gain loss (points in the diagonal region of **Figure 7**) were comparatively more numerous at low than at high frequencies (**Table 3**). The large majority of cases, however, were consistent with mixed OHC/IHC dysfunction, even though in some of these cases (Type 3 I/O curves) cochlear gain loss was unlikely to contribute to the audiometric loss (**Table 3**). Total cochlear gain loss (i.e., linear I/O curves), occurred more frequently at high frequencies than at low frequencies (**Table 3**).

POTENTIAL METHODOLOGICAL SOURCES OF BIAS

On the accuracy of the TMC method for estimating I/O curves

In inferring I/O curves from TMCs, the assumption has been made that the post-mechanical rate of recovery from forward masking is independent of masker frequency and level (Nelson et al., 2001). Evidence exists, however, that for NH listeners the recovery rate is twice as fast for masker levels below around 83 dB SPL than for higher masker levels (Wojtczak and Oxenham, 2009). This level effect, however, does not occur for HI listeners (Wojtczak and Oxenham, 2010). There also exists evidence that the recovery rate might be slower at low ($\leq$1 kHz) than at high probe frequencies (Stainsby and Moore, 2006), although this evidence is controversial (Lopez-Poveda and Alves-Pinto, 2008). Lopez-Poveda and Johannesen (2012) discussed that if these assumptions did not hold, Type 1 I/O curves (i.e., curves with a CT) would lead to larger HL_{IHC} and smaller HL_{OHC}. In the present context, this means that if the assumptions were not valid, the contribution of HL_{IHC} to the total hearing loss might be higher than reported in **Figure 6**.

Ambiguity of linear I/O curves

Linear I/O curves have been assumed indicative of total cochlear gain loss. This assumption may be inaccurate sometimes. Assuming that cochlear I/O curves become linear at high input levels (something still controversial, Robles and Ruggero, 2001, pp. 1308–1309), for cases with substantial IHC dysfunction, the mechanical cochlear response at the probe detection threshold might be so much higher with respect to NH that only the high-level linear segment of the I/O curve can be measured (e.g., Figure 1D of Lopez-Poveda and Johannesen, 2012). Hence, linear I/O curves at high input levels may indicate two different things: total cochlear gain loss or substantial IHC dysfunction. It is not possible to distinguish between these two cases. Therefore, some of the cases presently classified as "total cochlear gain loss" (or total OHC dysfunction) may actually reflect substantial IHC dysfunction.

An arbitrary slope criterion of 0.75 dB/dB has been used to separate Type 2 from Type 3 I/O curves. A sensitivity analysis was done to test to what extent results depended on the slope criterion value and we found that only five out of the 325 I/O curves would change type if the slope criterion were varied from 0.6 to 1 dB/dB. Therefore, I/O curve classification seems rather insensitive to slope criterion within these limits.

The impact of using a mean linear-reference TMC for some cases

A linear reference TMC could not be measured for eight participants (four of them from our previous study) because their hearing losses at the linear reference probe frequencies (**Table 1**) were so high that masker levels would have exceeded the maximum output level of our system. I/O curves for these cases were inferred using a mean linear reference TMC from all other subjects (see Methods). It is unlikely that this methodological difference affected the main results. First, CTs inferred using the mean linear reference TMC were within 5-dB of corresponding estimates inferred using the variant TMC method of Lopez-Poveda and Alves-Pinto (2008), a method that does not require a linear reference TMC (results not shown). Second, the number of I/O curves inferred using a mean linear reference TMC was only a very small fraction of the total number of I/O curves used in the present study.

Cochlear gain for normal hearing listeners and total OHC loss

Linear I/O curves were regarded as indicative of total cochlear gain loss (**Figures 4**, **5**). For these cases, HL_{OHC} was set equal to the mean cochlear gain of the reference, NH group. If the latter were inaccurate, this could have affected the present estimates of HL_{OHC} (i.e., the number and position of blue crosses in **Figure 7**). Gain for the NH group was calculated as described in section I/O Curve Analyses and Taxonomy and one might argue that this method underestimated gain for those NH I/O curves with absent CT or RLT; that is, for I/O cures that were still compressive at the lowest or the highest input levels in the I/O curve. The present NH gain values at high frequencies, however, compare well with previously reported values inferred using different psychoacoustical methods and with values inferred from direct BM recordings. For example, at 4 kHz, mean gain was 42.7 dB hence comparable to the value (43.5 dB) reported by Plack et al. (2004). Plack

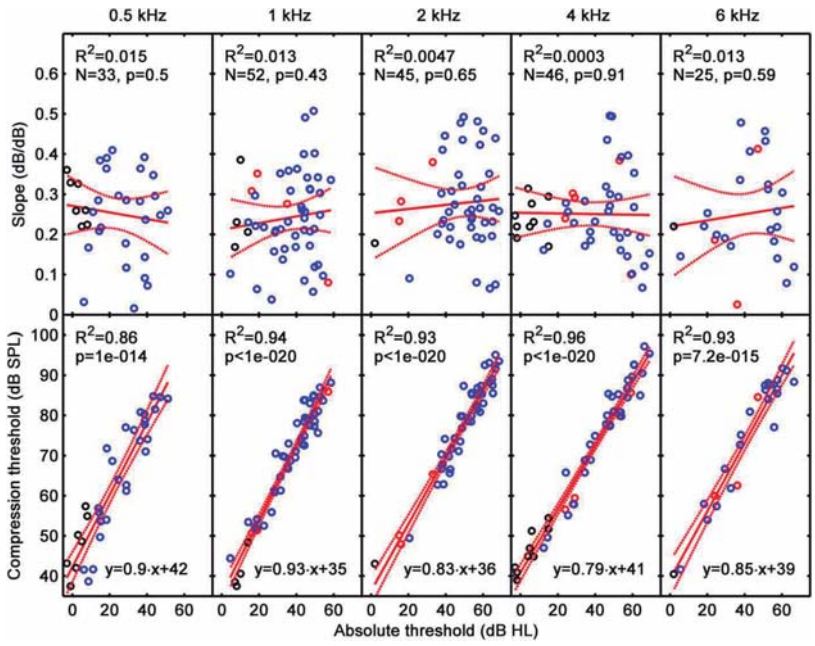

FIGURE 9 | Correlation of average slope (i.e., the slope of the I/O over the compressive segment) (top) and compression threshold (bottom) with absolute threshold. Each column is for a different test frequency, as indicated by the column title. Results for the present listeners are depicted as blue symbols; results for NH listeners and for listeners with mild-to-moderate loss from our earlier study (Lopez-Poveda and Johannesen, 2012) are depicted by black and red symbols, respectively. Continuous and dotted lines depict mean linear regression and 5–95% confidence intervals of the regression functions, respectively. The linear regression function and related statistics are shown in the insets.

et al. estimated gain as the difference between the masker levels of the linear-reference and on-frequency TMCs for the shortest gap, while gain was defined here as the sensitivity difference for low and high input levels (see Ruggero et al., 1997 for a discussion of different gain definitions). Gain for the present NH group would have been 48.9 dB had it been calculated using the definition of Plack et al. (2004), hence slightly higher than the value of Plack et al. The present NH gain compares well also with the value (35 dB at 6 kHz) that would be obtained from the I/O curves in Figure 2 of Oxenham and Plack (1997) that were inferred using a different psychoacoustical method known as growth of forward masking. Also, the present NH gain values at 4 kHz are within the value range suggested by direct basal BM recordings (range = 19–62 dB; median = 40 dB; mean = 38 dB; Table 1 of Robles and Ruggero, 2001). Altogether, this suggests that the present high-frequency NH gain values were reasonable.

Direct BM recording in animals suggest that cochlear gain is less for apical than for basal BM regions although it is possible that the difference is partly due to damage of apical cochlear mechanics during experimental recordings. For example, the change of chinchilla BM sensitivity at the characteristic frequency between low and high input levels is 10–20 dB at 500–800 Hz compared to 50 dB at 8–9 kHz (Tables 2, 3 in Robles and Ruggero, 2001). Previous psychoacoustical reports in humans using other methods and assumptions also suggest less gain at low frequencies but do not provide quantitative estimates (Plack et al., 2008). Gain estimates for the present NH group were 35.2 dB at 500 Hz and 42.7 dB at 4 kHz. The frequency trend in the present results is thus qualitatively consistent with direct BM observations, and quantitative differences might be due to differences in cochlear tonotopic mappings across species. If, however, the post-mechanical rate of recovery from forward masking were after all faster at lower frequencies (see previous sections), then cochlear gain would be smaller than reported here and the pattern of results would become more consistent with the animal data.

In summary, the NH gain values used here to quantify HL_{OHC} for cases of total OHC loss (linear I/O curves) seem reasonable at high frequencies but are less certain at low frequencies.

Incidentally, it is noteworthy that the present NH gain increased from 35.2 dB at 500 Hz to 43.5 dB at 1 kHz (unpaired, equal variance, t-test, $p = 0.014$) and then gain remained constant at higher frequencies (42.7 dB at 4 kHz). This pattern differed slightly from that reported by (Johannesen and Lopez-Poveda, 2008), from where some of the present NH data were taken. Indeed, in that study, gain increased gradually with increasing frequency from 37 dB at 500 Hz to 55 dB at 4 kHz (see their Figure 11A). This discrepancy is almost certainly due to methodological differences. First, the two studies used different

definitions of gain; Johannesen and Lopez-Poveda (2008) calculated gain as the difference between the RLT and CT. Second, the present NH data combined data from the 10 participants that took part in the study of Johannesen and Lopez-Poveda (2008) plus data for five more NH participants from Lopez-Poveda and Johannesen (2009); the latter contributed data particularly at 0.5 and 1 kHz. Third, Johannesen and Lopez-Poveda (2008) fitted their I/O curves with a third-order polynomial, which "forces" an RLT when a CT is present because the slopes of a third-order polynomial are identical below and above its inflection point. Indeed, fewer of the I/O curves from the study of Johannesen and Lopez-Poveda (2008) retained an RLT when they were re-analyzed using the present fitting approach.

The influence of conductive hearing loss on the results

Participants were controlled for conductive hearing loss. Nonetheless, their air-bone gaps could have differed by $\leq$15 dB at one frequency and/or $\leq$10 dB at any other frequency (see Methods). Small conductive losses might have increased probe absolute threshold and hence TMC masker levels by an amount equal to the conductive loss at the corresponding probe frequencies. The influence on the inferred I/O curve would be an upward vertical shift of the I/O curve equal to the conductive loss at the frequency of the linear reference probe and a rightward horizontal shift equal to the conductive loss at the frequency of the on-frequency masker. The CT would be affected only by the horizontal shift. Therefore, conductive loss at the particular frequency might lead to an overestimate of HL_{OHC} at that frequency. Pearson's correlation between HL_{OHC} and air-bone gap was significant only at 1 kHz and indicated decreasing HL_{OHC} for increasing air-bone gap. The direction of the effect was therefore opposite to the presumed effect of conductive hearing loss on HL_{OHC} and hence we concluded that conductive loss was unlikely to affect mean HL_{OHC} estimates in **Figure 6**.

The potential influence of dead regions on the results

A "dead region" is "a region in the cochlea where the IHCs and/or neurons are functioning so poorly that a tone which produces peak BM vibration in that region is detected via an adjacent region where the IHCs and/or neurons are functioning more efficiently" (p. 272 in Moore, 2007). In principle, dead regions could affect TMC measures as the probe presented in a dead region would be detected at a cochlear place removed from the probe place: e.g., at a place where the on-frequency masker might be subject to a compression regime different from compression at the normal probe place. For example, if the 4-kHz cochlear region was dead, a 4-kHz probe might be detected at the 2-kHz cochlear region where a 1.6-kHz (off-frequency) masker, which is typically regarded as a linear-reference condition, might be actually subject to significant compression.

Dead regions occur almost always for hearing losses above ~60 dB HL (Table 1 in Vinay and Moore, 2007) and the present listeners were roughly selected to have hearing losses <80 dB HL to be able to measure TMCs for a majority of test frequencies (**Figure 1**). Despite this, TMCs could not be measured for the higher losses. Of the 325 measured I/O curves, the number that may have been affected by dead regions can be roughly estimated from the data in Table 1 of Vinay and Moore (2007) (note that their data goes to 4 kHz only and we have assumed that the incidence of dead regions is identical at 4 and 6 kHz). Our analysis revealed that the expected incidence of dead regions was one, two and two at 2, 4, and 6 kHz, respectively. These numbers are so low that they are unlikely to have biased the reported HL_{OHC} and HL_{IHC}.

COMPARISON WITH EARLIER STUDIES

Based on our analysis of Type 1 I/O curves, we have shown that HL_{OHC} is 60–70% of HL_{TOTAL} across the frequency range from 0.5 to 6 kHz. This number is roughly consistent with that reported by earlier studies for more restricted frequency ranges, mostly at 4 kHz (Plack et al., 2004; Lopez-Poveda and Johannesen, 2012). It is, however, slightly lower than the 80–90% value reported elsewhere based on loudness models (Moore and Glasberg, 1997). Jürgens et al. (2011) showed that the two approaches (loudness model and TMCs) should give similar results. Therefore, the reason for this difference is uncertain.

We have also shown that even though the percentage of cases for which HL_{IHC} accounts entirely for HL_{TOTAL} (the percentage of Type 3 I/O curves) or the percentage of cases for which $HL_{OHC} \sim HL_{TOTAL}$ (the percentage of pure OHC dysfunction) are small, they are both larger for frequencies $\leq$1 kHz and decrease with increasing frequency (**Table 3**). To the best of the authors' knowledge, these trends have not been reported explicitly before, possibly due to the use of small sample sizes in earlier studies, but are not without precedent. For example, Moore and Glasberg (1997) used a model of loudness growth to estimate HL_{IHC} and found that it increased with decreasing frequencies for three listeners. Likewise, Jepsen and Dau (2011) reported greater HL_{IHC} at lower frequencies for a few subjects, although their average results were still consistent with the common notion that the most typical functional deficit is the loss of mechanical gain in the cochlear base.

An important distinction between the present and earlier analyses is that here, HL_{IHC} and HL_{OHC} were not always regarded as mutually exclusive, additive contributions to HL_{TOTAL}. Instead, the possibility has been contemplated that Equation (1) does not hold for cases where IHC dysfunction is so significant that it makes it impossible to measure a CT. In these cases, it was assumed that HL_{TOTAL} may be explained fully in terms of HL_{IHC} even though concomitant cochlear gain loss did probably occurred (**Figure 7**, bottom).

STRUCTURE-FUNCTION RELATIONSHIPS

Great care must be exercised at establishing a direct link between the behavioral deficits seen here (audiometric loss and cochlear gain loss) and hair cell pathophysiology in humans. Discussing potential relationships might be nonetheless useful.

We have shown that for a large percentage of cases (Type 1 I/O curves), 60–70% of HL_{TOTAL} is due to HL_{OHC} and 30–40% is due to HL_{IHC}, and that these percentages are roughly constant across frequencies (**Figure 6**). It would be probably wrong to conclude that this implies identical physical damage to OHCs and IHCs along the cochlear length. First, when physical hair cell damage occurs (e.g., after noise exposure), it is typically

greater in the cochlear base than in the apex (Møller, 2000). Second, the median age of the present participants was 61 years, hence for most of them the cause of hearing loss was probably presbycusis. Presbycusis is associated with a reduction of the endocochlear potential that causes high-frequency hearing loss (Schmiedt et al., 2002). This high-frequency loss is almost certainly due to concomitant, combined IHC and OHC dysfunction. A given reduction of the endocochlear potential causes greater loss of cochlear gain in the cochlear base than in the apex (Figure 8 of Saremi and Stenfelt, 2013), and a reduced response in the IHCs (Meddis et al., 2010; Panda et al., 2014). The present results for Type 1 I/O curves are consistent with concomitant IHC and OHC dysfunction characteristic of metabolic presbycusis and less so with the alternative and perhaps prevailing view that high-frequency loss is due to greater anatomical loss or damage of basal OHCs.

We have also shown, however, that the percentage of Type 2, linear I/O curves increases with increasing test frequency (**Figure 7**-top and **Table 3**). If metabolic presbycusis linearized cochlear responses (Saremi and Stenfelt, 2013), this might be indicative that metabolic presbycusis reduces the endocochlear potential more in the cochlear base than in the apex, something unlikely. A more parsimonious explanation for the higher percentage of linear I/O curves at high frequencies would be that they are actually due to severe physical OHC loss or damage. The latter explanation would be consistent with the prevailing view that physical OHC damage is greater in the cochlear base than in the apex (Møller, 2000).

Lastly, we have also shown that the percentage of Type 3 I/O curves is greatest for test frequencies ≤1 kHz and decreases with increasing frequency. This trend of more frequent IHC dysfunction at apical sites remains intriguing. A few studies have reported similar trends. For example, apical IHCs were found to be more labile than basal IHCs in guinea pigs treated with polypeptide antibiotics (Kohonen, 1965). Similarly, after administration of tobramycin, IHCs were found to be normal in the base but completely damaged in the apex whereas the OHCs were found to be normal in the apex and damaged in the base (Aran et al., 1982). Therefore, some Type 3 I/O curves might be indicative of antibiotic-induced hearing loss.

Unfortunately, confirmation of these conjectures was not possible due to the lack of accurate information regarding the etiology of hearing loss for the present participants.

CONCLUSIONS

With regard to the contribution of IHC and OHC dysfunction to the audiometric loss, the main conclusions are:

1. For cases where a CT is present, IHC and OHC dysfunction contribute on average to 30–40 and 60–70% to the total audiometric loss, and these contributions are approximately constant across the frequency range from 0.5 to 6 kHz.
2. The individual variability of the relative contributions of IHC and OHC dysfunction to the audiometric loss is, however, large particularly at low frequencies or mild-to-moderate hearing losses.

With regard to the incidence of dysfunction types, the main conclusions are:

3. The large majority of cases suffer from mixed IHC and OHC dysfunction, even though in some cases with presumably substantial IHC dysfunction, any concomitant OHC dysfunction does not contribute to the audiometric loss.
4. The percentage of cases for which the audiometric loss can be explained exclusively in terms of cochlear gain loss or of inefficient IHC processes (i.e., cases of pure OHC or IHC dysfunction, respectively) is higher at frequencies ≤1 kHz and decreases gradually with increasing frequency.
5. The percentage of cases suffering from total cochlear gain loss (i.e., linear I/O curves) increases gradually with increasing frequency.

Overall, the present results undermine the common view that high-frequency loss is typically due to greater physical damage of basal OHCs, and suggest that in a large percentage of cases, it is due to a common mechanism that concomitantly affects IHCs and OHCs, possibly reduced endocochlear potential. They further suggest that IHC processes may be more labile in the apex than in the base and/or that IHC dysfunction may have a greater impact on auditory threshold than cochlear gain loss at low frequencies.

ACKNOWLEDGMENTS

We thank Bill Woods and Sridhar Kalluri for insightful discussions, Almudena Eustaquio-Martin for technical support, and the staff of the ENT Service of Salamanca University Hospital and "La Alamedilla" Clinic (Salamanca, Spain) for their invaluable help with participant recruitment. Work supported by the Starkey Laboratories, (EEUU); Junta de Castilla y León; and the Spanish Ministry of Economy and Competitiveness (ref. BFU2012-39544-C02).

REFERENCES

AAO-HNS. (1993). American Academy of Otolaryngology – Head and Neck Surgery. *Bulletin* 16–17.

ANSI. (1996). *S3.6 Specification for Audiometers*. New York, NY: American National Standards Institute.

Aran, J. M., Erre, J. P., Guilhaume, A., and Aurousseau, C. (1982). The comparative ototoxicities of gentamicin, tobramycin and dibekacin in the guinea pig. A functional and morphological cochlear and vestibular study. *Acta Otolaryngol. Suppl.* 390, 1–30. doi: 10.3109/00016488209108895

Bacon, S. P., Fay, R. R., and Popper, A. N. (2004). *Compression: From Cochlea to Cochlear Implants*. New York, NY: Springer-Verlag.

Chen, G. D., and Fechter, L. D. (2003). The relationship between noise-induced hearing loss and hair cell loss in rats. *Hear. Res.* 177, 81–90. doi: 10.1016/S0378-5955(02)00802-X

Hicks, M. L., and Bacon, S. P. (1999). Effects of aspirin on psychophysical measures of frequency selectivity, two-tone suppression, and growth of masking. *J. Acoust. Soc. Am.* 106(3 Pt 1), 1436–1451. doi: 10.1121/1.427146

Huizing, E. H., and de Groot, J. C. (1987). Human cochlear pathology in aminoglycoside ototoxicity–a review. *Acta Otolaryngol. Suppl.* 436, 117–125. doi: 10.3109/00016488709124984

Jepsen, M. L., and Dau, T. (2011). Characterizing auditory processing and perception in individual listeners with sensorineural hearing loss. *J. Acoust. Soc. Am.* 129, 262–281. doi: 10.1121/1.3518768

Johannesen, P. T., and Lopez-Poveda, E. A. (2008). Cochlear nonlinearity in normal-hearing subjects as inferred psychophysically and from distortion-product otoacoustic emissions. *J. Acoust. Soc. Am.* 124, 2149–2163. doi: 10.1121/1.2968692

Jürgens, T., Kollmeier, B., Brand, T., and Ewert, S. D. (2011). Assessment of auditory nonlinearity for listeners with different hearing losses using temporal masking and categorical loudness scaling. *Hear. Res.* 280, 177–191. doi: 10.1016/j.heares.2011.05.016

Kohonen, A. (1965). Effect of some ototoxic drugs upon the pattern and innervation of cochlear sensory cells in the guinea pig. *Acta Otolaryngol. Suppl.* 208, l–70.

Levitt, H. (1971). Transformed up-down methods in psychoacoustics. *J. Acoust. Soc. Am.* 49(Suppl 2), 467–477. doi: 10.1121/1.1912375

Liberman, M. C., and Dodds, L. W. (1984). Single-neuron labeling and chronic cochlear pathology. III. Stereocilia damage and alterations of threshold tuning curves. *Hear. Res.* 16, 55–74. doi: 10.1016/0378-5955(84)90025-X

Lopez-Poveda, E. A., and Alves-Pinto, A. (2008). A variant temporal-masking-curve method for inferring peripheral auditory compression. *J. Acoust. Soc. Am.* 123, 1544–1554. doi: 10.1121/1.2835418

Lopez-Poveda, E. A., and Johannesen, P. T. (2009). Otoacoustic emission theories and behavioral estimates of human basilar membrane motion are mutually consistent. *J. Assoc. Res. Otolaryngol.* 10, 511–523. doi: 10.1007/s10162-009-0176-9

Lopez-Poveda, E. A., and Johannesen, P. T. (2012). Behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *J. Assoc. Res. Otolaryngol.* 13, 485–504. doi: 10.1007/s10162-012-0327-2

Lopez-Poveda, E. A., Plack, C. J., and Meddis, R. (2003). Cochlear nonlinearity between 500 and 8000 Hz in listeners with normal hearing. *J. Acoust. Soc. Am.* 113, 951–960. doi: 10.1121/1.1534838

Lopez-Poveda, E. A., Plack, C. J., Meddis, R., and Blanco, J. L. (2005). Cochlear compression in listeners with moderate sensorineural hearing loss. *Hear. Res.* 205, 172–183. doi: 10.1016/j.heares.2005.03.015

McGill, T. J., and Schuknecht, H. F. (1976). Human cochlear changes in noise induced hearing loss. *Laryngoscope* 86, 1293–1302. doi: 10.1288/00005537-197609000-00001

Meddis, R., Lecluyse, W., Tan, C. M., Panda, M., and Ferry, R. (2010). "Beyond the audiogram: identifying and modeling patterns of hearing loss," in *The Neurophysiological Bases of Auditory Perception*, eds E. A. Lopez-Poveda, A. R. Palmer, and R. Meddis (New York, NY: Springer), 631–640. doi: 10.1007/978-1-4419-5686-6_57

Mills, D. M. (2006). Determining the cause of hearing loss: differential diagnosis using a comparison of audiometric and otoacoustic emission responses. *Ear Hear.* 27, 508–525. doi: 10.1097/01.aud.0000233885.02706.ad

Møller, A. R. (ed.). (2000). "Disorders of the Cochlea," in *Hearing: Its Physiology and Pathophysiology* (San Diego, CA: Academic Press), 395–433.

Moore, B. C. J. (2007). *Cochlear Hearing Loss*. Chichester: John Wiley & Sons, Ltd. doi: 10.1002/9780470987889

Moore, B. C. J., and Glasberg, B. R. (1997). A model of loudness perception applied to cochlear hearing loss. *Aud. Neurosci.* 3, 289–311.

Muller, J., and Janssen, T. (2004). Similarity in loudness and distortion product otoacoustic emission input/output functions: implications for an objective hearing aid adjustment. *J. Acoust. Soc. Am.* 115, 3081–3091. doi: 10.1121/1.1736292

Nelson, D. A., Schroder, A. C., and Wojtczak, M. (2001). A new procedure for measuring peripheral compression in normal-hearing and hearing-impaired listeners. *J. Acoust. Soc. Am.* 110, 2045–2064. doi: 10.1121/1.1404439

Oxenham, A. J., and Plack, C. J. (1997). A behavioral measure of basilar-membrane nonlinearity in listeners with normal and impaired hearing. *J. Acoust. Soc. Am.* 101, 3666–3675. doi: 10.1121/1.418327

Panda, M. R., Lecluyse, W., Tan, C. M., Jürgens, T., and Meddis, R. (2014). Hearing dummies: individualized computer models of hearing impairment. *Int. J. Audiol.* doi: 10.3109/14992027.2014.917206. [Epub ahead of print].

Pickles, J. O. (ed.). (2008). "Sensorineural hearing loss," in *An Introduction to the Physiology of Hearing* (New York, NY: Academic Press), 309–342.

Plack, C. J., Drga, V., and Lopez-Poveda, E. A. (2004). Inferred basilar-membrane response functions for listeners with mild to moderate sensorineural hearing loss. *J. Acoust. Soc. Am.* 115, 1684–1695. doi: 10.1121/1.1675812

Plack, C. J., Oxenham, A. J., Simonson, A. M., O'Hanlon, C. G., Drga, V., and Arifianto, D. (2008). Estimates of compression at low and high frequencies using masking additivity in normal and impaired ears. *J. Acoust. Soc. Am.* 123, 4321–4330. doi: 10.1121/1.2908297

Robles, L., and Ruggero, M. A. (2001). Mechanics of the mammalian cochlea. *Physiol. Rev.* 81, 1305–1352.

Ruggero, M. A., Rich, N. C., Recio, A., Narayan, S. S., and Robles, L. (1997). Basilar-membrane responses to tones at the base of the chinchilla cochlea. *J. Acoust. Soc. Am.* 101, 2151–2163. doi: 10.1121/1.418265

Saremi, A., and Stenfelt, S. (2013). Effect of metabolic presbyacusis on cochlear responses: a simulation approach using a physiologically-based model. *J. Acoust. Soc. Am.* 134, 2833–2851. doi: 10.1121/1.4820788

Schmiedt, R. A., Lang, H., Okamura, H. O., and Schulte, B. A. (2002). Effects of furosemide applied chronically to the round window: a model of metabolic presbyacusis. *J. Neurosci.* 22, 9643–9650.

Selimoglu, E. (2007). Aminoglycoside-induced ototoxicity. *Curr. Pharm. Des.* 13, 119–126. doi: 10.2174/138161207779313731

Stainsby, T. H., and Moore, B. C. (2006). Temporal masking curves for hearing-impaired listeners. *Hear. Res.* 218, 98–111. doi: 10.1016/j.heares.2006.05.007

Trautwein, P., Hofstetter, P., Wang, J., Salvi, R., and Nostrant, A. (1996). Selective inner hair cell loss does not alter distortion product otoacoustic emissions. *Hear. Res.* 96, 71–82. doi: 10.1016/0378-5955(96)00040-8

van Ruijven, M. W., de Groot, J. C., and Smoorenburg, G. F. (2004). Time sequence of degeneration pattern in the guinea pig cochlea during cisplatin administration. A quantitative histological study.*Hear. Res.* 197, 44–54. doi: 10.1016/j.heares.2004.07.014

Vinay, and Moore, B. C. (2007). Prevalence of dead regions in subjects with sensorineural hearing loss. *Ear Hear.* 28, 231–241. doi: 10.1097/AUD.0b013e31803126e2

Wang, J., Powers, N. L., Hofstetter, P., Trautwein, P., Ding, D., and Salvi, R. (1997). Effects of selective inner hair cell loss on auditory nerve fiber threshold, tuning and spontaneous and driven discharge rate. *Hear. Res.* 107, 67–82. doi: 10.1016/S0378-5955(97)00020-8

Watson, C. S., and Gengel, R. W. (1969). Signal duration and signal frequency in relation to auditoy sensitivitiy. *J. Acoust. Soc. Am.* 46, 989–997. doi: 10.1121/1.1911819

Wojtczak, M., and Oxenham, A. J. (2009). Pitfalls in behavioral estimates of basilar-membrane compression in humans. *J. Acoust. Soc. Am.* 125, 270–281. doi: 10.1121/1.3023063

Wojtczak, M., and Oxenham, A. J. (2010). Recovery from on- and off-frequency forward masking in listeners with normal and impaired hearing. *J. Acoust. Soc. Am.* 128, 247–256. doi: 10.1121/1.3436566

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 14 May 2014; paper pending published: 27 May 2014; accepted: 02 July 2014; published online: 23 July 2014.

Citation: Johannesen PT, Pérez-González P and Lopez-Poveda EA (2014) Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. Front. Neurosci. ***8****:214. doi: 10.3389/fnins.2014.00214*

This article was submitted to Auditory Cognitive Neuroscience, a section of the journal Frontiers in Neuroscience.

Original Article

Forward-Masking Recovery and the Assumptions of the Temporal Masking Curve Method of Inferring Cochlear Compression

Trends in Amplification
2014, Vol. 18: 1–14

DOI: 10.1177/2331216514564253
tia.sagepub.com
SAGE

Patricia Pérez-González[1,2], Peter T. Johannesen[1,2], and Enrique A. Lopez-Poveda[1,2,3]

Abstract

The temporal masking curve (TMC) method is a behavioral technique for inferring human cochlear compression. The method relies on the assumptions that in the absence of compression, forward-masking recovery is independent of masker level and probe frequency. The present study aimed at testing the validity of these assumptions. Masking recovery was investigated for eight listeners with sensorineural hearing loss carefully selected to have absent or nearly absent distortion product otoacoustic emissions. It is assumed that for these listeners basilar membrane responses are linear, hence that masking recovery is independent of basilar membrane compression. TMCs for probe frequencies of 0.5, 1, 2, 4, and 6 kHz were available for these listeners from a previous study. The dataset included TMCs for masker frequencies equal to the probe frequencies plus reference TMCs measured using a high-frequency probe and a low, off-frequency masker. All of the TMCs were fitted using linear regression, and the resulting slope and intercept values were taken as indicative of masking recovery and masker level, respectively. Results for on-frequency TMCs suggest that forward-masking recovery is generally independent of probe frequency and of masker level and hence that it would be reasonable to use a reference TMC for a high-frequency probe to infer cochlear compression at lower frequencies. Results further show, however, that reference TMCs were sometimes shallower than corresponding on-frequency TMCs for identical probe frequencies, hence that compression could be overestimated in these cases. We discuss possible reasons for this result and the conditions when it might occur.

Keywords

cochlear nonlinearity, DPOAEs, otoacoustic emissions, middle-ear muscle reflex

Introduction

The mammalian cochlea compresses a wide range of sound pressure levels (SPLs) into a narrower range of mechanical responses. The amount of compression and the range of SPLs over which compression occurs depend on outer hair cell (OHC) function (Robles & Ruggero, 2001). Cochlear compression is thought to determine important auditory percepts such as absolute hearing threshold, the dynamic range of hearing, or auditory masking (Oxenham & Bacon, 2003, 2004). Detailed measurements of cochlear compression could thus be useful to diagnose hearing impairment (Lopez-Poveda & Johannesen, 2012; Plack, Drga, & Lopez-Poveda, 2004), to understand the impact of hearing loss on auditory perception (Bacon & Oxenham, 2004), or to fit hearing aids (Meddis, Lecluyse, Tan, Panda, & Ferry, 2010; Panda, Lecluyse, Tan, Jurgens, & Meddis, 2014). In humans, peripheral compression cannot be measured directly and so a number of psychoacoustical methods have been developed to infer it (Lopez-Poveda

[1]Instituto de Neurociencias de Castilla y León, Universidad de Salamanca, Salamanca, Spain
[2]Grupo de Audiología, Instituto de Investigación Biomédica de Salamanca, Salamanca, Spain
[3]Departamento de Cirugía, Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain

Corresponding author:
Enrique A. Lopez-Poveda, University of Salamanca, Calle Pintor Fernando Gallego 1, Salamanca 37007, Spain.
Email: ealopezpoveda@usal.es

& Alves-Pinto, 2008; Lopez-Poveda, Plack, & Meddis, 2003; Nelson, Schroder, & Wojtczak, 2001; Oxenham & Plack, 1997; Plack & Arifianto, 2010; Plack & O'Hanlon, 2003; Plack & Oxenham, 2000; Yasin, Drga, & Plack, 2013). These psychoacoustical techniques are indirect and hence are based on a number of assumptions. Here, we test the assumptions of a technique known as the temporal masking curve (TMC) method.

The TMC method (Nelson et al., 2001) consists of measuring the level of a tonal forward masker required to just mask a fixed tonal probe as a function of the time interval between the masker and the probe. A TMC is a graphical representation of the resulting masker levels against the corresponding masker-probe intervals. Because the probe level is fixed, the masker level increases with increasing masker-probe time interval and hence TMCs have positive slopes. Nelson et al. (2001) argued that the slope of any given TMC depends simultaneously on the amount of basilar membrane (BM) compression affecting the masker at a cochlear place whose characteristic frequency (CF) equals approximately the probe frequency *and* on the rate of recovery from the internal (postmechanical or compression free) masker effect. By assuming that the postmechanical recovery rate is the same across masker frequencies, BM input/output functions may be estimated by plotting the masker levels of a reference TMC (i.e., the TMC for a masker that is processed linearly by the cochlea) against the levels for any other masker frequency, paired according to masker-probe delays (Nelson et al., 2001).

In their original study, Nelson et al. (2001) used a masker frequency about an octave below the probe frequency as the reference TMC on the grounds that BM responses are linear for tones well below the CF. Lopez-Poveda et al. (2003) argued that the latter is true for basal cochlear regions but not for apical cochlear regions (Rhode & Cooper, 1996) and proposed inferring compression at low probe frequencies by using a reference TMC for a high probe frequency. This version of the TMC method has been used in many studies (e.g., Johannesen & Lopez-Poveda, 2008; Johannesen, Pérez-González, & Lopez-Poveda, 2014; Jurgens, Kollmeier, Brand, & Ewert, 2011; Lopez-Poveda & Alves-Pinto, 2008; Lopez-Poveda & Johannesen, 2012; Lopez-Poveda, Plack, Meddis, & Blanco, 2005; Nelson & Schroder, 2004; Panda et al., 2014; Plack & Drga, 2003; Plack et al., 2004). An implicit assumption of this approach is that the postmechanical rate of recovery from forward masking is independent of probe frequency.

The TMC method thus rests on two assumptions regarding the postmechanical rate of recovery from forward masking: (a) for a given probe frequency, it is independent of masker frequency; and (b) it is independent of probe frequency. These assumptions are controversial. Wojtczak and Oxenham (2009) questioned the first assumption by showing that the rate of postmechanical recovery is actually faster when masker and probe frequencies are equal (on-frequency condition) than when the masker frequency is about an octave below the probe frequency (reference condition). Given that masker levels are typically higher for the reference than for the on-frequency TMC, an alternative explanation for their findings is that forward-masking recovery is actually dependent upon masker level rather than masker frequency. Indeed, a third, less explicit assumption of the TMC method is that forward-masking recovery is independent of masker level. Wojtczak and Oxenham concluded that for normal-hearing listeners, the first assumption of the TMC method held for masker levels below 83 dB SPL but not for higher levels.

Stainsby and Moore (2006) questioned the second assumption of the TMC method. They showed that for hearing-impaired listeners with nearly absent distortion product otoacoustic emissions (DPOAEs), and hence presumably linear cochlear responses, TMCs are steeper for low than for high probe frequencies. On the other hand, other authors have provided experimental support for the second assumption using other psychoacoustical methods that do not require a reference TMC (Lopez-Poveda & Alves-Pinto, 2008; Plack et al., 2008). In an attempt to reconcile these seemingly disparate findings, Lopez-Poveda and Alves-Pinto (2008) argued that "absence of measurable DPOAEs at low frequencies is not necessarily indicative of linear cochlear responses because it is hard to measure DPOAEs at low frequencies due to physiological and ambient noise" (p. 1553). In other words, Lopez-Poveda and Alves-Pinto were suggesting that the absence of DPOAEs in the subjects used by Stainsby and Moore could be more apparent than real due to their using insufficiently sensitive DPOAE techniques. Indeed, Stainsby and Moore used primary tones with a single level of 70 dB SPL each even though DPOAEs depend strongly on the levels of the primary tones (e.g., Figure 7 in Lopez-Poveda & Johannesen, 2009), particularly at low frequencies (Figures 1 and 2 in Johannesen & Lopez-Poveda, 2010). Therefore, it is conceivable that DPOAEs may have appeared as *absent* to Stainsby and Moore but might have been present if they had used different primary levels. In addition, Stainsby and Moore used a fixed measurement time of 2 s across test frequencies even though DPOAE detectability increases with increasing measurement time (on average, the DPOAE signal-to-noise ratio improves by 3 dB for every doubling of the measurement time; e.g., see Figure 1 in Zurek, 1992; see also Figure 1 in Popelka, Osterhammel, Nielsen, & Rasmussen, 1993). The use of short recording times can hinder DPOAE detectability more at low

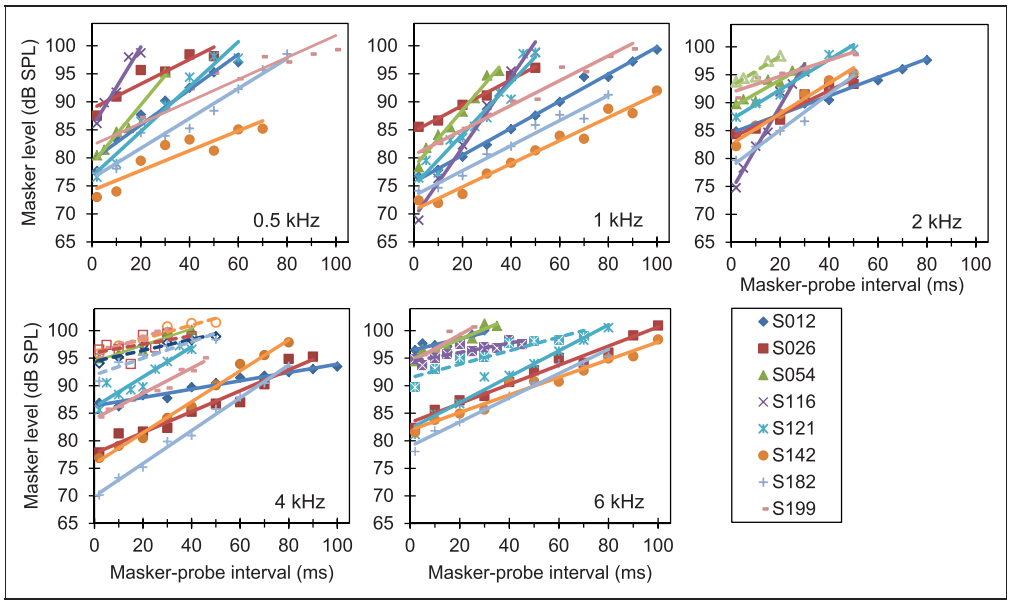

Figure 1. Experimental (symbols) and fitted (lines) TMCs. Each panel illustrates on-frequency TMCs (filled symbols, continuous lines) for a different probe frequency, as indicated by the numbers at the bottom-right corner of the panel. A panel also illustrates linear reference TMCs (dashed lines) if they were measured at the corresponding probe frequency.

frequencies where the physiological noise is comparatively higher. Therefore, it is conceivable that DPOAEs may have appeared as *absent* to Stainsby and Moore but might have been present if they had used longer recording times. An additional concern about the study of Stainsby and Moore is that they used only three subjects.

The aims of the present study were to revisit the two main assumptions of the TMC method using an approach inspired by Stainsby and Moore (2006) but with a larger sample size and improved methods to maximize DPOAE detectability.

Methods

Approach

The aim was to test if the postmechanical (i.e., compression free) rate of recovery from forward masking is independent of masker level and of probe frequency. To do it, we called back 68 hearing-impaired listeners who had participated in a related TMC study (Johannesen et al., 2014) and measured DPOAEs in these subjects at four test frequencies (0.5, 1, 2, and 4 kHz) and using eight different primary levels at each test frequency. Whenever possible, DPOAE primary levels were individually optimized to maximize DPOAE levels. Of the 68 listeners, we chose eight who showed absent or nearly absent DPOAEs and we assumed that they had linear cochlear responses. We analyzed the already available on-frequency TMCs for those listeners at test frequencies of 0.5, 1, 2, 4, and 6 kHz as well as their reference TMCs seeking correlations of TMC slope with probe frequency and masker level. Importantly, we overcame the limitations of the study by Stainsby and Moore (2006) by using a larger sample size ($N = 8$ vs. $N = 3$) and using improved DPOAE methods. Specifically, over a wide level range, we searched combinations of primary levels that maximize DPOAEs independently at each frequency compared with Stainsby and Moore who used primaries with only a fixed level of 70 dB SPL each; and we used longer measurement times of 30 s at 500 Hz and 10 s at higher frequencies compared with the 2s used by Stainsby and Moore. By including these improvements, we maximized the chance of detecting DPOAEs above the noise floor that might otherwise be missed, particularly at low frequencies. In other words, we were more confident that the lack of DPOAEs as observed using our methods was a better indicator of linear cochlear responses than a lack of DPOAEs as observed using the methods of Stainsby and Moore.

Experimental procedures were approved by the Ethics Review Board of the University of Salamanca. Informed consent was obtained from all participants.

DPOAE Measurements

Pairs of primary pure tones with frequencies (f_1, f_2) and corresponding levels (L_1, L_2) were presented, and the level of the $2f_1-f_2$ frequency component of the otoacoustic emission in the ear canal was recorded and regarded as the DPOAE level. DPOAEs were measured for f_2 of 0.5, 1, 2, and 4 kHz and for L_2 values from 35 to 70 dB SPL, in 5-dB steps (4 test frequencies × 8 levels = 32 conditions). For each test frequency f_2, f_1 was set equal to f_2/1.2. An attempt was made to individually set L_1 so as to maximize DPOAE levels. For L_2 values of 50 and 65 dB SPL, we empirically sought the L_1 value that maximized the DPOAE level, if any. When a pair of L_1 values was

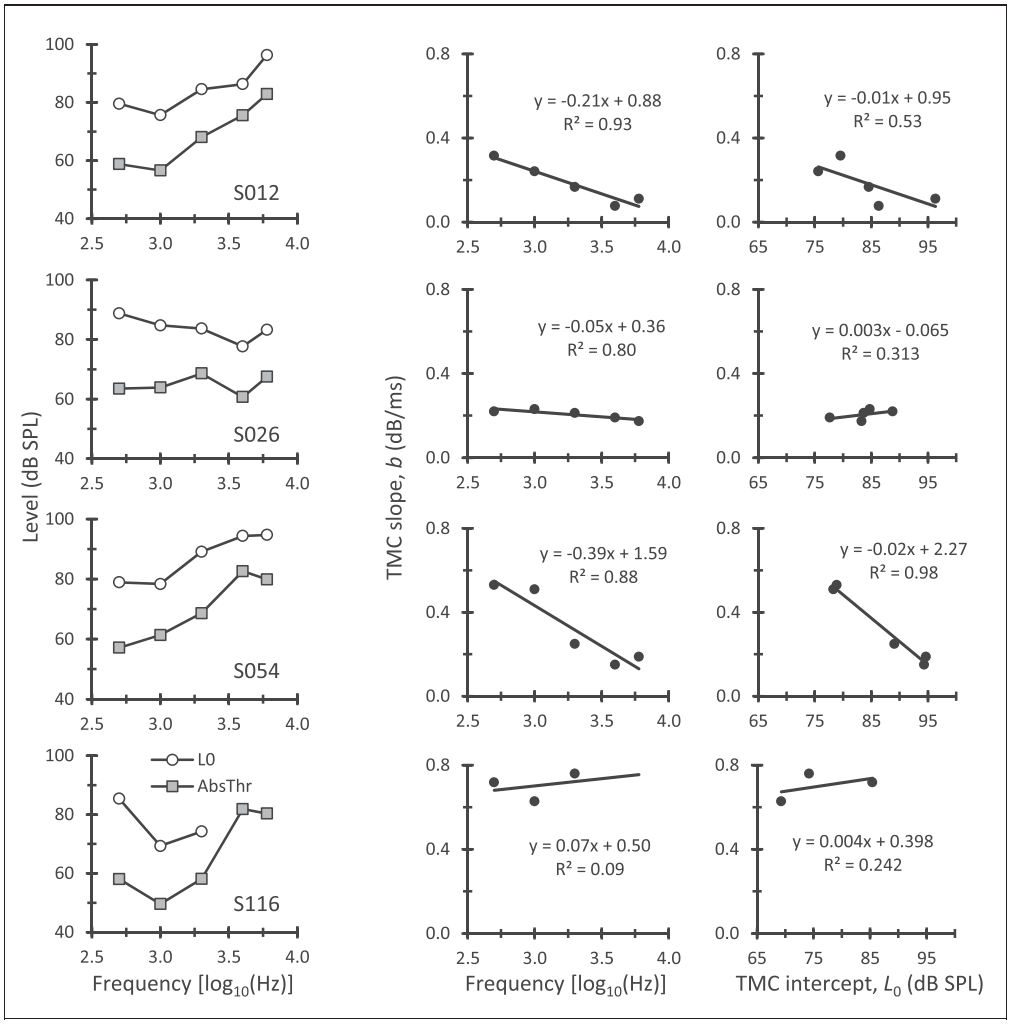

Figure 2. On-frequency TMC characteristics for four participants (S012, S026, S054, and S116). Left: Masker absolute thresholds (gray squares) and TMC intercept levels (L_0, open circles). Middle: TMC slope, b, as a function of frequency. Right: TMC slope, b, as a function of intercept level, L_0. Each row is for a different participant, as indicated in the bottom-right corner of the left panels. Straight lines and equations in the middle and right panels illustrate linear regression fits together with their corresponding equations and proportion of predicted variance (R^2).

found, then the values of L_1 for the other L_2 levels were obtained using linear regression. When individually optimal L_1 values were not found, we used the primary level rule of Neely, Johnson, and Gorga (2005) because it has been independently confirmed that this is the most appropriate rule to maximize DPOAE levels on average (cf. Figure 7 in Lopez-Poveda & Johannesen, 2009).

DPOAE measurements were obtained using an Intelligent Hearing System's Smart device (with SmartOAE software version 4.52) equipped with an Etymotic ER-10D probe. During the measurements, participants sat comfortably in a double-wall sound attenuating chamber and were asked to remain as steady as possible. The probe fit was checked before and after each recording session. The probe remained in the participant's ear throughout the whole measurement session to avoid measurement variance from probe fit. DPOAEs were measured for a preset measurement time of 30 s for $f_2 = 500$ Hz and 10 s for other f_2 frequencies. A DPOAE measurement was regarded as valid when it was 6 dB above the measurement noise floor (defined as the mean level over 10 frequency bins adjacent to the $2f_1 - f_2$ component in the OAE spectrum). When a response did not meet this criterion, the measurement was repeated. If the required criterion was not met for at least two of three successive tries, we concluded that DPOAEs were absent for that condition.

DPOAE measurements were regarded as valid only when they were 6 dB above the system's artifact response. The rationale behind this rather strict criterion and the details of the procedure for controlling for system's artifacts and calibration can be found elsewhere (Johannesen & Lopez-Poveda, 2008).

Participants

Eight listeners participated in the study (Table 1). They were selected from a sample of 68 listeners with symmetrical sensorineural hearing loss and no sign of middle-ear pathology (Johannesen et al., 2014). These eight listeners were selected because (a) they had absolute thresholds equal to or higher than 40 dB HL (American National Standards Institute, 1996) at the TMC test frequencies, a criterion also met by the three subjects of Stainsby and Moore (2006); and (b) they had absent DPOAEs for at least 29 of the 32 conditions (4 test frequencies × 8 primary levels) that were attempted, as shown in Table 2.

Middle-Ear Muscle Reflex Measurements

As a control, the threshold of activation of the middle-ear muscle reflex (MEMR) was measured using a clinical middle-ear analyzer (Interacoustics AT235h). Middle-ear compliance for a probe tone of 226 Hz and 85 dB SPL was measured in the presence and in the absence of ipsilateral MEMR elicitor tones with frequencies 500, 1000, 2000, and 4000 Hz and levels 75 to 100 dB HL in 5-dB steps. The MEMR activation threshold was regarded as the lowest elicitor level that evoked a detectable change in middle-ear compliance (re the non-elicitor condition) minus 2.5 dB, that is, minus half the elicitor intensity step. Measured MEMR activation thresholds are shown in Table 1.

Table 1. Participants' Data.

				Reference TMC	MEMR activation threshold (dB SPL)			
Participant	Sex	Age	Ear	(f_P, f_M)	500	1000	2000	4000
S012	M	80	Left	4, 1.6	n.p.	n.p.	n.p.	n.p.
S026	F	51	Left	4, 1.6	96	95	?	?
S054	M	79	Left	2, 0.8	106	?	n.p.	n.p.
S116	M	53	Right	6, 2.4	n.p.	105	106.5	n.p.
S121	M	60	Left	6, 2.4	96	95	106.5	n.p.
S142	M	51	Right	4, 2.0	101	95	96.5	104.5
S182	F	55	Right	4, 1.6	101	90	101.5	99.5
S199	F	73	Left	4, 2.0	?	?	?	?

Note. TMC = temporal masking curve; MEMR = middle-ear muscle reflex; n.p. = MEMR not present; ? = MEMR could not be measured reliably. Age is in years. Also shown is (a) the linear reference TMC condition measured for each listener, expressed as a pair of probe and masker frequencies (f_P, f_M) in kHz; and (b) the threshold of activation of the MEMR for different eliciting frequencies.

Table 2. DPOAE Levels (dB SPL) for Those Participants (S#), Test Frequencies (Columns), and L_2 Levels (Rows) for Which DPOAEs Were Measurable.

	F_2 (kHz)							
	0.5		1		2		4	
L_2 (dB SPL)	S#	dB SPL	S#	dB SPL	S#	dB SPL	S#	dB SPL
70	S054	−1.5						
65	S199	−1.7	S116	−4.0	S199	3.9	S026	10.6
							S199	−0.3
60	S116	2.8						
	S121	7.5						
55	S054	−7.8	S012	−3.5				
	S142	1.8						
50			S142	−9.4				
45							S026	−6.0
40			S012	−5.6	S054	−14.1	S142	−6.3
					S121	−9.6		
35			S116	−5.2	S182	−14.1		

Note. DPOAE = distortion product otoacoustic emission. Missing values indicate absent DPOAEs.

TMC Measurements

Temporal masking curves for the eight selected listeners were taken from a previously published study (Johannesen et al., 2014). Procedures are fully described in that study and hence only a summary is given here.

On-frequency TMCs were measured for probe frequencies (f_P) of 0.5, 1, 2, 4, and 6 kHz. Maskers and probes were sinusoids. The duration of the maskers was 210 ms including 5-ms cosine-squared onset and offset ramps. Probes had durations of 10 ms, including 5-ms cosine-squared onset and offset ramps with no steady-state portion, except for the 500-Hz probe, whose duration was 30 ms with 15-ms ramps and no steady-state portion. The level of the probes was fixed at 10 dB above the individual absolute threshold for the probe. Masker-probe time intervals, defined as the period from masker offset to probe onset, ranged from 10 to 100 ms in 10-ms steps with an additional gap of 2 ms. Masker levels sometimes reached the maximum permitted sound level output (105 dB SPL) for time intervals shorter than the maximum 100 ms. If the number of measured data points was insufficient for curve fitting (see later), masker levels were measured for additional intermediate intervals (e.g., 5, 15, 25 ms).

A single reference TMC was measured for each participant. The reference TMC was for a probe frequency of 2, 4, or 6 kHz and for a masker frequency equal to $0.4f_P$ or $0.5f_P$. The selection of the reference condition depended on the participant's hearing loss at the reference probe frequency and on the maximum permitted sound level output (105 dB SPL). Following the indications of earlier studies (Lopez-Poveda & Alves-Pinto, 2008; Lopez-Poveda et al., 2003), the reference conditions were sought in the following order of priority (Johannesen et al., 2014): (4, 1.6), (4, 2), (6, 2.4), (6, 3), (2, 0.8), (2, 1), where the numbers in each pair denote probe and masker frequency in kHz, (f_P, f_M), respectively. Table 1 shows the reference TMC conditions measured for each participant.

TMC Analysis

As in many previous studies (e.g., Lopez-Poveda et al., 2003, 2005; Nelson & Schroder, 2004; Nelson et al., 2001; Plack et al., 2004; Stainsby & Moore, 2006), TMCs were fitted using a straight line:

$$L_M(t) = L_0 + b \cdot t \quad (1)$$

where $L_M(t)$ is the masker level (in dB SPL) at masker-probe time interval t (in ms), b is the TMC slope (dB/ms), and L_0 is the intercept masker level (in dB SPL) for a masker-probe time interval of 0 ms. Given that the selected participants presumably had linear cochlear responses, parameter b was taken as indicative of forward-masking recovery rate. L_0 was used as indicative of the range of masker levels in a TMC.

Results

Distortion product otoacoustic emissions

Table 2 gives the DPOAE levels measured for each participant for each pair of test frequency, f_2, and primary level, L_2. Missing values indicate absent DPOAEs. DPOAEs were present for only 19 of the 256 possible cases (4 test frequencies × 8 primary levels × 8 participants). Furthermore, for no participant were DPOAEs present in more than 3 out of 32 conditions. The noise floor level was less than −4 dB SPL for all participants at 0.5 and 1 kHz, except for S121 at 500 Hz, for whom the noise floor was −1 dB SPL. The average noise floor level was −8.19 and −13.50 dB SPL at 0.5 and 1 kHz, respectively, and lower at higher frequencies. Altogether, these results suggest that the absence of DPOAEs for these participants is not due to high levels of noise. Therefore, we concluded the absence was due to their having linear (or almost linear) cochlear responses over the frequency range from 0.5 to 4 kHz. The accuracy of this conclusion will be discussed later.

Temporal masking curves

Figure 1 shows experimental (symbols) and fitted (lines) TMCs. On-frequency and reference fitted TMCs are illustrated using continuous and dashed lines, respectively. Note that 46 TMCs were measured (38 on-frequency plus 8 reference TMCs) and that on-frequency TMCs are missing for S116 at 4 and 6 kHz (Table 3). For S116, probe thresholds were so high at 4 kHz that we anticipated masker levels would be higher than the maximum system output level. Hence, we did not attempt measuring on-frequency TMCs at 4 kHz. For S116, we tried measuring on-frequency TMCs at 6 kHz but masker levels exceeded the maximum system output. Except for one case, missing points in Figure 1 are indicative that the corresponding masker levels would exceed the maximum system output level (105 dB SPL). The exception is the on-frequency TMC for S142 at 0.5 kHz. This TMC was nonmonotonic (i.e., masker levels decreased with increasing masker-probe time interval beyond 70 ms), probably because the subject had greater difficulty at keeping track of the probe for the longer masker-probe time intervals. We regarded the nonmonotonic trend as unrealistic and omitted the declining portion of the TMC.

Table 3 gives the parameters and goodness-of-fit statistics of the straight line fits to the TMCs (root mean square, RMS, errors and proportion of variance

Table 3. Linear Regression Parameters and Goodness-of-Fit for Each Subject (S#) and TMC.

		Linear regression model (equation (1))				
S#	kHz	L_0 (dB SPL)	b (dB/ms)	R^2	RMS (dB)	Num. points
S012	0.5	79.6	0.32	0.95	1.40	7
S026	0.5	88.8	0.22	0.86	1.45	6
S054	0.5	78.9	0.53	0.98	0.77	5
S116	0.5	85.4	0.72	0.94	1.13	5
S121	0.5	76.7	0.40	0.95	1.73	7
S142	0.5	74.2	0.18	0.83	1.80	8
S182	0.5	76.4	0.27	0.97	1.29	9
S199	0.5	82.3	0.20	0.89	2.18	11
S012	1	75.7	0.24	0.99	0.67	11
S026	1	84.7	0.23	0.99	0.41	6
S054	1	78.3	0.51	0.98	0.75	8
S116	1	69.3	0.63	0.98	1.29	6
S121	1	75.0	0.46	0.94	1.76	11
S142	1	70.7	0.21	0.97	1.07	11
S182	1	73.2	0.22	0.97	1.00	9
S199	1	80.5	0.22	0.97	1.02	10
S012	2	84.6	0.17	0.97	0.70	9
S026	2	83.7	0.21	0.94	0.88	6
S054	2	89.1	0.25	0.91	0.75	7
S116	2	74.2	0.76	0.97	1.24	7
S121	2	87.0	0.27	0.98	0.70	6
S142	2	82.6	0.27	0.98	0.70	6
S182	2	78.6	0.33	0.98	0.78	6
S199	2	91.9	0.14	0.90	0.78	6
S012	4	86.3	0.08	0.96	0.49	11
S026	4	77.7	0.19	0.96	1.16	10
S054	4	94.4	0.15	0.91	0.65	5
S116	4					
S121	4	86.1	0.27	0.86	1.39	9
S142	4	75.8	0.28	0.99	0.66	9
S182	4	69.9	0.30	0.99	0.63	9
S199	4	84.0	0.23	0.96	0.64	10
S012	6	96.3	0.11	0.82	0.49	7
S026	6	83.3	0.17	0.97	0.88	11
S054	6	94.7	0.19	0.91	0.65	8
S116	6					
S121	6	82.2	0.24	0.97	0.97	9
S142	6	81.9	0.16	0.96	0.97	11
S182	6	79.0	0.22	0.97	0.95	9
S199	6	94.2	0.25	0.80	1.00	6
S012	LR-4	94.4	0.10	0.92	0.49	6
S026	LR-4	96.0	0.08	0.29	1.44	8
S054	LR-2	92.9	0.27	0.92	0.51	5
S116	LR-6	94.4	0.08	0.74	0.69	10
S121	LR-6	91.4	0.12	0.87	1.07	8
S142	LR-4	96.0	0.13	0.93	0.56	6
S182	LR-4	92.0	0.15	0.88	0.93	6
S199	LR-4	95.5	0.16	0.91	0.49	7

Note. TMC = temporal masking curve; LR = linear reference. Each Line is for a different on-frequency or LR TMC. RMS is the root-mean-square error in decibels; R^2 is the proportion of variance explained by the linear regression model. Empty cells indicate that the corresponding TMC was not available (see main text).

explained, R^2). The variance explained by the fit was $\geqslant$90% for 36 of the 46 measured TMCs, between 80% and 90% for eight TMCs, and 74% and 29% for the remaining two TMCs. The RMS error was always less than 2.2 dB, with a mean value of 0.96 dB. These statistics justify the use of a linear regression model (Equation 1) to analyze the present TMCs.

Forward-Masking Recovery as a Function of Probe Frequency and TMC Intercept Level

The middle panels of Figures 2 and 3 show the slope of on-frequency TMCs (i.e., parameter b in equation (1)) as a function of probe frequency expressed as $\log_{10}$(Hz); the rightmost panels show TMC slope as a function of TMC intercept level (i.e., parameter L_0 in equation (1)). The leftmost panels in the two figures illustrate masker absolute thresholds and TMC intercept levels as a function of frequency. Each row of each figure shows results for an individual participant, as indicated in the leftmost panels of each figure. For some participants, TMC slope decreased with increasing frequency and with increasing L_0, while for other participants TMC slope remained approximately constant across frequencies and L_0. Linear regression functions were fitted to the trends in Figures 2 and 3. These are shown as straight lines together with their corresponding equations and proportion of explained variance (R^2). Note that a low value of R^2 does not necessarily imply a poor linear regression fit; indeed, low R^2 values also occur when TMC slope remains constant across frequencies or intercept levels.

Figure 4 shows the slopes of the linear regression fits for each participant. Different symbols illustrate the slope of the linear regression trends for frequency (triangles) and L_0 (circles). Negative and positive values indicate that TMC slope decreased and increased with increasing frequency or L_0, respectively. For five participants (S026, S116, S142, S182, and S199), TMC slope

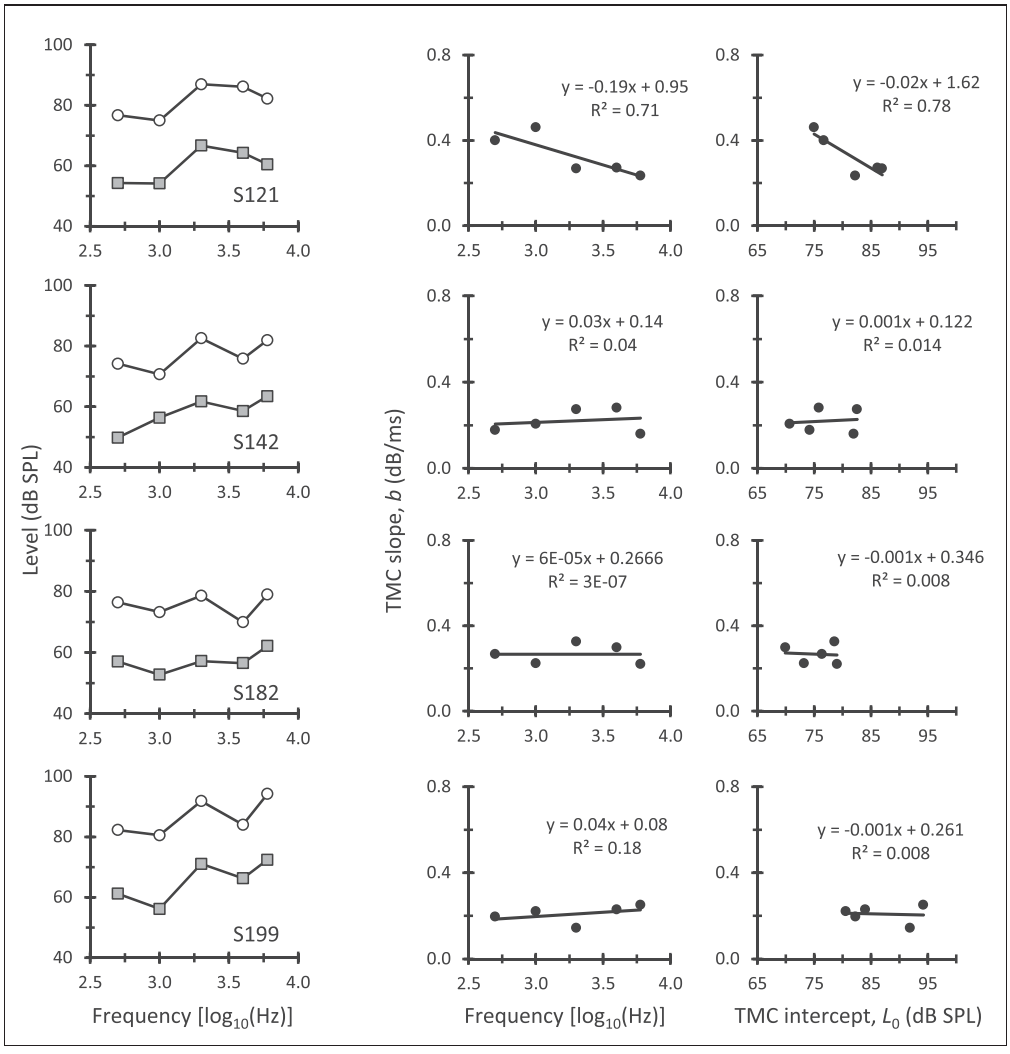

Figure 3. As Figure 2 but for four other participants (S121, S142, S182 and S199).

barely changed across frequencies or TMC intercept levels. For the remaining three participants (S012, S054, and S121), however, TMC slope decreased with increasing frequency and with increasing TMC intercept level. Interestingly, for the latter participants, TMC slope covaried with L_0 and with frequency, an aspect that will be further investigated later.

The filled symbols in Figure 4 show mean slopes of the linear regression trends across participants. On average, TMC slope decreased slightly with increasing frequency (mean $= -0.08$, $SD = 0.16$ dB/ms/$\log_{10}$(Hz)) indicating that on-frequency TMCs were on average about 10% shallower at 6000 than at 500 Hz. Mean TMC slope also decreased slightly with increasing L_0 (mean $= -0.005$, $SD = 0.0097$ dB/ms/dB) indicating that TMCs with $L_0 = 95$ dB SPL were on average about 10% shallower than those with $L_0 = 75$ dB SPL. Given the rather large variability across participants, however, the mean linear regression slopes were not statistically different from zero. In other words, mean TMC slope decreased slightly with increasing frequency and intercept level, across the probe frequency range

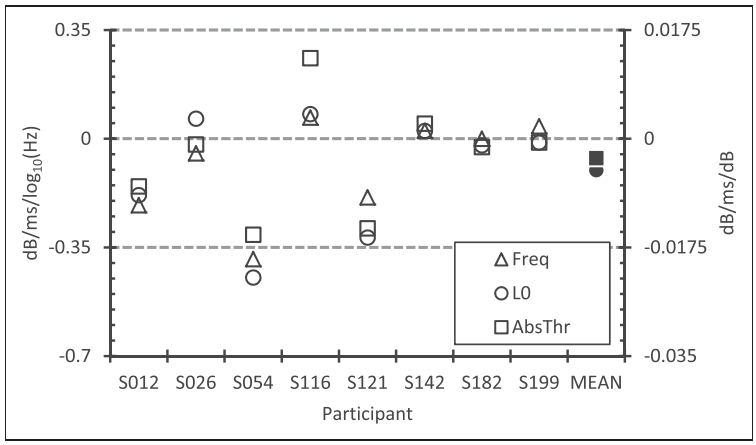

Figure 4. Trends of on-frequency TMC slope as a function of frequency or level for each participant or the mean. Each point depicts the slope of the linear regression lines in Figures 2 and 3. In other words, positive/negative values indicate that TMC slope increases/decreases with increasing frequency (left ordinate) or level (right ordinate).

(500–6000 Hz) and intercept level range (69–96 dB SPL) tested, but the trends were not significant.

Possible Frequency-Level Interactions on Forward-Masking Recovery

As shown in Figure 4, TMC slope covaried with frequency and with TMC intercept level. Probe frequency and intercept level were closely related with each other: Intercept level was higher at higher frequencies, particularly for those participants with sloping audiograms (left panels in Figures 2 and 3). An attempt was made to disentangle which of these two factors (probe frequency or intercept level) had a stronger influence on TMC slope. Our approach was based on the idea that if the main factor were level, then for a given probe frequency TMC slope should be negatively correlated with intercept level; however, if the main factor were frequency, then for TMCs with comparable intercept levels TMC slope should be negatively correlated with probe frequency. A third possibility could be that TMC slope concomitantly decreased with increasing probe frequency *and* intercept level.

Figure 5 illustrates the results of this analysis. The left panels show TMC slope against intercept level separately for each of the five frequencies tested. Note that the different points in a given panel correspond to different participants. TMC slope tended to be negatively correlated with level at frequencies of 1, 2, and 4 kHz. Despite the trends, however, the correlation was statistically significant only at 2 kHz (two-tailed t test, $N = 8$; $r = -.794$, $p = .0327$). The right panels in Figure 5 show TMC slope against probe frequency (expressed as $\log_{10}$(Hz)) for TMCs with intercept levels around approximately 76 (Figure 5(f)), 80 (Figure 5(g)), 85 (Figure 5(h)), and 89 dB SPL (Figure 5i), respectively. Slope also tended to be negatively correlated with frequency for intercept levels of 80, 85, and 89 dB SPL, but not for 76 dB SPL. Despite the trends, the correlations were not statistically significant at any of the four intercept levels.

In summary, the present data suggest that the rate of forward-masking recovery decreased with increasing level at frequencies of 1 to 4 kHz. They also suggest that the rate of forward-masking recovery decreased with increasing frequency, at least for TMCs that involved masker levels $\geqslant$80 dB SPL. Overall, however, the trends were not statistically significant possibly due to the small sample size.

To further assess the effect of level on forward-masking recovery while minimizing the potentially concomitant effect of frequency, we compared the slope of reference and on-frequency TMCs measured at the same probe frequency. If forward-masking recovery were independent of level, on-frequency and reference TMCs should have comparable slopes. The relevant data are shown in Figure 6. Note that only seven of the eight possible pairs of reference and on-frequency TMCs (Table 1) were available because the on-frequency TMC was missing for S116 at 6 kHz. In all cases, reference TMCs had higher intercept levels than corresponding on-frequency TMCs. For four of the seven participants (S026, S121, S142, and S182), reference TMCs had shallower slopes than their corresponding

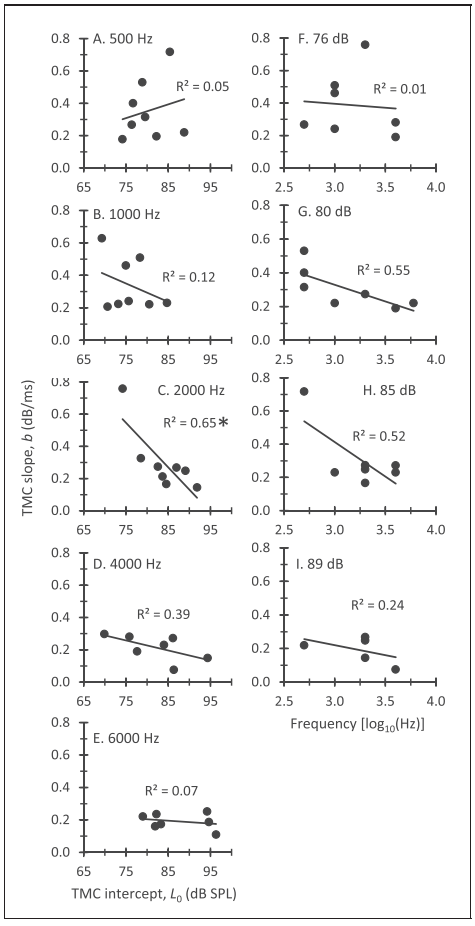

Figure 5. Left: On-frequency TMC slope as a function of intercept level. Each panel is for a different probe frequency, as indicated at the top of the panel. Right: On-frequency TMC slope as a function of frequency. Each panel is for a different intercept level, as indicated at the top of the panel. In each panel, different points are for different participants ($N = 8$). Missing points indicate that the corresponding TMC could not be measured. An asterisk (*) indicates a statistically significant correlation (two-tailed t test, $p < .05$).

on-frequency TMCs. For the remaining three participants (S012, S054, and S199), the slope of the reference TMC was comparable with or slightly greater than that of the corresponding on-frequency TMC. On average, reference TMCs had shallower slopes than on-frequency TMCs (0.15 vs. 0.22 dB/ms), but the difference was not statistically significant (two-tailed t test, $N = 7$, $p = .0851$).

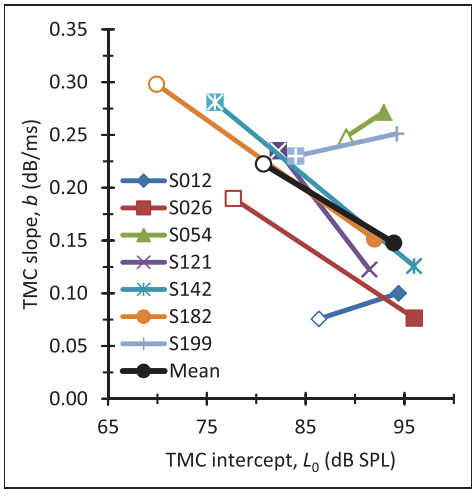

Figure 6. Slope of on-frequency (left symbols) and reference (right symbols) TMCs as a function of TMC intercept level. Each pair of data points is for a different participant.

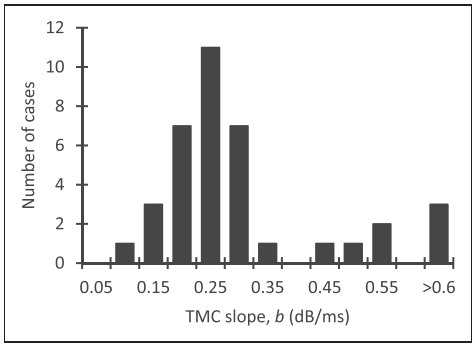

Figure 7. Histogram of on-frequency TMC slopes. Note that the total number of cases is 46 (8 participants × 6 frequencies minus two TMCs that could not be measured for S116, Table 3).

Discussion

We have investigated forward-masking recovery in a group of eight hearing-impaired listeners carefully selected to have absent or nearly absent DPOAEs over the range of primary L_2 levels from 35 to 70 dB SPL and over the range of primary f_2 frequencies from 500 to 4000 Hz (Table 2). We have shown that (a) for most cases, forward-masking recovery appeared constant across frequencies and levels; for some cases, however, forward-masking recovery decreased with increasing frequency and with increasing level (Figures 2 and 3);

(b) for those cases in which forward-masking recovery decreased with increasing frequency, forward-masking recovery also decreased with increasing level (Figure 4); (c) on average, however, forward-masking recovery did not change significantly across the range of probe frequencies (500–6000 Hz) or levels (70–100 dB SPL) tested; (d) for some individuals, forward-masking recovery measured using a fixed high-frequency probe was slower for low off-frequency maskers than for on-frequency maskers, while for others forward-masking recovery was comparable for on- and off-frequency maskers (Figure 6); and (e) on average, however, forward-masking recovery was not significantly different for on- and off-frequency maskers.

Limitations of the Present Data

Assuming that the absence of DPOAEs for levels below 70 dB SPL is indicative of linear cochlear responses, the present results would suggest that forward-masking recovery is frequency- and level-independent on average and for a majority of individuals but not for all individuals. One might argue, however, that the absence of DPOAEs below 70 dB SPL does not necessarily imply linear responses at the higher levels involved in the present TMCs (70–100 dB SPL, Figure 1). In other words, one might argue that the present TMCs could still be affected by compression. We could not rule this possibility out experimentally because the distortion generated by our DPOAE measurement system was too high at levels $L_2 > 70$ dB SPL to reliably assess the presence or absence of cochlear-generated DPOAEs at those levels. (We note that this limitation is common to most DPOAE measurements systems; see, e.g., Dorn et al., 2001.) In primates, however, cochlear gain, defined as the cochlear sensitivity at the CF premortem re postmortem, is about 40 dB at 6.5 to 8 kHz (see Table 1 of Robles & Ruggero, 2001). The present participants had hearing losses of at least 40 dB and typically greater at all test frequencies (Figures 2 and 3). Therefore, it is not unreasonable to assume that cochlear responses were linear for a majority of the present participants and conditions.

On the other hand, residual compression would lead to abnormally steep TMCs (Nelson et al., 2001). Figure 7 shows a histogram of the present on-frequency TMC slopes. The figure clearly suggests two groups of TMCs: a normally distributed group with slopes $\leqslant 0.35$ dB/ms and a group with higher slopes. It is tempting to speculate that the former group (with shallower slopes) possibly corresponds to TMCs unaffected by compression while the latter group (with steeper slopes) corresponds to TMCs that might be affected by residual compression. The latter group includes the steeper TMCs for participants S054, S116, and S121. These three participants had *sloping* audiograms; that is, greater losses at high than at low frequencies (left panels in Figures 2 and 3). Coincidentally, S054 and S121 are two of three cases for whom TMC slopes decreased with increasing frequency (S012, S054, and S121). If the present data were reanalyzed omitting slopes greater than 0.35 dB/ms, there would remain only one case (S012) for whom TMC slope would still change with frequency or level; for all other cases, TMC slope would be approximately constant across frequencies and levels. Therefore, it is tempting to conclude that TMC slope decreased with increasing frequency or level for some of the present participants because they had residual compression and that in the absence of compression forward-masking recovery would be constant across frequencies and levels.

In designing the present study, we have carried over the assumption from seminal reports that the TMC slope depends simultaneously on the amount of BM compression affecting the masker *and* on the rate of recovery from the internal (post-BM) masker effect (Nelson et al., 2001). Recent physiological, psychophysical, and modeling studies have shown or suggested sources of post-BM nonlinearity in the cochlea on responses that provide the input to the auditory nerve. For example, a recent study has shown that the motion of the reticular lamina shows more compression than the corresponding BM motion (Chen et al., 2011), indicating that the motion of the inner hair cell (IHC) stereocilia is not directly coupled to BM motion as is commonly thought (Guinan, 2012). In addition, Lopez-Poveda et al. (2005) noted that reference TMCs are shallower for some hearing-impaired than for normal-hearing listeners and argued that this could be due to frequency-unspecific compression in the IHCs that is present in normal-hearing listeners but reduced or absent in hearing-impaired listeners. This idea that IHC nonlinearities could be steepening the TMC slope has been later supported by model simulations of IHC potentials (Lopez-Poveda & Eustaquio-Martin, 2006) and by other psychoacoustical studies (Plack & Arifianto, 2010). This recent evidence suggests that in addition to BM compression, the slope of a TMC may also be affected (steepened) by compression added by the reticular lamina or the IHC. In the present context, this implies that even if the present TMCs were unaffected by BM compression (see the preceding paragraphs), they might still be affected by post-BM compression. In that case, the present analysis would still be correct if the post-BM compression were comparable across all the conditions tested here, something that is admittedly uncertain.

Of course, the TMC method was designed to infer BM compression specifically. Because it consists of comparing the slopes of two TMCs measured with different frequencies and because there is no evidence (to our knowledge) that post-BM compression is frequency

selective, post-BM compression effects on individual TMCs would be cancelled in the comparison and hence the TMC method may still be useful for its purpose.

Relationship With Earlier Studies

Using an approach similar to the present one, Stainsby and Moore (2006) concluded that forward-masking recovery was negatively correlated with frequency. The present study uses a larger sample selected with more rigorous DPOAE criteria and a different analysis. The present results suggest that the trends reported by Stainsby and Moore could be due to their participants having residual compression at low frequencies.

Implications for Estimating Compression From TMCs

In inferring peripheral cochlear compression from TMCs, it is assumed that the post-mechanical (or compression free) rate of recovery from the masker effect is independent of probe frequency and of masker level (Lopez-Poveda et al., 2003; Nelson et al., 2001). The present mean results support the assumptions of the TMC method. This is not to say, however, that it would be accurate to infer cochlear compression from comparisons of on-frequency and reference TMC slopes in all cases. Efferent effects might affect forward-masking recovery in normal-hearing listeners or in hearing-impaired listeners with residual OHC function (Jennings, Strickland, & Heinz, 2009; Wojtczak & Oxenham, 2009; Wojtczak & Oxenham, 2010; Yasin et al., 2013). Therefore, that post-mechanical forward-masking recovery is generally frequency- and level-independent for hearing-impaired listeners with absent compression does not imply that compression estimates inferred with the standard TMC method are accurate. Wojtczak and Oxenham (2009) showed that for normal-hearing listeners, forward-masking recovery is slower for levels above than below 83 dB SPL. They reasoned that the TMC method can overestimate compression by approximately a factor of 2 when reference TMCs involve levels above 83 dB SPL (i.e., in those cases, the actual compression exponent could be half of the inferred value). Wojtczak and Oxenham argued that this was possibly due to high-level off-frequency masker activating the MEMR.

The present results suggest that something similar may also happen for hearing-impaired listeners. Reference TMCs had shallower slopes than on-frequency TMCs measured with the same probe frequency (Figure 6). One explanation for this result might be that despite our precautions, the participants in question still had residual compression at high frequencies. On the other hand, the present reference TMCs always involved values higher than 90 to 95 dB SPL (their L_0 is illustrated by the rightmost points in the Figure 6), hence comparable with the threshold levels of activation of the MEMR for the present participants (shown in Table 1). Indeed, the actual activation threshold of the MEMR can be 8 to 14 dB lower than estimated with clinical methods similar to the one employed here (Feeney, Keefe, & Marryott, 2003; Neumann, Uppenkamp, & Kollmeier, 1996). The MEMR can be elicited by sounds with a duration of 116 ms (Keefe, Fitzpatrick, Liu, Sanford, & Gorga, 2010), which is approximately half the duration of the present maskers. The MEMR hinders the transmission of frequencies between 300 and 1000 Hz and has no significant effect on the transmission of frequencies higher than 2000 Hz but *facilitates* the transmission of frequencies between 1000 and 2000 Hz (see the top panels in Figure 1 of Feeney et al., 2003 and in Figure 2 of Feeney, Keefe, & Sanford, 2004). The maskers used to measure the reference TMCs were long enough that the MEMR could be active during the course of the masker and had frequencies (800–2000 Hz) within the range of the facilitating effect of MEMR. Therefore, it is conceivable that MEMR facilitated the transmission of the reference maskers, thereby reducing the masker level at the probe masked threshold. The MEMR would have a much lesser effect for corresponding on-frequency TMCs because the involved masker frequencies were higher than 2000 kHz, where the MEMR effect is negligible. Therefore, an alternative explanation for the shallower slopes of reference TMCs could be that forward-masking recovery did depend on masker level possibly due to the activation of the MEMR. If the latter explanation were correct, the present data (Figure 6) would indicate that compression inferred from comparisons of on-frequency and reference TMCs can be twice as much as the actual compression for hearing-impaired listeners whose reference TMCs involve masker levels above the individual threshold of activation of the MEMR.

Conclusions

On the basis of the analysis of TMCs for hearing-impaired listeners with presumably linear BM responses, we conclude that forward-masking recovery is independent of probe frequency and of masker level, hence that it is reasonable to use a reference TMC for a high-frequency probe to infer cochlear compression at lower frequencies.

Reference TMCs can be sometimes shallower than corresponding on-frequency TMCs for identical probe frequencies. The reason is uncertain. It might occur when the masker used to measure the reference TMC is of sufficient duration and intensity to activate the MEMR. Whatever the reason, BM compression could be overestimated in these cases by as much as a factor of two.

Acknowledgements

The authors thank Sridhar Kalluri and Bill Woods for their comments. The authors also thank two anonymous reviewers and the editor, Andrew J. Oxenham, for many useful suggestions during the review process.

Declaration of Conflict of Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was financially supported by Starkey Ltd. (USA), Junta de Castilla y León, and the Spanish Ministry of Economy and Competitiveness (ref. BFU2012-39544-C02).

References

American National Standards Institute. (1996). *S3.6 Specification for audiometers*. New York, NY: American National Standards Institute.

Bacon, S. P., & Oxenham, A. J. (2004). Psychophysical manifestations of compression: Hearing impaired listeners. In S. P. Bacon, R. R. Fay, & A. N. Popper (Eds.), *Compression: From cochlear to cochlear implants* (pp. 107–152). New York, NY: Springer-Verlag.

Chen, F., Zha, D., Fridberger, A., Zheng, J., Choudhury, N., Jacques, S. L., Wang, R. K., Shi, X., & Nuttall, A. L. (2011). A differentially amplified motion in the ear for near-threshold sound detection. *Nature Neuroscience*, *14*, 770–774.

Dorn, P. A., Konrad-Martin, D., Neely, S. T., Keefe, D. H., Cyr, E., & Gorga, M. P. (2001). Distortion product otoacoustic emission input/output functions in normal-hearing and hearing-impaired human ears. *The Journal of the Acoustical Society of America*, *110*, 3119–3131.

Feeney, M. P., Keefe, D. H., & Marryott, L. P. (2003). Contralateral acoustic reflex thresholds for tonal activators using wideband energy reflectance and admittance. *Journal of Speech, Language, and Hearing Research*, *46*, 128–136.

Feeney, M. P., Keefe, D. H., & Sanford, C. A. (2004). Wideband reflectance measures of the ipsilateral acoustic stapedius reflex threshold. *Ear and Hearing*, *25*, 421–430.

Guinan, J. J. (2012). How are inner hair cells stimulated? Evidence for multiple mechanical drives. *Hearing Research*, *292*, 35–50.

Jennings, S. G., Strickland, E. A., & Heinz, M. G. (2009). Precursor effects on behavioral estimates of frequency selectivity and gain in forward masking. *Journal of the Acoustical Society of America*, *125*, 2172–2181.

Johannesen, P. T., & Lopez-Poveda, E. A. (2008). Cochlear nonlinearity in normal-hearing subjects as inferred psychophysically and from distortion-product otoacoustic emissions. *Journal of the Acoustical Society of America*, *124*, 2149–2163.

Johannesen, P. T., & Lopez-Poveda, E. A. (2010). Correspondence between behavioral and individually "optimized" otoacoustic emission estimates of human cochlear input/output curves. *Journal of the Acoustical Society of America*, *127*, 3602–3613.

Johannesen, P. T., Pérez-González, P., & Lopez-Poveda, E. A. (2014). Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Frontiers in Nuroscience*, *8*, 214.

Jurgens, T., Kollmeier, B., Brand, T., & Ewert, S. D. (2011). Assessment of auditory nonlinearity for listeners with different hearing losses using temporal masking and categorical loudness scaling. *Hearing Research*, *280*, 177–191.

Keefe, D. H., Fitzpatrick, D., Liu, Y. W., Sanford, C. A., & Gorga, M. P. (2010). Wideband acoustic-reflex test in a test battery to predict middle-ear dysfunction. *Hearing Research*, *263*, 52–65.

Lopez-Poveda, E. A., & Alves-Pinto, A. (2008). A variant temporal-masking-curve method for inferring peripheral auditory compression. *Journal of the Acoustical Society of America*, *123*, 1544–1554.

Lopez-Poveda, E. A., & Eustaquio-Martin, A. (2006). A biophysical model of the inner hair cell: The contribution of potassium currents to peripheral auditory compression. *Journal of the Association for Research in Otolaryngology*, *7*, 218–235.

Lopez-Poveda, E. A., & Johannesen, P. T. (2009). Otoacoustic emission theories and behavioral estimates of human basilar membrane motion are mutually consistent. *Journal of the Association for Research in Otolaryngology*, *10*, 511–523.

Lopez-Poveda, E. A., & Johannesen, P. T. (2012). Behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Journal of the Association for Research in Otolaryngology*, *13*, 485–504.

Lopez-Poveda, E. A., Plack, C. J., & Meddis, R. (2003). Cochlear nonlinearity between 500 and 8000 Hz in listeners with normal hearing. *Journal of the Acoustical Society of America*, *113*, 951–960.

Lopez-Poveda, E. A., Plack, C. J., Meddis, R., & Blanco, J. L. (2005). Cochlear compression in listeners with moderate sensorineural hearing loss. *Hearing Research*, *205*, 172–183.

Meddis, R., Lecluyse, W., Tan, C. M., Panda, M., & Ferry, R. (2010). Beyond the audiogram: Identifying and modeling patterns of hearing loss. In E. A. Lopez-Poveda, A. R. Palmer, & R. Meddis (Eds.), *The neurophysiological bases of auditory perception* (pp. 631–640). New York, NY: Springer.

Neely, S. T., Johnson, T. A., & Gorga, M. P. (2005). Distortion-product otoacoustic emission measured with continuously varying stimulus level. *Journal of the Acoustical Society of America*, *117*, 1248–1259.

Nelson, D. A., & Schroder, A. C. (2004). Peripheral compression as a function of stimulus level and frequency region in normal-hearing listeners. *Journal of the Acoustical Society of America*, *115*, 2221–2233.

Nelson, D. A., Schroder, A. C., & Wojtczak, M. (2001). A new procedure for measuring peripheral compression in normal-hearing and hearing-impaired listeners. *Journal of the Acoustical Society of America*, *110*, 2045–2064.

Neumann, J., Uppenkamp, S., & Kollmeier, B. (1996). Detection of the acoustic reflex below 80 dB HL. *Audiol Neurootol*, *1*, 359–369.

Oxenham, A. J., & Bacon, S. P. (2003). Cochlear compression: Perceptual measures and implications for normal and impaired hearing. *Ear & Hearing*, *24*, 352–366.

Oxenham, A. J., & Bacon, S. P. (2004). Psychophysical manifestations of compression: Normal-hearing listeners. In S. P. Bacon, R. R. Fay, & A. N. Popper (Eds.), *Compression: From cochlea to cochlear implants* (pp. 62–106). New York, NY: Springer.

Oxenham, A. J., & Plack, C. J. (1997). A behavioral measure of basilar-membrane nonlinearity in listeners with normal and impaired hearing. *Journal of the Acoustical Society of America*, *101*, 3666–3675.

Panda, M. R., Lecluyse, W., Tan, C. M., Jürgens, T., & Meddis, R. (2014). Hearing dummies: Individualized computer models of hearing impairment. *International Journal of Audiology*, *53*, 699–709.

Plack, C. J., & Arifianto, D. (2010). On- and off-frequency compression estimated using a new version of the additivity of forward masking technique. *Journal of the Acoustical Society of America*, *128*, 771–786.

Plack, C. J., & Drga, V. (2003). Psychophysical evidence for auditory compression at low characteristic frequencies. *Journal of the Acoustical Society of America*, *113*, 1574–1586.

Plack, C. J., Drga, V., & Lopez-Poveda, E. A. (2004). Inferred basilar-membrane response functions for listeners with mild to moderate sensorineural hearing loss. *Journal of the Acoustical Society of America*, *115*, 1684–1695.

Plack, C. J., & O'Hanlon, C. G. (2003). Forward masking additivity and auditory compression at low and high frequencies. *Journal of the Association for Research in Otolaryngology*, *4*, 405–415.

Plack, C. J., & Oxenham, A. J. (2000). Basilar-membrane nonlinearity estimated by pulsation threshold. *Journal of the Acoustical Society of America*, *107*, 501–507.

Plack, C. J., Oxenham, A. J., Simonson, A. M., O'Hanlon, C. G., Drga, V., & Arifianto, D. (2008). Estimates of compression at low and high frequencies using masking additivity in normal and impaired ears. *Journal of the Acoustical Society of America*, *123*, 4321–4330.

Popelka, G. R., Osterhammel, P. A., Nielsen, L. H., & Rasmussen, A. N. (1993). Growth of distortion product otoacoustic emissions with primary-tone level in humans. *Hearing Research*, *71*, 12–22.

Rhode, W. S., & Cooper, N. P. (1996). Nonlinear mechanics in the apical turn of the chinchilla cochlea in vivo. *Auditory Cognitive Neuroscience*, *3*, 101–121.

Robles, L., & Ruggero, M. A. (2001). Mechanics of the mammalian cochlea. *Physiological Reviews*, *81*, 1305–1352.

Stainsby, T. H., & Moore, B. C. (2006). Temporal masking curves for hearing-impaired listeners. *Hearing Research*, *218*, 98–111.

Wojtczak, M., & Oxenham, A. J. (2009). Pitfalls in behavioral estimates of basilar-membrane compression in humans. *Journal of the Acoustical Society of America*, *125*, 270–281.

Wojtczak, M., & Oxenham, A. J. (2010). Recovery from on- and off-frequency forward masking in listeners with normal and impaired hearing. *Journal of the Acoustical Society of America*, *128*, 247–256.

Yasin, I., Drga, V., & Plack, C. J. (2013). Estimating peripheral gain and compression using fixed-duration masking curves. *Journal of the Acoustical Society of America*, *133*, 4145–4155.

Zurek, P. M. (1992). Detectability of transient and sinusoidal otoacoustic emissions. *Ear and Hearing*, *13*, 307–310.

Trends in Hearing
2016, Vol. 20: 1–14

DOI: 10.1177/2331216516641055
tia.sagepub.com
SAGE

The Influence of Cochlear Mechanical Dysfunction, Temporal Processing Deficits, and Age on the Intelligibility of Audible Speech in Noise for Hearing-Impaired Listeners

Peter T. Johannesen[1,2], Patricia Pérez-González[1,2], Sridhar Kalluri[3], José L. Blanco[1], and Enrique A. Lopez-Poveda[1,2,4]

Abstract

The aim of this study was to assess the relative importance of cochlear mechanical dysfunction, temporal processing deficits, and age on the ability of hearing-impaired listeners to understand speech in noisy backgrounds. Sixty-eight listeners took part in the study. They were provided with linear, frequency-specific amplification to compensate for their audiometric losses, and intelligibility was assessed for speech-shaped noise (SSN) and a time-reversed two-talker masker (R2TM). Behavioral estimates of cochlear gain loss and residual compression were available from a previous study and were used as indicators of cochlear mechanical dysfunction. Temporal processing abilities were assessed using frequency modulation detection thresholds. Age, audiometric thresholds, and the difference between audiometric threshold and cochlear gain loss were also included in the analyses. Stepwise multiple linear regression models were used to assess the relative importance of the various factors for intelligibility. Results showed that (a) cochlear gain loss was unrelated to intelligibility, (b) residual cochlear compression was related to intelligibility in SSN but not in a R2TM, (c) temporal processing was strongly related to intelligibility in a R2TM and much less so in SSN, and (d) age per se impaired intelligibility. In summary, all factors affected intelligibility, but their relative importance varied across maskers.

Keywords

hearing impairment, cochlear hearing loss, auditory masking, ageing, temporal fine structure

Date received: 23 October 2015; revised: 1 March 2016; accepted: 1 March 2016

Hearing-impaired (HI) listeners vary widely in their ability to understand speech in noisy backgrounds, even when the detrimental effect of their hearing loss on intelligibility is compensated for with frequency-specific amplification (e.g., Peters, Moore, & Baer, 1998). The aim of the present study was to shed some light on the relative importance of cochlear mechanical dysfunction, temporal processing deficits, and age on the ability of HI listeners to understand audible speech in noisy backgrounds.

Several factors can affect the ability of HI listeners to understand audible speech in noise (reviewed by Lopez-Poveda, 2014). One of them is outer hair cell (OHC) loss or dysfunction. OHC dysfunction would degrade the representation of the speech spectrum in the mechanical response of the cochlea, particularly in noisy environments, for various reasons. First, OHC dysfunction reduces cochlear frequency selectivity (Robles & Ruggero, 2001). This can smear the cochlear

[1]Instituto de Neurociencias de Castilla y León, Universidad de Salamanca, Spain
[2]Instituto de Investigación Biomédica de Salamanca, Universidad de Salamanca, Spain
[3]Starkey Hearing Research Center, Berkeley, CA, USA
[4]Departamento de Cirugía, Facultad de Medicina, Universidad de Salamanca, Spain

Corresponding author:
Enrique A. Lopez-Poveda, Instituto de Neurociencias de Castilla y León, Universidad de Salamanca, Calle Pintor Fernando Gallego 1, 37007 Salamanca, Spain.
Email: ealopezpoveda@usal.es

representation of the acoustic spectrum, making it harder for HI listeners to separately perceive the spectral cues of speech from those of interfering sounds (Moore, 2007). Several behavioral studies have supported this idea (Baer & Moore, 1994; Festen & Plomp, 1983; ter Keurs, Festen, & Plomp, 1992). Second, in the healthy cochlea, suppression might facilitate the encoding of speech in noise by enhancing the most salient spectral features of speech against those of the background noise (Deng, Geisler, & Greenberg, 1987; Young, 2008). OHC dysfunction reduces suppression and this might hinder speech-in-noise intelligibility. Third, cochlear mechanical compression might facilitate the understanding of speech in interrupted or fluctuating noise by amplifying the speech in the low-level noise intervals, a phenomenon known as *listening in the dips* (e.g., Gregan, Nelson, & Oxenham, 2013; Rhebergen, Versfeld, & Dreschler, 2009). OHC loss or dysfunction reduces compression (i.e., linearizes cochlear responses; Ruggero, Rich, Robles, & Recio, 1996) and thus could hinder *dip listening* (Gregan et al., 2013). Fourth, medial olivocochlear efferents possibly facilitate the intelligibility of speech in noise by increasing the discriminability of transient sounds in noisy backgrounds (Brown, Ferry, & Meddis, 2010; Guinan, 2010; Kim, Frisina, & Frisina, 2006). Medial olivocochlear efferents exert their action via OHCs, and so OHC dysfunction could reduce the unmasking effects of medial olivocochlear efferents.

The degree of OHC dysfunction could be different across different HI listeners and this might contribute to the wide variability in their ability to understand audible speech in noise. While seemingly reasonable, however, this view is almost certainly only partially correct. First, for HI listeners, there appears to be no significant correlation between residual cochlear compression and the benefit from dip listening (Gregan et al., 2013), which undermines the influence of compression on the intelligibility of suprathreshold speech in noise. Second, at high intensities, cochlear tuning for healthy cochleae is reduced and is only moderately sharper than that of impaired cochleae (Robles & Ruggero, 2001) and yet HI listeners still perform more poorly than do normal-hearing (NH) listeners in speech-in-noise intelligibility tests (reviewed in pp. 205–208 of Moore, 2007).

A second factor that may affect speech-in-noise intelligibility is age. Elderly listeners with normal audiometric thresholds and presumably healthy OHCs have more difficulty in understanding speech in noise than young, NH listeners (Committee on Hearing, Bioacoustics, and Biomechanics, 1988; Kim et al., 2006; Peters et al., 1998), which suggests that age per se or mechanisms other than OHC dysfunction can limit the intelligibility of audible speech.

A third factor that might contribute to the ability of HI listeners to understand suprathreshold speech in noise is temporal processing ability. Several studies support this view. First, for HI listeners, speech-in-noise intelligibility is correlated with their ability to use the information conveyed in the rapid temporal changes that occur in speech, known as *temporal fine structure* (TFS; Lorenzi, Gilbert, Carn, Garnier, & Moore, 2006; Strelcyk & Dau, 2009). Second, both stochastic undersampling of a noisy speech waveform, as might occur after cochlear synaptopathy or deafferentation (Lopez-Poveda & Barrios, 2013), and temporally jittering the frequency components in speech (Pichora-Fuller, Schneider, Macdonald, Pass, & Brown, 2007) decrease speech-in-noise intelligibility with negligible effects on absolute threshold. Third, Henry and Heinz (2012) showed that the synchronization of auditory nerve discharges to a sound's waveform decreases in noise backgrounds and that the decrease is greater for cochleae with OHC dysfunction than for healthy cochleae. Therefore, it is possible that OHC dysfunction causes temporal processing deficits that manifest in noise. Altogether this suggests that normal processing of speech temporal cues is required for understanding audible speech in noise. Temporal processing abilities could vary across HI listeners and this could contribute to the wide variability in their ability to understand speech in noise.

The present study was aimed at assessing the relative importance of cochlear mechanical dysfunction, temporal processing deficits, and age for understanding audible speech in noisy environments by HI listeners. In a previous study, we reported behaviorally inferred estimates of cochlear mechanical gain loss and residual compression for 68 HI listeners (Johannesen, Perez-Gonzalez, & Lopez-Poveda, 2014). Those estimates were used in the present study as indicators of cochlear dysfunction and the participants from that study were invited back into the laboratory to assess their ability to understand audible speech in various types of noise, as well as their ability to process temporal information. After Moore and Sek (1996), temporal processing ability was assessed using frequency modulation detection thresholds (FMDTs), defined as the minimum detectable excursion in frequency for a pure tone carrier. FMDTs are thought to be dependent on the quality with which frequencies are coded in the phase locking of auditory nerve discharges and on the ability of a listener to discriminate frequencies based on such a code (Moore & Sek, 1996). Speech-in-noise intelligibility was assessed using the speech reception threshold (SRT), defined as the speech-to-noise ratio (SNR) required to understand 50% of the sentences that listeners were presented within a noise background (e.g., Peters et al., 1998). When measuring SRTs, stimuli were linearly amplified in a frequency-specific manner to minimize the effect of reduced audibility on intelligibility. SRTs were measured

for two types of maskers: a steady noise with a speech--shaped long-term spectrum (speech-shaped noise [SSN]) and two-talker masker played in reverse (R2TM). The latter masker was used because it has the same temporal and spectral properties as forward speech and was thus expected to have the same energetic masking properties as speech but without semantic information that may contribute to informational masking (e.g., Hornsby & Ricketts, 2007). Stepwise multiple linear regression models (MLRs) were used to predict SRTs from a linear combination of cochlear dysfunction indicators, FMDTs, and age and to quantify the relative importance of these factors for speech-in-noise intelligibility.

Material and Methods

Subjects

The 68 subjects (43 males) with symmetrical sensorineural hearing losses who participated in the study of Johannesen et al. (2014) participated in the present study. Their ages ranged from 25 to 82 years, with a median of 61 years. The present study was part of a larger hearing-aid study and hence all participants were required to be hearing-aid users or candidates. Speech-in-noise intelligibility was assessed in bilateral listening conditions (see later). Indicators of cochlear mechanical status and temporal processing ability, however, were measured for one ear only. For most participants, the test ear was the ear with better audiometric thresholds in the frequency range of 2 to 6 kHz (30 left ears and 38 right ears). See Johannesen et al. for further details of the subject sample. All procedures were approved by the human experimentation ethical review board of the University of Salamanca. Subjects gave their signed informed consent prior to their inclusion in the study.

Indicators of Cochlear Mechanical Dysfunction

OHC dysfunction linearizes cochlear mechanical responses (Ruggero et al., 1996). Johannesen et al. (2014) compared behaviorally inferred cochlear input/output curves for each HI listener at each of five test frequencies (0.5, 1, 2, 4, and 6 kHz) with corresponding reference input/output curves for NH listeners. They reported three main variables from their analyses. One variable was cochlear mechanical gain loss (also referred to as OHC loss or HL_{OHC}) expressed in decibels (dB). It was defined as the contribution of cochlear gain loss to the audiometric threshold and was inferred from the difference (in dB) between the compression threshold for an individual input/output curve and the reference compression threshold for NH listeners at the corresponding test frequency corrected for compression (see Equation (2) in Lopez-Poveda & Johannesen, 2012). A second variable was inner hair cell (IHC) loss or HL_{IHC}. It was defined as the difference (in dB) between the audiometric loss (in dB HL) and HL_{OHC}. This difference was reported after earlier studies where the audiometric loss was assumed to be the sum of a cochlear mechanical component, HL_{OHC}, and an additional component of an uncertain nature termed HL_{IHC} (Moore & Glasberg, 1997). A third variable reported by Johannesen et al. was the basilar-membrane compression exponent (BMCE). It was defined as the slope (in dB/dB) of an inferred cochlear input/output curve over its compressive segment. See Johannesen et al. for further details on how these variables were inferred.

HL_{OHC} and BMCE were readily available for most participants and test frequencies from the study of Johannesen et al. (2014) and were used in the present context as indicators of cochlear mechanical dysfunction. Specifically, HL_{OHC} was regarded here as an indicator of cochlear mechanical gain loss and the BMCE as an indicator of residual cochlear compression. For completeness, HL_{IHC} was also used in the present analysis. Note that the three variables had values at each of the five test frequencies.

Johannesen et al. (2014) reported that they could not infer input/output curves for listeners and test frequencies where the audiometric loss was too high. For the present analysis, we assumed that those cases were indicative of total cochlear gain loss. Therefore, for those cases, BMCE was set equal to 1 dB/dB, corresponding to a linear input/output curve, and HL_{OHC} was set equal to the maximum cochlear gain values for NH listeners. These were assumed to be 35.2, 43.5, 42.7, 42.7, and 42.7 dB at 0.5, 1, 2, 4, and 6 kHz, respectively, as reported on p. 11 of Johannesen et al.

Frequency Modulation Detection Thresholds

Temporal processing ability was assessed using FMDTs. The complete justification for this can be found in Moore and Sek (1996). We followed the procedure of Strelcyk and Dau (2009). In short, a FMDT was defined as the minimum detectable excursion in frequency for a tone carrier and was estimated using a three alternative forced choice adaptive procedure. The three intervals contained a pure tone with a frequency of 1500 Hz and a duration of 750 ms, including 50-ms raised cosine onset and offset ramps. The level of the tone was set 30 dB above the absolute threshold for the tone (30 dB sensation level). The tones in all intervals were also sinusoidally amplitude modulated (AM) with a modulation depth of 6 dB and with an instantaneous modulation rate that either increased or decreased linearly with time. The initial and final AM modulation rates were randomized in the interval between 1 and 3 Hz under

the constraint that the modulation rate change was always above 1 Hz. In one interval, chosen at random, the tone's frequency was additionally sinusoidally varied with a rate of 2 Hz and with a certain maximum frequency excursion. The listeners' task was to identify the interval containing the frequency modulation. The use of a low rate of frequency variation (2 Hz), a moderately low-frequency carrier (1500 Hz), and the randomized AM were intended to emphasize the dependency of FMDT on temporal information (*phase locking* to the carrier) rather than on changes in the excitation patterns (Moore & Sek, 1996); the use of a carrier tone frequency of 1500 Hz, thus in the middle of the speech frequency range, was intended to emphasize the dependency of FMDT on the listeners' ability to follow the temporal cues in speech. The listeners were provided with feedback about the correctness of their response. The logarithm of the maximum frequency excursion was varied in successive trials according to an adaptive one-up two-down rule to estimate the 71% correct point in the psychometric function (Levitt, 1971). The initial frequency excursion was set, so the target interval was always easily identified. The initial step size of the frequency excursion was $\log_{10}(1.5)$. This was decreased to $\log_{10}(1.26)$ after four reversals. The adaptive procedure continued until a total of 12 reversals in frequency excursion had occurred. The FMDT was calculated as the mean of the logarithms of the frequency excursions at the last eight reversals. A measurement was discarded if the standard deviation of the logarithm of the frequency excursions at the last eight reversals exceeded 0.15. Three threshold estimates were obtained in this way and their mean was taken as the threshold. If the standard deviation of these three measurements exceeded 0.15, one or more additional threshold estimates were obtained and included in the mean.

Prior to the FMDT task, the absolute threshold of the carrier tone was measured using a three alternative forced choice procedure in which the level of the tone was varied in successive trials according to an adaptive two-down, one-up rule to estimate the 71% correct point in the psychometric function (Levitt, 1971). The duration of the carrier tone was 750 ms, including 50-ms raised cosine onset and offset ramps.

Speech Reception Thresholds

SRTs were measured using the hearing-in-noise test (HINT; Nilsson, Soli, & Sullivan, 1994). Sentences uttered by a male speaker were presented to the listener in the presence of a masker. The sentences were those in the Castilian Spanish version of the HINT (Huarte, 2008). Two different maskers were used. One masker consisted of a steady Gaussian noise filtered in frequency to have the long-term average spectrum of speech (Table 2 in Byrne et al., 1994). This masker will be referred to as SSN and the corresponding SRT as SRT_{SSN}. The second masker consisted of two simultaneous talkers (one male and one female) played in reverse. This masker will be referred to as time-reversed two-talker masker (R2TM) and the corresponding SRT as SRT_{R2TM}.

To generate the R2TM, the Spanish HINT sentences were uttered by a male and a female native Castilian-Spanish speaker in a sound booth and recorded with a Brüel & Kjaer type 4192 microphone with its amplifier (Brüel & Kjaer Nexus) connected to an RME Fireface 400 sound card. The recorded sentences were segmented and pauses between sentences removed. For each speaker, the sentences were equalized in root mean square amplitude, time reversed, and concatenated. Finally, the concatenated sentences of the male and the female speaker were mixed digitally. A different segment (chosen at random) of the resulting R2TM was used to mask each HINT sentence during an SRT measurement. We note that the long-term spectra of the R2TM, the SSN, and the target speech could have been slightly different because the speakers used to generate the R2TM and the target sentences were different, and the filter used to produce the SSN, though speech shaped, was not based on the long-term spectrum of the specific target sentences.

To measure an SRT, the speech was fixed in level at 65 dB SPL and the masker level was varied adaptively using a one-up, one-down rule to find the SNR (in dB) at which the listener correctly identified 50% of the sentences (i.e., to find the SRT in dB SNR units). After setting the levels of the speech and the masker, the two sounds were mixed digitally and filtered to simulate a free-field listening condition where the speech and the masker were colocated 1 m away in front of the listener at eye level (i.e., 0° azimuth and 0° elevation) and had a spectrum according to Table 3 in American National Standards Institute (ANSI, 1997). The filtering included corrections for the frequency response of the headphones. The resulting stimulus was linearly amplified individually for each participant according to the National Acoustics Laboratory Revised (NAL-R) rule (Byrne & Dillon, 1986) and played diotically to the listeners. The masker started 500 ms before and ended 250 ms after the target sentence. Twenty sentences were played to the listeners for each SRT measurement. In the adaptive procedure, the masker level was varied with a step size of 4 dB for the first 5 sentences and of 2 dB for the last 15 sentences. The SRT was calculated as the mean SNR used for the last 15 sentences. For each masker, three SRT estimates were obtained and the mean was taken as the final result. All other details of the procedure were as for the original HINT test (Nilsson et al., 1994). Feedback on the correctness of the listener's response was not provided.

Stimuli and Apparatus

For all measurements, stimuli were digitally generated or stored as digital files with a sampling rate of 44100 Hz. They were digital to analog converted using an RME Fireface 400 sound card with a 24-bit resolution and were played through Sennheiser HD-580 headphones. Subjects sat in a double-wall sound-attenuating booth during data collection.

Statistical Analyses

Audiometric pure-tone thresholds (PTT, in dB HL), HL_{OHC}, HL_{IHC}, BMCE, FMDTs, and age were used as potential predictors (independent variables) of the aided SRT_{SSN} and SRT_{R2TM} (dependent variables). Pairwise Pearson correlations were first calculated between each of the six independent variables and each of the two dependent variables. Statistically significant correlations were regarded as indicative that the independent variable could be a potential predictor of the dependent variable. This type of analysis, however, does not reveal the relative importance of the identified predictors. Indeed, sometimes several potential predictors might reflect a common underlying factor, a phenomenon known as colinearity. In such cases, often only one of the colinear predictors is sufficient to explain the variance in the dependent variable. To better assess the relative importance of potential predictors while minimizing the impact of colinearity, we conducted a stepwise MLR analysis. In a MLR model, it is assumed that the dependent variable may be expressed as a linear combination of independent variables. If the MLR model is constructed in a stepwise fashion (i.e., by gradually adding new potential predictors to the model in each step), the final model omits colinear variables and, most importantly, provides information about the relative importance of the various predictors. Here, we used MLR models to predict the SRT_{SSN} and SRT_{R2TM} independently. As is common practice, the variance explained by the models was adjusted for the number of predictors used in the model (i.e., the explained variance was reduced more as more predictors were included in the model; Theil & Goldberger, 1961).

Unlike FMDTs, which were measured for one carrier frequency only, PTT, HL_{OHC}, HL_{IHC}, and BMCE were available for each of the five test frequencies. Because the correlation and MLR analyses required that the independent variables be single valued, multivalued variables were combined into a single value by weighting the value at each test frequency according to the importance of that frequency for speech recognition (speech-intelligibility index (SII) weightings; ANSI, 1997) and summing the SII-weighted values across all frequencies. The weights were 0.18, 0.25, 0.28, 0.23, and 0.06 for the test frequencies 0.5, 1, 2, 4, and 6 kHz, respectively (from Tables 3 and 4 of ANSI, 1997). The implications of this approach are addressed in the Discussion section.

Results

Raw Data

Figure 1 shows distributions of absolute thresholds for the test ears and for each test frequency. Note that high-frequency losses were more frequent than other type of losses. The 5, 25, 50, 75, and 95th percentiles of age were 38, 54, 61, 74, and 81 years, respectively. The mean age was 62 years and the standard deviation was 14 years. Although the distribution of the ages was slightly skewed toward higher ages, it was not significantly different from Gaussian ($p = .40$, Chi-squared test).

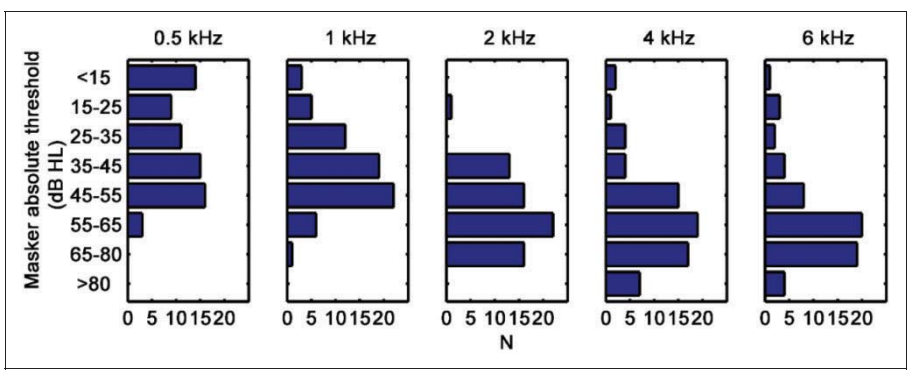

Figure 1. Distribution of hearing losses in categories for the test ears of all participants for each of the test frequencies. Replotted with permission from Johannesen et al. (2014).

For most listeners, SRT_{SSN} values were in the range −5 to 1 dB SNR (Figure 2), thus in line with values reported by earlier studies for SSN maskers (George, Festen, & Houtgast, 2006; Gregan et al., 2013; Peters et al., 1998). SRT_{R2TM} values were in the range −2 to 5 dB SNR and generally higher than SRT_{SSN} values (Figure 2). This trend and range of values are consistent with those reported elsewhere for HI listeners for a R2TM (e.g., Festen & Plomp, 1990 reported SRT_{R2TM} values from −4 to 2 dB SNR). The present SRT_{R2TM} values were about 3, 5, and 5 dB higher than the SRTs for interrupted or modulated noise backgrounds reported by George et al. (2006), Peters et al. (1998), and Gregan et al. (2013), respectively. The fact that SRTs differ for different types of fluctuating maskers is consistent with previous studies (e.g., Festen & Plomp, 1990).

FMDTs for the present participants were in the range of 0.7 to 2 (in units of $\log_{10}$(Hz); Figure 2) and thus similar to the range of values reported by Strelcyk and Dau (2009; 0.7–1.7, when converted to the present units). The participants in the study of Strelcyk and Dau had almost normal audiometric thresholds at frequencies $\leqslant 1$ kHz while the present listeners typically had greater hearing losses over that frequency range (Figure 1), which might explain the higher upper limit in the present FMDTs.

Pairwise Pearson Correlations

Table 1 shows squared Pearson correlation coefficients (R^2 values) for pairs of variables. HL_{OHC} and HL_{IHC} were significantly correlated with PTT but were uncorrelated with each other. This supports the idea put forward elsewhere that listeners with similar audiometric losses can suffer from different degrees of mechanical cochlear gain loss (e.g., Johannesen et al., 2014; Lopez-Poveda & Johannesen, 2012; Lopez-Poveda, Johannesen, & Merchán, 2009; Moore & Glasberg, 1997; Plack, Drga, & Lopez-Poveda, 2004).

BMCE was positively correlated with PTT and HL_{OHC}, indicating that the greater the audiometric loss or the loss of cochlear gain, the more linear (greater BMCE) the cochlear input/output curves. The positive correlation between BMCE and PTT appears inconsistent with earlier studies that reported no correlation between those two variables (Johannesen et al., 2014; Plack et al., 2004). Indeed, Johannesen et al. (2014) reported no correlation between BMCE and audiometric loss based on the same data as were used here. Differences in the data analyses might explain this discrepancy. First, the cited studies based their conclusions on frequency-by-frequency correlation analyses, whereas the present result is based on across-frequency SII-weighted averages. Second, BMCE was set here to 1 dB/dB whenever the audiometric loss was so high that a corresponding input/output curve could not be measured, something that possibly biased and increased the correlation slightly.

Table 1 also shows that FMDTs were not correlated with PTT, HL_{IHC}, or BMCE and were only slightly positively correlated with HL_{OHC}. Furthermore, FMDTs were not correlated with age. This suggests that FMDTs were assessing auditory processing aspects unrelated (or only slightly related) to cochlear mechanical dysfunction or age.

Potential Predictors of Speech-in-Noise Intelligibility

Table 1 shows that all of the independent variables used in the present study were significantly correlated with SRT_{SSN} and SRT_{R2TM}, except for BMCE which was significantly correlated with SRT_{SSN} only. Therefore, virtually all of them could in principle be related to the measured SRTs. Figure 2 shows scatter plots of SRT_{SSN} (left) and SRT_{R2TM} (right) against each of the six predictor variables (one variable per row), together with linear regression functions (fitted by least squares) and corresponding statistics. The plots suggest a linear relationship between each of the predictors and the aided SRTs. PTT explained slightly more SRT_{R2TM} variance ($R^2 = .17$) than SRT_{SSN} variance ($R^2 = .14$; compare Figure 2(C) and 2(D)). This trend and values are consistent with those reported by Peters et al. (1998), who found R^2 values in the range of 0.07 to 0.11 for SSN and 0.11 to 0.25 for fluctuating maskers, although they did not specifically use R2TMs (see their Table IV).

Figure 2 suggests that PTT, HL_{OHC}, and HL_{IHC} had only a small influence on aided SRTs, as the largest amount of variance explained by any of these three predictors for either of the two SRTs was 17%; this was the variance in SRT_{R2TM} predicted by PTT (Figure 2(D)). For both SRT_{SSN} and SRT_{R2TM}, HL_{OHC} and HL_{IHC} predicted less variance than PTT, which suggests that specific knowledge about the proportion of the PTT that is due to cochlear mechanical gain loss (HL_{OHC}) or other uncertain factors (HL_{IHC}) does not provide much more information than the PTT alone about aided speech-in-noise intelligibility deficits.

BMCE predicted 23% of SRT_{SSN} variance (Figure 2(I)) but was not a significant predictor of SRT_{R2TM} (Figure 2(J)), while FMDTs predicted 28% of the SRT_{R2TM} variance (Figure 2(L)) but only 7% of the SRT_{SSN} variance (Figure 2(K)). This suggests that residual cochlear compression could be more important than temporal processing abilities for understanding speech in steady noise backgrounds while temporal processing abilities could be more important for understanding speech in fluctuating backgrounds.

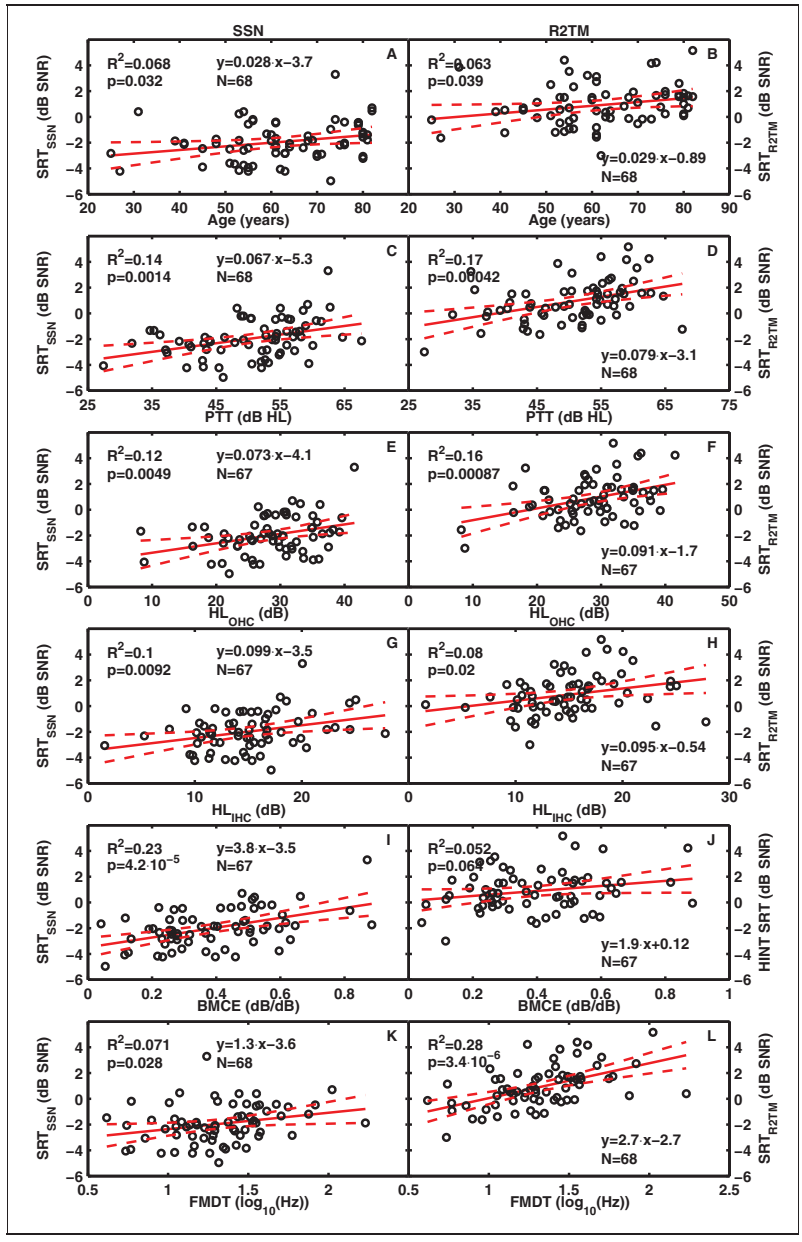

Figure 2. Aided speech reception thresholds for SSN (left column) and R2TM (right column) against across-frequency SII-weighted predictor variables. Each row is for a different predictor (age, PTT, HL_{OHC}, HL_{IHC}, BMCE, and FMDT) as indicated in the abscissa of each panel. Solid lines depict linear regression lines; dashed lines depict the 5 and 95% confidence interval of the regression line. The upper left inset in each panel informs of the proportion of variance of aided HINT SRTs (R^2) explained by the different predictors and the probability (p) for the value to occur by chance. The lower inset presents the regression equation and the number of cases (N). *Note.* SRT = speech reception threshold; SSN = speech-shaped noise; R2TM = time-reversed two-talker masker; SII = speech-intelligibility index; HLOHC: contribution of cochlear gain loss to the audiometric loss; HLIHC: contribution of inner hair cell dysfunction to the audiometry loss; BMCE = basilar-membrane compression exponent; FMDT = frequency modulation detection threshold; HINT = hearing-in-noise test.

Table 1. Squared Pairwise Pearson Correlations (R^2) and Significance Levels (p) Between All Potential Predictors and Aided HINT SRTs for SSN and R2TM.

		Age	PTT	HL_{OHC}	HL_{IHC}	BMCE	FMDT	SRT_{SSN}	SRT_{R2TM}
Age (years)	R^2	–	.01	.02	.00	.02	.00	**.07**	**.06**
	p	.40	.48	.28	.62	.22	.57	**.032**	**.039**
PTT (dB HL)	R^2	–	–	**.63**	**.30**	**.15**	.03	**.14**	**.17**
	p	–	.09	$\mathbf{8.9 \cdot \times 10^{-16}}$	$\mathbf{1.4 \cdot \times 10^{-6}}$	$\mathbf{1.0 \times 10^{-3}}$	.13	$\mathbf{1.4 \times 10^{-3}}$	$\mathbf{4.2 \times 10^{-4}}$
HL_{OHC} (dB)	R^2	–	–	–	.01	**.39**	**.06**	**.12**	**.16**
	p	–	–	.25	.50	$\mathbf{1.5 \times 10^{-8}}$	**.04**	$\mathbf{4.9 \times 10^{-3}}$	$\mathbf{8.7 \times 10^{-4}}$
HL_{IHC} (dB)	R^2	–	–	–	–	.00	.02	**.10**	**.08**
	p	–	–	–	**.03**	.76	.30	$\mathbf{9.2 \times 10^{-3}}$	**.020**
BMCE (dB/dB)	R^2	–	–	–	–	–	.01	**.23**	.05
	p	–	–	–	–	**.04**	.38	$\mathbf{4.2 \times 10^{-5}}$	.064
FMDT ($\log_{10}$(Hz))	R^2	–	–	–	–	–	–	**.07**	**.28**
	p	–	–	–	–	–	.26	**.028**	$\mathbf{3.4 \times 10^{-6}}$
SRT_{SSN} (dB SNR)	R^2	–	–	–	–	–	–	–	**.51**
	p	–	–	–	–	–	–	.17	$\mathbf{1.1 \times 10^{-11}}$
SRT_{R2TM} (dB SNR)	R^2	–	–	–	–	–	–	–	–
	p	–	–	–	–	–	–	–	.31

Note. SRT = speech reception threshold; SSN = speech-shaped noise; R2TM = time-reversed two-talker masker; HLOHC: contribution of cochlear gain loss to the audiometric loss; HLIHC: contribution of inner hair cell dysfunction to the audiometry loss; BMCE = basilar-membrane compression exponent; FMDT = frequency modulation detection threshold; HINT = hearing-in-noise test. The p-values in the diagonal indicate the probability for a Gaussian distribution of the corresponding variable. Statistical significance ($p < .05$) is indicated with bold font.

Stepwise MLR Models

Stepwise MLR models for SRT_{SSN} and SRT_{R2TM} are shown in Table 2. Each model includes only those predictors whose contribution to the predicted variance was statistically significant. For each model, the predictors' priority order was established according to how much the corresponding predictor contributed to the predicted variance (higher priority was given to larger contributions).

The top part of Table 2 shows that, in the MLR model for aided SRT_{SSN}, the most significant predictor was cochlear compression (BMCE), which explained 22% of the SRT_{SSN} variance, followed by HL_{IHC} and age, which explained 10% and 7% more of the predicted variance, respectively. The model predicted a total of 39% of the SRT_{SSN} variance. Including FMDT, PTT, or HL_{OHC} as additional predictors did not increase the variance predicted by the model. Also, despite the correlation between HL_{OHC} and BMCE ($R^2 = .39$, Table 1), these two variables could not be interchanged in the MLR model. In other words, HL_{OHC} alone explained less variance that BMCE alone. Indeed, BMCE remained as a significant predictor of SRT_{SSN} when HL_{OHC} was included as the first predictor in the stepwise approach but HL_{OHC} became a nonsignificant predictor as soon as BMCE was included in the model.

The MLR model for aided SRT_{R2TM} was strikingly different from the model for SRT_{SSN} (compare the top and bottom parts of Table 2). The most significant predictor of SRT_{R2TM} was FMDT, which explained 27% of the SRT_{R2TM} variance, followed by PTT and age, which explained 10% and 2% more of the variance, respectively. Altogether, the model accounted for 39% of the SRT_{R2TM} variance. Neither HL_{OHC} or BMCE, the two indicators of cochlear mechanical dysfunction, was found to be a significant predictor of SRT_{R2TM}. HL_{IHC} did not increase the variance predicted by this model.

The Role of Audibility

Reduced audibility decreases speech-in-noise intelligibility (e.g., Peters et al., 1998). Here, we tried to minimize the effects of reduced audibility on the SRTs by individually amplifying the target sentences (and the noise) used in the SRT measurements according to the NAL-R linear amplification rule (Byrne & Dillon, 1986). The NAL-R amplification rule, however, compensates at most for half of the audiometric loss. Therefore, it is possible that the low-level portions of the amplified speech spectrum might have been below absolute threshold, something that might have reduced the intelligibility. We attempted to verify that this was not the case by using the SII (ANSI, 1997).

Table 2. Stepwise MLR Models of Aided SRT_{SSN} and SRT_{R2TM}.

Priority	Predictor	Coefficient	*t*-value	*p*	Accum. R^2
SRT_{SSN}					
n/a	Intercept	−7.7	−8.0	4.1×10^{-11}	–
1	BMCE	3.46	4.5	3.2×10^{-5}	.22
2	HL_{IHC}	0.104	3.4	1.0×10^{-3}	.32
3	Age	0.031	2.9	5.8×10^{-3}	.39
SRT_{R2TM}					
n/a	Intercept	−6.6	−5.5	7.0×10^{-7}	–
1	FMDT	2.34	4.7	1.3×10^{-5}	.27
2	PTT	0.060	3.2	1.9×10^{-3}	.37
3	Age	0.022	2.0	4.9×10^{-2}	.39

Note. MLR = multiple linear regression; SRT = speech reception threshold; SSN = speech-shaped noise; R2TM = time-reversed two-talker masker; HLIHC: contribution of inner hair cell dysfunction to the audiometry loss; BMCE = basilar-membrane compression exponent; FMDT = frequency modulation detection threshold. Columns indicate the predictor's priority order and name, the regression coefficient, the *t*-value, and corresponding probability for a significant contribution (*p*), and the accumulated proportion of total variance explained (Accum. R^2), respectively. The priority order is established according to how much the corresponding predictor contributed to the predicted variance (higher priority is given to larger contributions). The accumulated R^2 is the predicted variance adjusted for the number of variables included in the regression model.

The SII is an estimate of the proportion of the speech spectrum that is above the absolute threshold *and* above the background noise (ANSI, 1997). Here, however, the SII was calculated using only the listeners' absolute thresholds, the speech spectrum, and the NAL-R amplification but disregarding the maskers; that is, here, the SII indicated the proportion of the speech spectrum that was above absolute threshold. The rationale was that if the full speech spectrum were audible, then performance deficits in noise would be due to the presence of the noise rather than to reduced audibility and would thus reflect suprathreshold deficits. The resulting SII will be referred to as SII_Q to emphasize that it corresponds to the value in quiet. In all other aspects, the SII calculations conformed to ANSI (1997) for 1/3 octave bands. Our analysis was identical to that of Peters et al. (1998).

As shown in Table 3, 95% of the participants had SII_Q values above 0.52. An SII value of 0.52 corresponds to an intelligibility of almost 90% for NH listeners (e.g., see Figure 3 in Eisenberg, Dirks, Takayanagi, & Martinez, 1998). This suggests that audibility could have affected SRT_{SSN} or SRT_{R2TM} slightly. To further assess the influence of reduced audibility on the present SRTs, new MLR models of SRT_{SSN} and SRT_{R2TM} that included the SII_Q as a potential predictor were explored. The resulting models were identical to those reported in Table 2 and the SII_Q was not a significant predictor in the final MLR model for SRT_{SSN} ($p = .51$) or in the model for SRT_{R2TM} ($p = .75$). Therefore, it is concluded that reduced audibility was unlikely to have a substantial influence on the present SRTs.

Table 3. Distribution of SII_Q Values for Individually NAL-R Amplified Speech.

	Percentile (%)						
	0	5	25	50	75	95	100
SII_Q	0.37	0.52	0.58	0.66	0.74	0.86	0.88

Note. SII = speech-intelligibility index.

Discussion

The aim of the present study was to assess the relative importance of cochlear mechanical dysfunction, temporal processing deficits, and age for the ability of HI listeners to understand individually amplified speech in SSN (SRT_{SSN}) and a R2TM (SRT_{R2TM}). The main findings were:

1. For the present sample of HI listeners, age, PTT, BMCE, and FMDTs were virtually uncorrelated with each other (Table 1) and yet they were significant predictors of SRTs in noisy backgrounds (Table 2).
2. Residual cochlear compression (BMCE) was the most important single predictor of SRT_{SSN}, while FMDT was the most important single predictor of SRT_{R2TM} (Figure 2, Table 2).
3. Cochlear mechanical gain loss (HL_{OHC}) was correlated with SRT_{SSN} and SRT_{R2TM} (Table 1) but did not improve the MLR models of SRT_{SSN} or SRT_{R2TM} once the previously mentioned predictors were included in the models.
4. Age was a significant predictor of SRT_{SSN} and SRT_{R2TM}, and it was independent of FMDTs and virtually independent of BMCE (Table 1).

The absence of a correlation between age and PTT in the present sample of HI listeners was surprising, given the well-established relationship between those two variables (reviewed by Gordon-Salant, Frisina, Popper, & Fay, 2010). One possible explanation is that our participants were required to be hearing-aid candidates (something necessary for an aspect of the study not reported here) while having mild-to-moderate audiometric losses in the frequency range from 0.5 to 6 kHz, something necessary to infer HL_{OHC} estimates using behavioral masking methods (Johannesen et al., 2014). Thus, it is possible that their hearing losses spanned a narrower range than would be observed across the same age span in a random sample. Our across-frequency SII-weighted averaging of audiometric thresholds

(see Methods section) may have contributed to the lack of correlation between age and PTT.

The absence of a correlation between age and FMDTs is not unprecedented (Strelcyk & Dau, 2009) but was nevertheless unexpected, given that several studies have reported lower (better) FMDTs for younger than for middle-aged or older NH listeners (e.g., Grose & Mamo, 2012; Grose, Mamo, Buss, & Hall, 2015; He, Mills, & Dubno, 2007; Hopkins & Moore, 2011; Moore, Vickers, & Mehta, 2012). The number of synapses between IHCs and auditory nerve fibers is known to decrease gradually with increasing age, even in cochleae with normal IHC and OHC counts and thus presumably normal PTTs (Makary, Shin, Kujawa, Liberman, & Merchant, 2011). Insofar as audiometric loss can be caused by noise exposure and noise exposure decreases the number of afferent synapses (Kujawa & Liberman, 2009), audiometric loss is also thought to be associated with a reduction in the number of synapses. A reduced synapse count (or synaptopathy) is thought to impair auditory temporal processing (Lopez-Poveda, 2014; Lopez-Poveda & Barrios, 2013; Plack, Barker, & Prendergast, 2014; Shaheen, Valero, & Liberman, 2015). The absence of a correlation between age and FMDTs (Table 2) suggests either that our participants did not suffer from synaptopathy (something unlikely given the wide range of their ages and audiometric losses, Figure 1) or that FMDTs reflect temporal processing abilities not directly (or not solely) related to synaptopathy. On the other hand, the effect of age on FMDTs is greater for low- (500 Hz) than for high-frequency (4 kHz) carrier tones (He et al., 2007) and the coding of frequency modulation detection cues in the temporal discharge pattern of auditory nerve responses (phase locking) deteriorates gradually with increasing frequency (Johnson, 1980; Palmer & Russell, 1986). Therefore, another explanation for the present lack of correlation between age and FMDTs might be that the frequency of carrier tone used here was perhaps too high (1500 Hz) to unveil any relationship between age and FMDTs. Another explanation might be that both cochlear mechanical dysfunction and aging can independently impair frequency-modulation detection cues but that in the present case (because all listeners had moderate to moderately severe sensorineural audiometric loss), the detrimental effect of cochlear dysfunction on those cues dominated over the (possibly more modest) effect of aging.

The finding that age, PTT, FMDT, and BMCE were correlated with speech-in-noise intelligibility was expected (Table 1) for the reasons reviewed in the Introduction section. A significant, though incidental aspect of the present study is, however, that for the present group of HI listeners those factors were uncorrelated or barely correlated with each other (Table 1) and yet they all affected intelligibility in different proportions for the two types of maskers (Table 2).

Of the two indicators used here to characterize cochlear mechanical dysfunction, cochlear gain loss (HL_{OHC}) was correlated with speech intelligibility in SSN and a R2TM, while residual compression (BMCE) was correlated with speech intelligibility in SSN. The two indicators (HL_{OHC} and BMCE) were correlated with each other (Table 1). However, HL_{OHC} did not remain as a significant predictor of intelligibility for either of the two maskers when other variables were included in the MLR model, while BMCE was the most significant predictor of intelligibility only for SSN (Table 2). The present estimates of HL_{OHC} and BMCE are indirect and based on numerous assumptions (Johannesen et al., 2014; see also Pérez-González, Johannesen, & Lopez-Poveda, 2014). Assuming nonetheless that these estimates are reasonable, the present findings suggest that cochlear mechanical gain loss and residual compression are not equivalent predictors of the impact of cochlear mechanical dysfunction on intelligibility in SSN. This further suggests that residual compression might be more significant than cochlear gain loss, perhaps because the impact of HL_{OHC} on intelligibility may be compensated with linear amplification but the impact of BMCE may not.

The importance of compression for intelligibility in SSN appears inconsistent with the findings reported in some studies. For example, Noordhoek, Houtgast, and Festen (2001) found little influence of residual compression on the intelligibility of narrow-band speech centered on 1 kHz. Similarly, Summers, Makashay, Theodoroff, and Leek (2013) reported that compression was not clearly associated with understanding intense speech (at a fixed level of 92 dB SPL) in steady noise. This inconsistency may be partly due to methodological differences across studies. First, Summers et al. assessed intelligibility using the percentage of sentences identified correctly for a fixed SNR rather than the SRT (in dB SNR). Second, Summers et al. reported correlations between intelligibility and estimates of compression at single frequencies, while we have reported correlations between SRTs and across-frequency SII-weighted averages of compression. Finally, and perhaps most importantly, although Summers et al. inferred compression from temporal masking curves (TMCs), as we did, they did not take into account important precautions that are necessary to infer accurate compression estimates using the TMC method. This method is based on the assumption that cochlear compression may be inferred from comparisons of the slopes of TMCs unaffected by compression (linear references) with those of TMCs affected by compression. Summers et al. used different linear reference TMCs for different test frequencies and their linear references were TMCs for a masker frequency equal to

0.55 times the probe frequency. It has been shown that this almost certainly underestimates compression, particularly at lower frequencies (e.g., Lopez-Poveda & Alves-Pinto, 2008; Lopez-Poveda, Plack, & Meddis, 2003; Pérez-González et al., 2014). As a result, Summers et al. almost certainly underestimated compression, particularly for their NH listeners, something that might have contributed to hiding differences in compression across listeners with different audiometric thresholds.

For the present sample of HI listeners, BMCE was the most significant predictor of aided speech intelligibility in SSN, while FMDT was the most significant predictor of aided intelligibility in a R2TM (Table 2). Hopkins and Moore (2011) investigated the effects of age and cochlear hearing loss on TFS sensitivity, frequency selectivity, and speech reception in noise for a sample of NH and HI listeners. They reported that once absolute threshold was partialled out, TFS sensitivity was the only significant predictor of speech intelligibility in modulated noise while auditory filter bandwidth was the only significant predictor of intelligibility in steady SSN (see their Table IV). The present results appear broadly consistent with those of Hopkins and Moore considering (a) that FMDT may be thought to index the quality of the internal representation of the TFS at the outputs of the cochlear filters (Moore & Sek, 1996) and (b) that auditory filter bandwidth is a psychoacoustical correlate of cochlear frequency selectivity (e.g., Evans, 2001; Shera, Guinan, & Oxenham, 2002) and thus an indicator of cochlear dysfunction.

Of course, peripheral compression (BMCE) and auditory filter bandwidth are both indirect and different behavioral indicators of cochlear dysfunction but are related. A behavioral study has shown that the auditory filter bandwidth increases as the compression decreases (Moore, Vickers, Plack, & Oxenham, 1999) and physiological studies have shown that OHC dysfunction reduces both cochlear frequency selectivity and compression (Ruggero et al., 1996). In the light of this evidence, the mechanism behind intelligibility in SSN for the present HI listeners might be poorer spectral separation of the speech cues due to increased filter bandwidth (Moore, 2007). It seems puzzling, however, that the same mechanism is not at least slightly involved in the intelligibility of speech in modulated noise (Hopkins & Moore, 2011) or R2TMs (present results).

The present finding that TFS sensitivity (as assessed by FMDT) is less important for intelligibility in steady than in fluctuating maskers appears consistent with the results of Hopkins and Moore (2009), who showed that SRTs improved less with increasing TFS information for steady than for fluctuating backgrounds. Perhaps good TFS sensitivity is unhelpful or unnecessary to understand speech in backgrounds where the TFS of the background is uninformative (as would be the case for SSN) but is required to separate a TFS-rich signal from a TFS-rich masker (as would be the case for a R2TM). If this were the case, intelligibility would be better when the TFS information of the signal and the masker are well represented internally.

The finding that age remained as a significant predictor of intelligibility after the effects of BMCE on SRT_{SNN} and of FMDT on SRT_{R2TM} were partialled out suggests that age per se affects intelligibility in noise. This result is consistent with that of Füllgrabe, Moore, and Stone (2015), who showed that for audiometrically matched young and old listeners, age was a significant contributor for intelligibility in various types of maskers also after the effect of TFS sensitivity was accounted for.

The present conclusions are based on MLR models where all of the predictors were the SII-weighted sum of parameters across frequency. One might wonder whether conclusions would hold if the across-frequency weightings had been different for different parameters. For example, cochlear filter bandwidths tend to increase with increasing HL_{OHC} or BMCE (e.g., Moore et al., 1999) and broader filters can interact with TFS processing (Hopkins & Moore, 2011). Such an interaction could affect intelligibility and would be greater at low frequencies, where phase locking is more significant, than at high frequencies (Hopkins & Moore, 2010). This suggests that predictors of cochlear dysfunction (HL_{OHC} and BMCE) might need to have more weight at low frequencies than suggested by the SII and conclusions might be different in this case. This, however, was unlikely. Alternative MLR models were constructed using the unweighted mean predictors at low (0.5, 1, and 2 kHz) and at high (4 and 6 kHz) frequencies simultaneously. The alternative models (Table 4) suggested (a) that intelligibility depends mostly on the parameter values at low frequencies (something not surprising considering that most subjects had moderate-to-severe audiometric losses at high frequencies) and (b) that the relative importance of the predictors differed from that in the SII-weighted models (Table 2). Nonetheless, the predictors in these alternative models were the same as in the models with SII-weighted parameters across frequency (compare the predictors in Tables 2 and 4).

Speech intelligibility is often analyzed using the SII, which, when calculated taking into account the background noise (ANSI, 1997), provides a measure of the proportion of the speech spectrum that is audible and *above* the noise. The SII is often combined with an additional *proficiency* index that accounts for the effect on intelligibility of factors unrelated to audibility but related to the speaker's enunciation, the type of speech material, and the experience of the listeners with that particular speaker (e.g., Fletcher & Galt, 1950; Studebaker, McDaniel, & Sherbecoe, 1995). Using such a SII/

Table 4. As Table 2 but for MLR Models Where Separate Unweighted Means of the Predictors' Values at 0.5, 1, and 2 kHz (LF), and 4 and 6 kHz (HF) Were Simultaneously Available as Predictors, While SII-Weighted Means Across All Frequencies Were Not.

Priority	Predictor	Coefficient	*t*-value	*p*	Accum. R^2
SRT_{SSN}					
n/a	Intercept	−7.73	−7.8	7.9×10^{-11}	—
1	HL_{IHC} (HF)	0.0347	2.9	5.4×10^{-3}	.13
2	BMCE (LF)	3.81	4.1	1.2×10^{-4}	.21
3	HL_{IHC} (LF)	0.113	3.6	6.5×10^{-4}	.28
4	Age	0.037	3.3	1.6×10^{-3}	.38
SRT_{R2TM}					
n/a	Intercept	−6.80	−6.5	1.6×10^{-8}	—
1	PTT (LF)	0.0812	4.5	2.7×10^{-5}	.29
2	Age	0.033	3.1	2.7×10^{-3}	.43
3	FMDT	1.59	3.1	2.8×10^{-3}	.50

Note. MLR = multiple linear regression; SRT = speech reception threshold; SSN = speech-shaped noise; SII = speech-intelligibility index; R2TM = time-reversed two-talker masker; HL = audiometric loss; IHC = inner hair cell; BMCE = basilar-membrane compression exponent; FMDT = frequency modulation detection threshold.

proficiency model, intelligibility for HI listeners has been reasonably well predicted/explained for quiet and noise backgrounds and for aided and unaided conditions (e.g. Humes, 2002; Pavlovic & Studebaker, 1984; Scollie, 2008; Woods, Kalluri, Pentony, & Nooraei, 2013). Here, we did not opt for such an approach for several reasons. First, the SII is not sufficiently validated for fluctuating backgrounds like the R2TM employed here (a revised SII has been proposed that works also for fluctuating noise; Rhebergen, Versfeld, & Dreschler, 2006). Second, in the present study, audibility was largely achieved by providing individualized amplification (see the Results section); hence only the effects of proficiency would remain if the present SRTs were to be explained using the SII/proficiency model. Third, and most importantly, the proficiency index would inform of the magnitude of intelligibility deficits unrelated to audibility while we intended to assess the relative contributions of the physiological causes for those deficits.

Conclusions

1. Estimated cochlear gain loss is unrelated to the ability to understand speech in steady noise.
2. Residual cochlear compression is related to speech understanding in speech-shaped steady noise but not in a time-reversed two-talker masker..
3. Auditory temporal processing ability, as estimated by frequency-modulation detection thresholds, is related to good speech understanding in a time-reversed two-talker masker but has only minor importance for intelligibility in steady noise.
4. Age per se reduces the intelligibility of speech in any of the two maskers tested here, regardless of absolute thresholds, cochlear mechanical dysfunction, or temporal processing deficits.

Acknowledgments

We thank William S. Woods, Brent Edwards, and Olaf Strelcyk for useful suggestions. We also thank Andrew J. Oxenham, Brian C. J. Moore, and an anonymous reviewer for their comments during the review process.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work is supported by Starkey Ltd. (USA), Junta de Castilla y León, MINECO (ref. BFU2012-39544-C02), and European Regional Development Funds.

References

American National Standards Institute. (1997). *S3.5 methods for calculation of the speech intelligibility index*. New York, NY: Author.

Baer, T., & Moore, B. C. J. (1994). Effects of spectral smearing on the intelligibility of sentences in the presence of interfering speech. *Journal of the Acoustical Society of America*, *95*, 2277–2280.

Brown, G. J., Ferry, R. T., & Meddis, R. (2010). A computer model of auditory efferent suppression: Implications for the recognition of speech in noise. *Journal of the Acoustical Society of America*, *127*, 943–954.

Byrne, D., & Dillon, H. (1986). The national acoustic laboratories' (NAL) new procedure for selecting the gain and frequency response of a hearing aid. *Ear and Hearing*, *7*, 257–265.

Byrne, D., Dillon, H., Tran, K., Arlinger, S., Wilbraham, K., Cox, R., . . . Ludvidsen, C. (1994). An international comparison of long-term average speech spectra. *Journal of the Acoustical Society of America*, *96*, 2108–2120.

Committee on Hearing, Bioacoustics, and Biomechanics. (1988). Speech understanding and aging. Working group on speech understanding and aging. *Journal of the Acoustical Society of America*, *83*, 859–895.

Deng, L., Geisler, C. D., & Greenberg, S. (1987). Responses of auditory-nerve fibers to multiple-tone complexes. *Journal of the Acoustical Society of America*, *82*, 1989–2000.

Eisenberg, L. S., Dirks, D. D., Takayanagi, S., & Martinez, A. S. (1998). Subjective judgements of clarity and intelligibility for filtered stimuli with equivalent speech intelligibility index predictions. *Journal of Speech, Language, and Hearing Research*, *41*, 327–339.

Evans, E. F. (2001). Latest comparison between physiological and behavioral frequency selectivity. In A. J. M. Houtsma, A. Kohlraush, V. F. Prijs, R. Schoonhoven, & J. Breebaart (Eds.), *Physiological and psychophysical bases of auditory function* (pp. 382–387). Maastricht, The Netherlands: Shaker.

Festen, J. M., & Plomp, R. (1983). Relations between auditory functions in impaired hearing. *Journal of the Acoustical Society of America*, *73*, 652–662.

Festen, J. M., & Plomp, R. (1990). Effects of fluctuating noise and interfering speech on the speech-reception threshold for impaired and normal hearing. *Journal of the Acoustical Society of America*, *88*, 1725–1736.

Fletcher, H., & Galt, R. (1950). Perception of speech and its relation to telephony. *Journal of the Acoustical Society of America*, *22*, 89–151.

Füllgrabe, C., Moore, B. C. J., & Stone, M. A. (2015). Age-group differences in speech identification despite matched audiometrically normal hearing: contributions from auditory temporal processing and cognition. *Frontiers in Aging Neuroscience*, *6*, 347.

George, E. L., Festen, J. M., & Houtgast, T. (2006). Factors affecting masking release for speech in modulated noise for normal-hearing and hearing-impaired listeners. *Journal of the Acoustical Society of America*, *120*, 2295–2311.

Gordon-Salant, S., Frisina, R. D., Popper, A. N., & Fay, R. R. (2010). *The aging auditory system*. New York, NY: Springer.

Gregan, M. J., Nelson, P. B., & Oxenham, A. J. (2013). Behavioral measures of cochlear compression and temporal resolution as predictors of speech masking release in hearing-impaired listeners. *Journal of the Acoustical Society of America*, *134*, 2895–2912.

Grose, J. H., & Mamo, S. K. (2012). Frequency modulation detection as a measure of temporal processing: Age-related monaural and binaural effects. *Hearing Research*, *294*, 49–54.

Grose, J. H., Mamo, S. K., Buss, E., & Hall, J. W. (2015). Temporal processing deficits in middle age. *American Journal of. Audiology*, *24*, 91–93.

Guinan, J. J. (2010). Cochlear efferent innervation and function. *Current Opinion in Otolaryngology & Head and Neck Surgery*, *18*, 447–453.

He, N. J., Mills, J. H., & Dubno, J. R. (2007). Frequency modulation detection: Effects of age, psychophysical method, and modulation waveform. *Journal of the Acoustical Society of America*, *122*, 467–477.

Henry, K. S., & Heinz, M. G. (2012). Diminished temporal coding with sensorineural hearing loss emerges in background noise. *Nature Neuroscience*, *15*, 1362–1364.

Hopkins, K., & Moore, B. C. J. (2009). The contribution of temporal fine structure to the intelligibility of speech in steady and modulated noise. *Journal of the Acoustical Society of America*, *125*, 442–446.

Hopkins, K., & Moore, B. C. J. (2010). The importance of temporal fine structure information in speech at different spectral regions for normal-hearing and hearing-impaired subjects. *Journal of the Acoustical Society of America*, *127*, 1595–1608.

Hopkins, K., & Moore, B. C. J. (2011). The effects of age and cochlear hearing loss on temporal fine structure sensitivity, frequency selectivity, and speech reception in noise. *Journal of the Acoustical Society of America*, *130*, 334–349.

Hornsby, B. W. Y., & Ricketts, T. A. (2007). Directional benefit in the presence of speech and speech like maskers. *Journal of the American Academy of Audiology*, *18*, 5–16.

Huarte, A. (2008). The Castilian Spanish hearing in noise test. *International Journal of Audiology*, *47*, 369–370.

Humes, L. E. (2002). Factors underlying the speech-recognition performance of elderly hearing-aid wearers. *Journal of the Acoustical Society of America*, *112*, 1112–1132.

Johannesen, P. T., Perez-Gonzalez, P., & Lopez-Poveda, E. A. (2014). Across-frequency behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Frontiers in Neuroscience*, *8*, 214.

Johnson, D. H. (1980). The relationship between spike rate and synchrony in responses of auditory-nerve fibers to single tones. *Journal of the Acoustical Society of America*, *68*, 1115–1122.

Kim, S. H., Frisina, R. D., & Frisina, D. R. (2006). Effects of age on speech understanding in normal hearing listeners: Relationship between the auditory efferent system and speech intelligibility in noise. *Speech Communication*, *48*, 855–862.

Kujawa, S. G., & Liberman, M. C. (2009). Adding insult to injury: Cochlear nerve degeneration after "temporary" noise-induced hearing loss. *Journal of Neuroscience*, *29*, 14077–14085.

Levitt, H. (1971). Transformed up-down methods in psychoacoustics. *Journal of the Acoustical Society of America*, *49*(Suppl. 2): 467–477.

Lopez-Poveda, E. A. (2014). Why do I hear but not understand? Stochastic undersampling as a model of degraded neural encoding of speech. *Frontiers in Neuroscience*, *8*, 348.

Lopez-Poveda, E. A., & Alves-Pinto, A. (2008). A variant temporal-masking-curve method for inferring peripheral auditory compression. *Journal of the Acoustical Society of America*, *123*, 1544–1554.

Lopez-Poveda, E. A., & Barrios, P. (2013). Perception of stochastically undersampled sound waveforms: A model of auditory deafferentation. *Frontiers in Neuroscience*, *7*, 124.

Lopez-Poveda, E. A., & Johannesen, P. T. (2012). Behavioral estimates of the contribution of inner and outer hair cell dysfunction to individualized audiometric loss. *Journal of the Association for Research in Otolaryngology*, *13*, 485–504.

Lopez-Poveda, E. A., Johannesen, P. T., & Merchán, M. A. (2009). Estimation of the degree of inner and outer hair cell dysfunction from distortion product otoacoustic emission input/output functions. *Audiological Medicine*, *7*, 22–28.

Lopez-Poveda, E. A., Plack, C. J., & Meddis, R. (2003). Cochlear nonlinearity between 500 and 8000 Hz in listeners with normal hearing. *Journal of the Acoustical Society of America*, *113*, 951–960.

Lorenzi, C., Gilbert, G., Carn, H., Garnier, S., & Moore, B. C. J. (2006). Speech perception problems of the hearing impaired reflect inability to use temporal fine structure. *Proceedings of the National Academy of Science of the United States of America*, *103*, 18866–18869.

Makary, C. A., Shin, J., Kujawa, S. G., Liberman, M. C., & Merchant, S. N. (2011). Age-related primary cochlear

neuronal degeneration in human temporal bones. *Journal of the Association for Research in Otolaryngology*, *12*, 711–717.

Moore, B. C. J. (2007). *Cochlear hearing loss*. Chichester, England: John Wiley.

Moore, B. C. J., & Glasberg, B. R. (1997). A model of loudness perception applied to cochlear hearing loss. *Auditory Neuroscience*, *3*, 289–311.

Moore, B. C. J., & Sek, A. (1996). Detection of frequency modulation at low modulation rates: Evidence for a mechanism based on phase locking. *Journal of the Acoustical Society of America*, *100*, 2320–2331.

Moore, B. C. J., Vickers, D. A., & Mehta, A. (2012). The effects of age on temporal fine structure sensitivity in monaural and binaural conditions. *International Journal of Audiology*, *51*, 715–721.

Moore, B. C. J., Vickers, D. A., Plack, C. J., & Oxenham, A. J. (1999). Inter-relationship between different psychoacoustic measures assumed to be related to the cochlear active mechanism. *Journal of the Acoustical Society of America*, *106*, 2761–2778.

Nilsson, M., Soli, S. D., & Sullivan, J. A. (1994). Development of the hearing in noise test for the measurement of speech reception thresholds in quiet and in noise. *Journal of the Acoustical Society of America*, *95*, 1085–1099.

Noordhoek, I. M., Houtgast, T., & Festen, J. M. (2001). Relations between intelligibility of narrow-band speech and auditory functions, both in the 1-kHz frequency region. *Journal of the Acoustical Society of America*, *109*, 1197–1212.

Palmer, A. R., & Russell, I. J. (1986). Phase-locking in the cochlear nerve of the guinea-pig and its relation to the receptor potential of inner hair-cells. *Hearing Research*, *24*(1), 1–15.

Pavlovic, C. V., & Studebaker, G. A. (1984). An evaluation of some assumptions underlying the articulation index. *Journal of the Acoustical Society of America*, *75*, 1606–1612.

Pérez-González, P., Johannesen, P. T., & Lopez-Poveda, E. A. (2014). Forward-masking recovery and the assumptions of the temporal masking curve method of inferring cochlear compression. *Trends in Hearing*, *18*, 1–14.

Peters, R. W., Moore, B. C. J., & Baer, T. (1998). Speech reception thresholds in noise with and without spectral and temporal dips for hearing-impaired and normally hearing people. *Journal of the Acoustical Society of America*, *103*, 577–587.

Pichora-Fuller, M. K., Schneider, B. A., Macdonald, E., Pass, H. E., & Brown, S. (2007). Temporal jitter disrupts speech intelligibility: A simulation of auditory aging. *Hearing Research*, *223*, 114–121.

Plack, C. J., Barker, D., & Prendergast, G. (2014). Perceptual consequences of "hidden" hearing loss. *Trends in Hearing*, *18*, 1–11.

Plack, C. J., Drga, V., & Lopez-Poveda, E. A. (2004). Inferred basilar-membrane response functions for listeners with mild to moderate sensorineural hearing loss. *Journal of the Acoustical Society of America*, *115*, 1684–1695.

Rhebergen, K. S., Versfeld, N. J., & Dreschler, W. A. (2006). Extended speech intelligibility index for the prediction of the speech reception threshold in fluctuating noise. *Journal of the Acoustical Society of America*, *120*, 3988–3997.

Rhebergen, K. S., Versfeld, N. J., & Dreschler, W. A. (2009). The dynamic range of speech, compression, and its effect on the speech reception threshold in stationary and interrupted noise. *Journal of the Acoustical Society of America*, *126*, 3236–3245.

Robles, L., & Ruggero, M. A. (2001). Mechanics of the mammalian cochlea. *Physiological Reviews*, *81*, 1305–1352.

Ruggero, M. A., Rich, N. C., Robles, L., & Recio, A. (1996). The effects of acoustic trauma, other cochlear injury and death on basilar-membrane responses to sound. In A. Axelson, H. Borchgrevink, P. -A. Hellström, D. Henderson, R. P. Hamernik, & R. J. Salvi (Eds.), *Scientific basis of noise-induced hearing loss* (pp. 23–35). New York, NY: Medical Publishers.

Scollie, S. D. (2008). Children's speech recognition scores: The speech intelligibility index and proficiency factors for age and hearing level. *Ear and Hearing*, *29*, 543–556.

Shaheen, L. A., Valero, M. D., & Liberman, M. C. (2015). Towards a diagnosis of cochlear neuropathy with envelope following responses. *Journal of the Association for Research in Otolaryngology*, *16*, 727–745.

Shera, C. A., Guinan, J. J., & Oxenham, A. J. (2002). Revised estimates of human cochlear tuning from otoacoustic and behavioral measurements. *Proceedings of the National Academy of Science*, *99*, 3318–3323.

Strelcyk, O., & Dau, T. (2009). Relations between frequency selectivity, temporal fine-structure processing, and speech reception in impaired hearing. *Journal of the Acoustical Society of America*, *125*, 3328–3345.

Studebaker, G. A., McDaniel, D. M., & Sherbecoe, R. L. (1995). Evaluating relative speech recognition performance using the proficiency factor and rationalized arcsine differences. *Journal of the American Academy of Audiology*, *6*, 173–182.

Summers, V., Makashay, M. J., Theodoroff, S. M., & Leek, M. R. (2013). Suprathreshold auditory processing and speech perception in noise: Hearing-impaired and normal-hearing listeners. *Journal of the American Academy of Audiology*, *24*, 274–292.

ter, Keurs, M., Festen, J. M., & Plomp, R. (1992). Effect of spectral envelope smearing on speech reception. I. *Journal of the Acoustical Society of America*, *91*, 2872–2880.

Theil, H., & Goldberger, A. S. (1961). On pure and mixed statistical estimation in economics. *International Economic Review*, *2*, 65–78.

Woods, W. S., Kalluri, S., Pentony, S., & Nooraei, N. (2013). Predicting the effect of hearing loss and audibility on amplified speech reception in a multi-talker listening scenario. *Journal of the Acoustical Society of America*, *133*, 4268–4278.

Young, E. D. (2008). Neural representation of spectral and temporal information in speech. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *363*, 923–945.

La Relación entre la Disfunción Mecánica Coclear y la Inteligibilidad del Habla en Ruido para Personas Hipoacúsicas

TESIS DOCTORAL

APÉNDICE B

RESUMEN EN ESPAÑOL

Patricia Pérez González

Instituto de Neurociencias de Castilla y León

Universidad de Salamanca

Julio 2017

RESUMEN CORTO

El objetivo principal de la presente tesis es investigar por qué la capacidad para entender el habla en entornos ruidosos varía ampliamente de unas personas hipoacúsicas a otras, incluso tras compensar la pérdida auditiva con amplificación. Nuestra hipótesis es que la disfunción de las células ciliadas externas (CCEs) afecta a la inteligibilidad del habla audible en ruido, y que personas hipoacúsicas con pérdidas audiométricas idénticas pueden presentar gran variabilidad en el grado de disfunción de las CCEs. Para comprobar estas hipótesis, se ha inferido la proporción de pérdida audiométrica que es debida a la pérdida de ganancia mecánica coclear (HL_{CCE}), y se ha investigado la correlación entre la HL_{CCE} y la compresión coclear residual con el umbral de recepción verbal (URVs) en ruido. La HL_{CCE} y la compresión residual se estimaron comparando las curvas de entrada/salida cocleares (E/S) de oyentes hipoacúsicos con curvas de referencia para personas normoyentes. Las curvas de E/S se infirieron empleando una técnica psicoacústica conocida como el método de las *curvas de enmascaramiento temporal* (CETs). Un último objetivo de la tesis fue validar los supuestos de este último método.

En el estudio, participaron 68 personas con pérdidas auditivas neurosensoriales simétricas. Para cada uno de ellos, se midieron los umbrales audiométricos por vía aérea y vía ósea, CETs, y emisiones otoacústicas de productos de distorsión a múltiples frecuencias (0.5, 1, 2, 4 y 6 kHz). También se midieron URVs para dos tipos de ruido: uno estacionario con espectro igual al espectro promedio del habla, y una máscara de dos hablantes invertida en el tiempo.

Los resultados muestran que (1) es razonable usar el método CET para inferir las curvas de E/S cocleares en humanos; (2) la gran mayoría de personas hipoacúsicas sufren una combinación de disfunción de las células ciliadas internas como de las externas; (3) la HL_{CCE} contribuye entre un 30–40% y un 60–70% a la pérdida auditiva total, y esta contribución es aproximadamente constante en el rango de frecuencias de 0.5 a 6 kHz; (4) la contribución de la HL_{CCE} a la pérdida auditiva total es muy variable de unas personas a otras, en particular a bajas frecuencias o en casos de pérdidas auditiva leves o moderadas; (5) la disfunción de las CCE no está correlacionada con los URVs en

ruido estacionario; (6) la compresión coclear residual, sin embargo, está correlacionada con los URVs en ruido estacionario pero no con la máscara de dos hablantes invertida en el tiempo; (7) la edad del oyente *per se* reduce la inteligibilidad del habla en cualquiera de los dos ruidos empleados en este estudio, independientemente de los umbrales absolutos o de la disfunción coclear mecánica.

ABREVIACIONES Y ACRÓNIMOS

ANSI	Instituto Nacional Americano de Estándares
CCE	Célula Ciliada Externa
CCI	Célula Ciliada Interna
CET	Curva de Enmascaramiento Temporal
dB	Decibelios
DS	Desviación Estándar
E/S	Entrada/Salida
ECMB	Exponente de Compresión de la Membrana Basilar
f_1, f_2	Frecuencias de los Tonos Primarios de OEAPD
FC	Frecuencia Característica
f_M	Frecuencia de Máscara
f_P	Frecuencia de Sonda
HI	Hipoacúsico
HL	Nivel de Audición
HL_{CCE}	Cantidad de pérdida auditiva (en dB) asociada a disfunción de CCE
HL_{CCI}	Cantidad de pérdida auditiva (en dB) asociada a disfunción de CCI
L_1, L_2	Niveles de f_1 y f_2
L_M	Nivel de Máscara
MB	Membrana Basilar
NH	Normoyente
OEAPD	Otoemisiones Acústicas de Productos de Distorsión
R2TM	Máscara de dos Hablantes Invertida en el Tiempo

RMS	Raíz de la Media Cuadrática
SII	Índice de Inteligibilidad del Habla
SPL	Nivel de Presión Sonora
SSN	Ruido con Forma del Habla
TFS	Estructura Temporal Fina
UATP	Umbrales Audiométricos de Tonos Puros

Índice

1. Introducción 1

Inteligibilidad del Habla en Ruido para Personas con Pérdida Auditiva 1

La Importancia de la Disfunción Mecánica Coclear para Entender el Habla en Ruido 2

Evaluación de la Disfunción Mecánica Coclear a partir de Curvas de Entrada / Salida 4

Inferencia de las Curvas de Entrada/Salida Coclear en Humanos 5

Hipótesis 7

Objetivos 8

2. Material y Métodos 9

Sujetos ..... **¡Error! Marcador no definido.**

Consideraciones Éticas 9

Umbrales de Recepción Verbal 9

CET Estímulo y Procedimiento ..... **¡Error! Marcador no definido.**

Indicadores de la Disfunción Mecánica Coclear 11

Medidas de las OEAPD ..... **¡Error! Marcador no definido.**

Estímulos y Aparatos 12

3. Discusión 13

Estimaciones Conductuales de la Contribución de la Disfunción de Células Ciliadas Internas y Externas a la Pérdida Audiométrica Individualizada 13

Potenciales Fuentes de Sesgo Metodológico 14

Comparación con Estudios Previos 18

Sobre la Validez del Método de CET para inferir las curvas de E/S Coclear. 20

Limitaciones de los Presentes Datos 21

Relación con Estudios Previos 23

Implicaciones de Estimar la Compresión a partir de CETs 23

La Influencia de la Disfunción Mecánica Coclear en la Inteligibilidad del Habla en Ruido 25

Conclusiones..... 31

1. INTRODUCCIÓN

Se dice que una persona tiene pérdida auditiva cuando oye peor que alguien con audición normal. Técnicamente, se dice que una persona tiene una pérdida auditiva, o que es hipoacúsica, cuando el promedio de sus umbrales audiométricos para tonos puros de frecuencias 0.5, 1 y 2 kHz, expresados en decibelios de nivel de audición (dB HL), supera los 25 dB HL en ambos oídos. Por otro lado, una persona tiene discapacidad auditiva cuando su pérdida auditiva en el mejor oído supera los 40 dB HL en adultos, o 30 dB HL en niños. Se denomina normoyentes a las personas que no presentan estas pérdidas auditivas.

Según la Organización Mundial de la Salud (OMS, 2017), más del 5% de la población mundial - 360 millones de personas - sufre hipoacusia (328 millones de adultos y 32 millones de niños). Aproximadamente un tercio de las personas mayores de 65 años de edad se ven afectadas por pérdida auditiva discapacitante. La pérdida auditiva puede ser leve, moderada, grave o profunda (Goodman, 1965), dependiendo de los umbrales audiométricos. Además, puede afectar a un oído o a ambos, y puede dificultar la percepción del habla conversacional o los sonidos fuertes.

INTELIGIBILIDAD DEL HABLA EN RUIDO PARA PERSONAS CON PÉRDIDA AUDITIVA

La capacidad de entender el habla en ambientes ruidosos puede medirse de diversas maneras (revisado por Schoepflin, 2012). Una de ellas consiste en presentar listas de elementos del habla (por ejemplo, consonantes, palabras u oraciones) a diferentes relaciones de señal-ruido (RSR) y medir el porcentaje

de elementos identificados correctamente por el oyente. Otra medida fiable y sensible de la inteligibilidad es el umbral de recepción verbal (URV). El URV puede definirse como la RSR a la que un oyente puede identificar correctamente el 50%, u otro porcentaje especificado, de los elementos de habla presentados (Nilsson, Solli y Sullivan, 1994). EL URV puede medirse empleando monosílabos, bisílabos, palabras, palabras clave u oraciones.

Las personas hipoacúsicas muestran peores porcentajes de reconocimiento de palabras y/o URV más altos (en dB RSR) que las personas normoyentes, sobre todo en ambientes ruidosos. Peters, Moore y Baer (1998) demostraron que los ancianos con pérdida auditiva coclear entre moderada y severa tienen URVs en ambientes ruidosos entre 2 y 19 dB más altos que los jóvenes normoyentes, dependiendo del tipo de ruido (véase su Tabla I).

La capacidad para entender el habla en ambientes ruidosos varía ampliamente entre las personas con deficiencia auditiva, incluso cuando usan audífonos para compensar el efecto perjudicial de su pérdida auditiva sobre la inteligibilidad. Mientras que algunas de estas personas son capaces de reconocer el 100% de las palabras monosílabas en ruido, con o sin sus audífonos, otras ni siquiera alcanzan el 10% de reconocimiento de palabras.

La Importancia de la Disfunción Mecánica Coclear para Entender el Habla en Ruido

Diversos factores pueden afectar la capacidad de las personas hipoacúsicas para entender el habla en ambientes ruidosos (revisado por Lopez-Poveda, 2014). Uno de ellos es la disfunción de las células ciliadas externas (CCEs). La disfunción de las CCEs podría degradar la representación del espectro del habla en la vibración mecánica de la cóclea, particularmente en ambientes ruidosos, por diversas razones. En primer lugar, la disfunción de las CCEs reduce la selectividad frecuencial de la cóclea (Robles y Ruggero, 2001). Esto podría difuminar la representación del espectro acústico en la vibración de la cóclea, dificultando a los oyentes hipoacúsicos percibir por separado las señales espectrales del habla de las del ruido o de las de otras interferencias acústicas (Moore, 2007). Varios estudios conductuales han apoyado esta idea (Baer y Moore, 1994; Festen y Plomp, 1983; Keurs ter, Festen y Plomp, 1990). En

segundo lugar, la supresión que ocurre en la cóclea sana podría facilitar la codificación del habla en el ruido, realzando las características espectrales más sobresalientes del habla frente a las del ruido de fondo (Deng, Geisler y Greenberg, 1987; Young, 2008). La disfunción de las CCE reduce la supresión, y esto podría dificultar la inteligibilidad del habla en el ruido. En tercer lugar, la compresión mecánica coclear podría facilitar la comprensión del habla en ruido fluctuante, amplificando el habla en los intervalos de silencio (o de bajo nivel de ruido), un fenómeno conocido como 'escucha en huecos' o '*dip listening*' (Greberg, Nelson, y Oxenham, 2013, Rhebergen, Versfeld y Dreschler, 2009). La disfunción de las CCEs reduce la compresión (es decir, hace más lineales las respuestas cocleares; Ruggero, Rich, Robles, y Recio, 1996) y, por lo tanto, podría dificultar la 'escucha en huecos' (Gregan et al., 2013). Cuarto, los eferentes olivococleares mediales posiblemente facilitan la inteligibilidad del habla en el ruido aumentando la discriminabilidad de los sonidos transitorios en ambientes ruidosos (Brown, Ferry, y Meddis, 2010; Guinan, 2010; Kim, Frisina y Frisina, 2006). Los eferentes olivococleares mediales ejercen su acción a través de las CCEs, y por lo tanto la disfunción de las CCE podría reducir los efectos desenmascarantes de estos eferentes.

El grado de disfunción de las CCEs podría ser diferente para diferentes personas hipoacúsicas (Lopez-Poveda y Johannesen, 2012) y esto podría contribuir a la gran variabilidad en su capacidad de entender el habla audible en ambientes ruidosos. Aunque razonable, sin embargo, esta idea es casi con toda seguridad sólo parcialmente correcta. En primer lugar, para los personas hipoacúsicos, no parece haber correlación significativa entre la compresión coclear residual y el beneficio de la 'escucha en los huecos' (Gregan et al., 2013), lo que socava la influencia de la compresión en la inteligibilidad del habla supraliminal en el ruido. En segundo lugar, la sintonización frecuencial de las cócleas sanas se reduce a altas intensidades, y es sólo ligeramente mayor que la de las cócleas dañadas (Robles y Ruggero, 2001). A pesar de ello, sin embargo, las personas hipoacúsicos todavía muestran peor inteligibilidad en ruido que las normoyentes a altas intensidades (revisado por Moore, 2007, pp. 205-28).

El objetivo principal de la presente tesis es arrojar algo de luz sobre la importancia relativa de la disfunción de las CCE en la capacidad de las personas hipoacúsicas para entender el habla audible en ambientes ruidosos.

EVALUACIÓN DE LA DISFUNCIÓN MECÁNICA COCLEAR A PARTIR DE CURVAS DE ENTRADA / SALIDA

En la cóclea sana, las células ciliadas internas (CCIs) transducen las vibraciones mecánicas de la membrana basilar (MB) en señales nerviosas. Por otro lado, las CCEs amplifican las respuestas de la MB a sonidos de bajo nivel y son las responsables de nuestra alta sensibilidad auditiva (Bacon et al., 2004). Una reducción en el número de CCEs, o un daño en las CCEs (o de las estructuras asociadas) puede reducir la ganancia coclear a sonidos de bajo nivel sonoro y, por tanto, provocar una pérdida auditiva. Del mismo modo, una reducción en el número de CCI, o un daño en las CCI o sus estructuras asociadas, puede requerir de un aumento de la excitación de la MB para detectar una señal, lo que también puede causar una pérdida auditiva (Moore, 2007). Aunque generalmente no es posible establecer una correspondencia uno a uno entre la pérdida auditiva y el grado de pérdida o lesión física de las CCI/CCE (Chen y Fechter, 2003; Lopez-Poveda y Johannesen, 2012), es razonable suponer que la pérdida auditiva de las personas con hipoacusia coclear puede deberse a una pérdida o disfunción combinada de CCIs y CCEs. De hecho, algunos autores han supuesto que la pérdida auditiva (HL_{TOTAL}, del inglés *Hearing Loss*) para una frecuencia dada, puede expresarse como la suma de dos contribuciones: una asociada con la pérdida de ganancia mecánica coclear, o disfunción de las CCE (HL_{CCE}) más una asociada con una transducción ineficiente de las CCI, o con una disfunción de las CCI (HL_{CCI}), donde HL_{TOTAL}, HL_{CCI} y HL_{CCE} están medidas en decibelios (dB) (Moore y Glasberg, 1997; Plack et al., 2004; Moore, 2007; Jepsen y Dau, 2011; Lopez-Poveda y Johannesen, 2012).

La disfunción mecánica coclear hace más lineales las curvas de entrada/salida (E/S) de la MB (Ruggero y Robles, 2001). Por lo tanto, HL_{CCE} puede calcularse mediante la comparación de las curvas de E/S de la MB para un oyente hipoacúsico con las curvas de E/S de referencia para normoyentes. Plack et al. (2004) han sugerido que la curva de E/S mecánica coclear se puede modelar mediante una función que consiste en un primer segmento lineal (pendiente ~1 dB/dB) a bajos niveles de entrada, seguido de un segmento compresivo en niveles medios (pendiente < 1 dB/dB), seguido de un segundo segmento lineal a altos niveles de entrada. El límite entre el segmento lineal de bajo nivel y el segmento compresivo se denomina el 'umbral de compresión' (UC), mientras

que el límite entre el segmento compresivo y el segmento lineal de alto nivel se denomina 'umbral de retorno a la linealidad' (RLT). Según Plack et al. (2004), una disfunción mecánica coclear desplaza el primer segmento lineal de la curva de E/S de la MB hacia niveles más altos sin cambiar la pendiente de la curva E/S sobre su segmento compresivo. Por lo tanto, es posible calcular HL_{CCE} como el desplazamiento horizontal (en decibelios) del primer segmento lineal de la curva de E/S para cualquier oyente hipoacúsico, con respecto al segmento correspondiente de las curvas de E/S de referencia media para los normoyentes. HL_{CCI} puede estimarse (en decibelios) como la diferencia entre HL_{TOTAL} y HL_{CCE} (Moore y Glasberg, 1997; Plack et al., 2004; Moore, 2007; Jepsen y Dau, 2011; Lopez Poveda y Johannesen, 2012).

Teóricamente, diferentes personas con idéntica pérdida audiométrica pueden sufrir de diferentes grados de disfunción de CCI y CCE. Un objetivo específico de la presente tesis es estimar el grado de HL_{CCI} y HL_{CCE} para oyentes con pérdida auditiva coclear utilizando un enfoque basado en el modelo de Plack et al. (2004).

INFERENCIA DE LAS CURVAS DE ENTRADA/SALIDA COCLEAR EN HUMANOS

En humanos, las curvas de E/S de la MB no se pueden medir directamente, por lo que se han desarrollado una serie de métodos psicoacústicos para inferirlas (Lopez-Poveda y Alves-Pinto, 2008; Lopez-Poveda, Plack, y Meddis, 2003; Nelson, Schroder, y Wojtczak, 2001; Oxenham y Plack, 1997; Plack y Arifianto, 2010; Plack y O'Hanlon, 2003; Plack y Oxenham, 2000; Yasin, Drga, y Plack, 2013). Una de las técnicas más usadas se conoce como el método de la curva de enmascaramiento temporal (CET).

El método CET (Nelson et al., 2001) consiste en medir el nivel sonoro umbral de un tono enmascarador previo, llamado máscara, necesario para enmascarar una sonda tonal fija en función del intervalo de tiempo entre la máscara y la sonda. Una CET es la representación gráfica de los niveles de máscara necesarios para enmascarar una determinada sonda en función de los diferentes intervalos de tiempo entre máscara y sonda. Debido a que el nivel de la sonda es fijo, el nivel requerido de la máscara aumenta con el aumento del

intervalo de tiempo y, por tanto, las CET tienen pendientes positivas. Nelson et al. (2001) argumentaron que la pendiente de cualquier CET depende simultáneamente de *a*) la cantidad de compresión de MB que afecta a la máscara en la región de la cóclea cuya frecuencia característica (FC) es aproximadamente igual la frecuencia de la sonda, y *b*) la tasa de recuperación del efecto enmascarador interno (post-mecánico o libre de compresión). Suponiendo que la tasa de recuperación post-mecánica es la misma para todas las frecuencias de la máscara, las funciones de E/S de la MB pueden inferirse trazando los niveles de la máscara de una CET de referencia (es decir, la CET para una máscara procesada linealmente por la cóclea) frente a los niveles para cualquier otra frecuencia de máscara, emparejados de acuerdo a los intervalos de separación entre la sonda y la máscara (Nelson et al., 2001).

El método CET se basa en dos suposiciones relativas a la tasa de recuperación del efecto interno enmascarante: a saber, (1) para una frecuencia de sonda dada, esta tasa es independiente de la frecuencia de la máscara; y (2) es independiente de la frecuencia de la sonda. Ambas suposiciones son controvertidas. Wojtczak y Oxenham (2009) cuestionaron la primera suposición, mostrando que la tasa de recuperación post-mecánica es más rápida cuando las frecuencias de la máscara y de la sonda son iguales (condición de igual-frecuencia) que cuando la frecuencia de la máscara es aproximadamente una octava menor que la frecuencia de la sonda (condición de referencia). Dado que los niveles de máscara normalmente son más altos para la referencia que para la condición igual-frecuencia, una explicación alternativa es que la recuperación del enmascaramiento anterógrado depende del nivel sonoro de la máscara y no de su frecuencia. De hecho, una tercera suposición menos explícita del método de CET es que la recuperación de enmascaramiento anterógrado es independiente del nivel sonoro de la máscara. Wojtczak y Oxenham concluyeron que para las personas normoyentes, la primera suposición del método de CET es válida para niveles de máscara por debajo de 83 dB SPL, pero no para niveles superiores.

Stainsby y Moore (2006) cuestionaron la segunda hipótesis del método de CET. Mostraron que para oyentes hipoacúsicos sin otoemisiones de productos de distorsión (OEAPDs), es decir, para oyentes con respuestas cocleares lineales, las CETs son más pendientes para las sondas de frecuencia bajas que para las

de frecuencia alta. Por otro lado, otros autores han proporcionado apoyo experimental para la segunda hipótesis, utilizando otros métodos psicoacústicos que no requieren de una CET de referencia (Lopez-Poveda y Alves-Pinto, 2008; Plack et al., 2008). Lopez-Poveda y Alves-Pinto (2008) argumentaron que "*la ausencia de OEAPDs a bajas frecuencias no es necesariamente indicativa de respuestas cocleares lineales porque es difícil medir las OEAPD a bajas frecuencias debido al ruido fisiológico y ambiental*" (p. 1553). En otras palabras, Lopez-Poveda y Alves-Pinto sugirieron que Stainsby y Moore usaron técnicas OEAPD poco sensibles y, por tanto, que la ausencia de OEAPDs en sus sujetos podría no ser real. De hecho, Stainsby y Moore usaron tonos primarios a un solo nivel de 70 dB SPL, y es conocido que las OEAPD dependen fuertemente de los niveles de los tonos primarios, especialmente a bajas frecuencias. Por lo tanto, parece razonable que las OEAPDs que se muestran como *ausentes* a Stainsby y Moore, podrían haber estado presentes si se hubieran utilizado diferentes niveles de tonos primarios.

Por otro lado, Stainsby y Moore utilizaron un tiempo de medición fijo de 2 segundos para todas las frecuencias, incluso sabiendo que la detección de las OEAPD aumenta al aumentar el tiempo de medición (en promedio, la relación señal/ruido de OEAPDs mejora en 3 dB al duplicar el tiempo de medición). El uso de tiempos de registro cortos puede dificultar la detección de las OEAPDs y más a frecuencias bajas, donde el ruido fisiológico es comparativamente más alto. Por lo tanto, es de suponer que las OEAPDs que se mostraron como ausentes a Stainsby y Moore, podrían haber estado presentes si se hubieran utilizado tiempo de registro más largos. Además de esto, una preocupación adicional sobre el estudio de Stainsby y Moore es que sólo utilizaron tres sujetos.

Otro objetivo específico de la presente tesis es verificar las suposiciones del método de CET utilizando un enfoque similar al de Stainsby y Moore, pero resolviendo sus limitaciones metodológicas en la medida de lo posible.

HIPÓTESIS

La presente tesis tiene por objeto explorar tres hipótesis:

1. Diferentes personas con hipoacusia coclear (neurosensorial) y con umbrales auditivos comparables pueden mostrar diferentes grados de disfunción mecánica coclear.
2. Los supuestos del método psicoacústico de las curvas de enmascaramiento temporal empleado para inferir las curvas de E/S cocleares humanas son razonables.
3. La inteligibilidad de las personas con discapacidad auditiva en entornos ruidosos está correlacionada positivamente con su grado de disfunción mecánica coclear.

OBJETIVOS

El objetivo general de esta tesis es evaluar la importancia de la disfunción mecánica coclear para entender el habla audible en ambientes ruidosos.

Para lograr este objetivo general, se establecieron tres objetivos específicos:

1. Inferir el grado de disfunción mecánica coclear en un gran grupo de personas con hipoacusia neurosensorial, a partir de la comparación de las curvas cocleares E/S inferidas psicoacústicamente con las correspondientes curvas de referencia de personas normoyentes. Específicamente, medir la contribución de HL_{CCE} y HL_{CCI} a la pérdida auditiva de estas personas. Un objetivo secundario relacionado fue investigar la distribución de HL_{CCE} y HL_{CCI} en el rango de frecuencias de 500 a 8000 Hz. Un tercer objetivo relacionado fue investigar la variabilidad de HL_{CCE} y HL_{CCI} entre las personas hipoacúsicas.
2. Validar los supuestos del método de CET para inferir las curvas de E/S cocleares humanas. En particular, verificar la suposición de que la tasa de recuperación post-mecánica del enmascaramiento anterógrado es independiente de la frecuencia del tono de la sonda, así como del nivel de la máscara.
3. Investigar la correlación entre el grado de disfunción mecánica coclear y la inteligibilidad del habla en el ruido para personas hipoacúsicas.

2. MATERIAL Y MÉTODOS

PARTICIPANTES

En el estudio, participaron 68 personas (43 varones) con pérdida auditiva neurosensorial simétrica. Sus edades oscilaron entre los 25 y los 82 años, con una media de 61 años. Los umbrales audiométricos por vía aérea se midieron utilizando un audiómetro clínico (Interacoustics AD229e) a las frecuencias de 0.125, 0.25, 0.5, 1, 2, 3, 4, 5 y 8 kHz (ANSI, 1996). Los umbrales por vía ósea se midieron a 0.5, 1, 2, 3 y 4 kHz. Para muchos de los participantes, se midieron, además, los umbrales audiométricos por vía aérea y ósea a las frecuencias de 0.75 y 1.5 kHz. Se consideró que la pérdida auditiva era neurosensorial cuando la timpanometría era normal y la diferencia entre vía aérea y vía ósea era menor o igual a 15 dB en una de las frecuencias medidas.

CONSIDERACIONES ÉTICAS

Todos los procedimientos fueron aprobados por el Comité de Ética de la Universidad de Salamanca. Los participantes fueron informados y firmaron su consentimiento para participar antes de ser incluidos en el estudio.

UMBRALES DE RECEPCIÓN VERBAL

Los URVs se midieron mediante la prueba de escucha en ruido o '*Hearing-In-Noise Test*' (HINT, Nilsson et al., 1994). Para ello, se presentaron oraciones pronunciadas por un hablante masculino en presencia de un sonido enmascarante. Las frases presentadas fueron las correspondientes a la versión

en castellano del HINT (Huarte, 2008). Se usaron dos máscaras diferentes. Una de ellas, consistía en un ruido gaussiano constante filtrado en frecuencia para tener el espectro promedio a largo plazo del habla (Tabla 2 en Byrne et al., 1994). Nos referiremos a esta máscara como 'ruido con forma de habla' (SSN) y a su correspondiente URV como URV_{SSN}. La segunda máscara consistía en dos locutores simultáneos (un varón y una mujer) reproducidos a la inversa. Nos referiremos a esta máscara como 'máscara de dos hablantes invertida en el tiempo' (R2TM) y a su correspondiente URV como URV_{R2TM}.

CURVAS DE ENMASCARAMIENTO TEMPORAL: ESTÍMULOS Y PROCEDIMIENTO

Las CETs se midieron utilizando estímulos y procedimientos similares a los utilizados por Lopez-Poveda y Johannesen (2012). Las CET de igual-frecuencia se midieron para las frecuencias de sonda (f_P) de 0.5, 1, 2, 4 y 6 kHz, siendo tanto las máscaras como las sondas sinusoidales. La duración de la máscara fue de 210 ms, incluyendo rampas de encendido y apagado de 5 ms con forma de coseno al cuadrado. La sonda tenía una duración de 10 ms, incluyendo rampas de encendido y apagado de 5 ms con forma de coseno al cuadrado y sin ninguna porción de estado estacionario, excepto para la sonda de 500 Hz, cuya duración fue de 30 ms con rampas de 15 ms y sin ninguna porción de estado estacionario. El nivel sonoro de las sondas se fijó a 10 dB por encima del umbral absoluto individual para la frecuencia de la sonda. Los intervalos de tiempo entre la máscara y la sonda, definidos como el período desde el final de la máscara hasta el inicio de la sonda, oscilaban entre 5 y 100 ms en pasos de 10 ms, con un intervalo adicional de 2 ms. Los niveles umbrales de máscara se midieron siguiendo un procedimiento adaptativo de doble intervalo, doble alternativa, y elección forzosa (Levitt, 1971). Los niveles de la máscara alcanzaron, en ocasiones, el nivel de sonido de salida máximo permitido (105 dB SPL). Si el número de puntos de datos medidos era insuficiente para el ajuste de curvas, se midieron los niveles de máscara para intervalos intermedios adicionales (por ejemplo, 5, 15, 25 ms). En algunos casos, los niveles de máscara fueron atípicamente bajos para un intervalo de tiempo de 100 ms. En estos casos, los niveles de máscara se midieron para intervalos adicionales en el rango de 110-140 ms.

INDICADORES DE LA DISFUNCIÓN MECÁNICA COCLEAR

Se compararon las curvas de E/S coclear para los sujetos hipoacúsicos con las correspondientes curvas de E/S de referencia para los normoyentes, tomadas de estudios previos publicados por nuestro grupo (Lopez-Poveda y Johannesen, 2012) a cinco frecuencias: 0.5, 1, 2, 4 y 6 kHz. A partir de la comparación, se infirieron tres indicadores de disfunción mecánica coclear:

1. Pérdida audiométrica asociada a una pérdida de ganancia mecánica coclear (HL_{CCE}).
2. Pérdida audiométrica asociada a una disfunción de las células ciliadas internas (HL_{CCI}).
3. Exponente de compresión de la membrana basilar (ECMB).

Siguiendo el razonamiento de Moore y Glasberg (1997), supusimos que la pérdida auditiva total se puede dividir en dos aportaciones: una relativa a la reducción de la ganancia mecánica coclear, debida a la disfunción de las CCEs, y otro componente que, por conveniencia, supondremos debido a procesos ineficientes de las células ciliadas internas (CCI), o disfunción de CCIs:

$$HL_{TOTAL} = HL_{CCE} + HL_{CCI}, \quad (1)$$

Donde HL_{TOTAL}, HL_{CCE} y HL_{CCI} están medidos en decibelios. En adelante, nos referiremos a HL_{CCE} y HL_{CCI} como 'pérdida de CCEs' y 'pérdida de CCIs', respectivamente, y deben interpretarse como la contribución funcional de la disfunción de ambos tipos de células a la pérdida auditiva (en dB) en lugar de como lesiones anatómicas o recuentos celulares reducidos.

OTOEMISIONES ACÚSTICAS DE PRODUCTOS DE DISTORSIÓN

Se presentaron pares de tonos puros primarios con frecuencias (f_1, f_2) y sus niveles correspondientes (L_1, L_2) y se registró el nivel de la componente de frecuencia $2f_1-f_2$ de la emisión otoacústica en el conducto auditivo, que fue considerado como el nivel de la OEAPD. Se midieron OEAPDs para f_2 de 0.5, 1, 2 y 4 kHz y para valores de L_2 de 35 a 70 dB SPL, en pasos de 5 dB (4 frecuencias × 8 niveles = 32 condiciones). Para cada frecuencia f_2, f_1 se fijó igual a $f_2/1.2$. Primeramente se realizó un intento para ajustar L_1 de forma individualizada

para maximizar los niveles de OEAPD. Para los valores de L_2 de 50 y 65 dB SPL, buscamos empíricamente el valor de L_1 que maximizara el nivel de OEAPDs, si lo hubiera. Cuando se encontró ese par de valores de L_1, los valores de L_1 para el resto de niveles de L_2 se obtuvieron usando una regresión lineal. Cuando no se encontraron los valores individuales óptimos de L_1, el nivel L_1 se determinó siguiendo la regla de Neely, Johnson y Gorga (2005), ya que se ha confirmado que ésta es la regla más apropiada para maximizar los niveles de OEAPDs en promedio (véase la Figura 7 en Lopez-Poveda y Johannesen, 2009).

ESTÍMULOS Y APARATOS

Para todas las medidas psicoacústicas, los estímulos fueron generados digitalmente (medidas de CET) o almacenados como archivos digitales (medidas de URVs) con una frecuencia de muestreo de 44100 Hz. Se transformaron de formato digital a analógico utilizando una tarjeta de sonido RME Fireface 400 con una resolución de 24 bits y se reprodujeron a través de unos auriculares Sennheiser HD-580. Durante la realización de los experimentos, los sujetos se sentaron en una cabina sono-amortiguada de doble muro.

Los niveles de presión sonora (SPL) se calibraron colocando los auriculares en un maniquí KEMAR equipado con un oído artificial Zwislocki DB-100 conectado a un medidor de nivel sonoro (Bruel y Kjaer, tipo 2238). La calibración se realizó sólamente a 1 kHz, y la sensibilidad obtenida se usó en todas las demás frecuencias.

3. RESULTADOS Y DISCUSIÓN

ESTIMACIONES DE LA CONTRIBUCIÓN DE LA DISFUNCIÓN DE CÉLULAS CILIADAS INTERNAS Y EXTERNAS A LA PÉRDIDA AUDIOMÉTRICA

Un objetivo de la presente tesis es evaluar hasta qué punto la pérdida audiométrica se debe a una reducción en la ganancia mecánica coclear (es decir, a una disfunción de CCEs) y/o a un componente adicional, denominado aquí disfunción de CCIs. Un segundo objetivo es investigar la distribución de frecuencias de las dos contribuciones potenciales. Un tercer objetivo es investigar el grado de variabilidad de las dos contribuciones entre los oyentes. Nuestro enfoque se basó en el análisis de las curvas de E/S coclear inferidas conductualmente, propuestas por Lopez-Poveda y Johannesen (2012).

Con respecto a los objetivos primero y segundo, los resultados basados en el análisis del subconjunto de curvas de E/S con un UC sugieren que, en promedio, la disfunción de CCI y CCE contribuye un 30-40 y 60-70% a la pérdida audiométrica, respectivamente, y que estos porcentajes se mantienen aproximadamente constantes a lo largo del rango de frecuencias entre 500 Hz y 6 kHz (**Figura 6**). Con respecto al tercer objetivo, los resultados sugieren que la proporción de la pérdida audiométrica atribuida a la pérdida de ganancia coclear puede variar ampliamente entre los hipoacúsicos con pérdidas auditivas similares, sin un patrón de frecuencia claro (**Figura 8**). Los casos para los cuales los umbrales audiométricos podían explicarse exclusivamente en términos de una disfunción de CCIs o en términos de pérdida de ganancia coclear (puntos en la región diagonal de la **Figura 7**) fueron comparativamente más numerosos a bajas que a altas frecuencias (**Tabla 4**). Sin embargo, la gran

mayoría de los casos eran consistentes con la disfunción mixta CCE/CCI, incluso aunque en algunos de estos casos era improbable que la pérdida de ganancia coclear contribuyera a la pérdida audiométrica (**Tabla 4**). La pérdida de ganancia coclear total (es decir, curvas lineales de E/S), ocurrió más frecuentemente en frecuencias altas que en frecuencias bajas (**Tabla 4**).

POTENCIALES FUENTES DE SESGO METODOLÓGICO

Sobre la precisión del método CET para la estimación de curvas de E/S

Al inferir las curvas de E/S de las CETs, se ha supuesto que la tasa post-mecánica de recuperación de enmascaramiento anterógrado es independiente de la frecuencia y el nivel de la máscara (Nelson et al., 2001). Sin embargo, existe evidencia de que para los normoyentes la tasa de recuperación es dos veces más rápida para niveles de máscara por debajo de 83 dB SPL que para niveles más altos (Wojtczak y Oxenham, 2009). Este efecto de nivel, sin embargo, no ocurre para los oyentes hipoacúsicos (Wojtczak y Oxenham, 2010). Existe también evidencia de que la tasa de recuperación podría ser más lenta para frecuencias de sonda bajas (≤1 kHz) que altas (Stainsby y Moore, 2006), aunque esta evidencia es polémica (Lopez-Poveda y Alves-Pinto, 2008). Lopez-Poveda y Johannesen (2012) discutieron que si estas suposiciones no se mantenían, las curvas de E/S con un UC conducirían a una mayor HL_{CCI} y una menor HL_{CCE}. En el contexto actual, esto significa que si las suposiciones no eran válidas, la contribución de HL_{CCI} a la pérdida auditiva total podría ser mayor que la indicada en la **Figura 6**.

Sin embargo, según el presente análisis de CETs para los oyentes hipoacúsicos con respuestas de la MB presumiblemente lineales (**Capítulo 4**), podemos concluir que la recuperación del enmascaramiento es independiente de la frecuencia de la sonda y del nivel de máscara, por lo que es razonable utilizar un CET para una alta frecuencia de sonda y una máscara de baja frecuencia como una referencia lineal para inferir la compresión coclear en frecuencias más bajas. En otras palabras, los resultados del presente análisis apoyan las estimaciones de la disfunción mecánica coclear.

Ambigüedad de las curvas de E/S lineales

Se ha supuesto que las curvas de E/S lineales son indicativas de una pérdida total de ganancia coclear. Esta suposición puede ser inexacta en algunas situaciones. Suponiendo que las curvas de E/S cocleares se vuelven lineales a niveles de entrada altos (algo todavía controvertido, Robles y Ruggero, 2001, pág. 1308-1309), para los casos con una disfunción significativa de las CCI, la respuesta coclear mecánica en el umbral de detección de sonda podría ser tan grande con respecto a los normoyentes, que sólo podría ser medido el segmento lineal de alto nivel de la curva E/S (por ejemplo, la Figura 1D de Lopez-Poveda y Johannesen, 2012). Por lo tanto, las curvas lineales de E/S a altos niveles de entrada pueden indicar dos cosas diferentes: la pérdida total de ganancia coclear o la disfunción significativa de las CCIs. No es posible distinguir entre estos dos casos. Por lo tanto, algunos de los casos clasificados como 'pérdida total de ganancia coclear' (o disfunción total de CCEs) pueden en realidad ser debidos a una disfunción significativa de CCIs.

Ganancia coclear para normoyentes y pérdida total de CCEs

Las curvas de E/S lineales se consideraron indicativas de pérdida total de ganancia coclear (**Figura 4** y **Figura 5**). Para estos casos, se estableció HL_{CCE} igual a la ganancia coclear media para un grupo de normoyentes. Si esto hubiera sido inexacto, podría haber afectado las estimaciones de HL_{CCE} (es decir, el número y la posición de cruces azules en la **Figura 7**). La ganancia para el grupo de normoyentes se calculó como se describe en el **Capítulo 3** (sección 'Análisis de curvas de E/S y taxonomía') y se podría argumentar que este método subestimó la ganancia para aquellas curvas de E/S de normoyentes con UC o RLT ausentes, es decir, para curas de E/S que todavía eran compresivas a los niveles de entrada más bajos o más altos en la curva de E/S. Sin embargo, los valores de ganancia de normoyentes en altas frecuencias fueron comparables a los inferidos por otros autores usando diferentes métodos psicoacústicos, así como a los obtenidos de los registros directos de la MB. Por ejemplo, a 4 kHz, la ganancia media fue de 42.7 dB, por lo tanto comparable al valor (43.5 dB) que reportaron Plack et al. (2004). La ganancia empleada aquí como referencia para normoyentes también es comparable con el valor de 35 dB a 6 kHz que se obtendría de las curvas de E/S de la Figura 2 de Oxenham y Plack (1997) que se inferieron usando un método psicoacústico

diferente conocido como crecimiento enmascaramiento anterógrado. Además, los valores de ganancia de normoyentes a 4 kHz se encuentran dentro del rango de valores sugerido por las mediciones directas de la MB (rango = 19-62 dB, mediana = 40 dB, media = 38 dB, tabla 1 de Robles y Ruggero, 2001). En conjunto, esto sugiere que los valores actuales de ganancia a alta frecuencia fueron razonables para normoyentes.

El registro directo de la MB en animales sugiere que la ganancia coclear es menor para las regiones apicales que para las basales, aunque es posible que la diferencia se deba parcialmente al daño de la mecánica coclear apical durante las mediciones experimentales. Por ejemplo, el cambio de la sensibilidad de la MB de la chinchilla para la frecuencia característica entre niveles de entrada bajos y altos es de 10-20 dB a 500-800 Hz frente a 50 dB a 8-9 kHz (Tablas 2, 3 en Robles y Ruggero, 2001). Informes psicoacústicos previos en los seres humanos utilizando otros métodos y suposiciones también sugieren menos ganancia a bajas frecuencias, pero no proporcionan estimaciones cuantitativas (Plack et al., 2008). Las estimaciones de ganancia para el presente grupo de normoyentes fueron de 35.2 dB a 500 Hz y 42.7 dB a 4 kHz. La tendencia de la frecuencia en los resultados actuales es, pues, cualitativamente coherente con las observaciones directas de la MB, y las diferencias cuantitativas podrían deberse a diferencias en los mapas tonotópicos cocleares entre especies. Sin embargo, si la velocidad de recuperación post-mecánica del enmascaramiento anterógrado fuese después de todo más rápida a frecuencias más bajas, entonces la ganancia coclear sería menor que la reportada en este documento y el patrón de resultados sería más consistente con los datos de los animales.

En resumen, los valores de ganancia de normoyentes usados para cuantificar la HL_{CCE} para casos de pérdida total de CCE (curvas lineales de E/S) parecen razonables a altas frecuencias, pero son menos seguros en frecuencias bajas.

Cabe destacar que la ganancia en normoyentes aumentó de 35.2 dB a 500 Hz a 43.5 dB a 1 kHz (*t*-test, $p = 0.014$, muestras no apareadas e igualdad de varianza) y la ganancia se mantuvo constante a frecuencias más altas (42.7 dB a 4 KHz). Este patrón difiere ligeramente de lo reportado por Johannesen y Lopez-Poveda (2008), de donde se tomaron algunos de los datos actuales de normoyentes. De hecho, en ese estudio, la ganancia aumentó gradualmente con frecuencia de 37 dB a 500 Hz a 55 dB a 4 kHz (véase su Figura 11A). Esta

discrepancia se debe, casi con seguridad, a diferencias metodológicas entre los dos estudios. En primer lugar, los dos estudios utilizaron definiciones de ganancia diferentes; Johannesen y Lopez-Poveda (2008) calcularon la ganancia como la diferencia entre el RLT y el UC. En segundo lugar, los datos de normoyentes actuales combinaron datos de los 10 participantes que participaron en el estudio de Johannesen y Lopez-Poveda (2008), además de datos para cinco participantes más de Lopez-Poveda y Johannesen (2009). Este último estudio aportó datos a 0.5 y 1 kHz. En tercer lugar, Johannesen y Lopez-Poveda (2008) ajustaron sus curvas de E/S a un polinomio de tercer orden, que 'fuerza' un RLT cuando existe UC, ya que las pendientes del polinomio de tercer orden son idénticas por debajo y por encima de su punto de inflexión. De hecho, un menor número de curvas de E/S del estudio de Johannesen y Lopez-Poveda (2008) mantuvieron el RLT cuando fueron re-analizados usando nuevo el enfoque de ajuste.

La influencia de la pérdida auditiva conductiva sobre los resultados

Se permitió tuvieran una diferencia entre umbrales audiométricos por vía aérea y vía ósea de hasta ≤15 dB a una frecuencia y/o ≤10 dB en cualquier otra frecuencia. Las pequeñas pérdidas conductivas podrían haber aumentado el umbral absoluto para la sonda empleada para medir las CETs y, por lo tanto, los niveles de las máscaras correspondientes en una cantidad igual a la pérdida conductiva en las frecuencias correspondientes. La influencia en la curva de E/S inferida sería de, un desplazamiento vertical ascendente de la curva E/S igual a la pérdida conductiva en la frecuencia de la sonda de la referencia lineal, y de un desplazamiento horizontal hacia la derecha igual a la pérdida conductiva a la frecuencia de la máscara en la condición en frecuencia. El UC sólo se vería afectado por el desplazamiento horizontal. Por lo tanto, la pérdida conductiva a la frecuencia en particular podría conducir a una sobre-estimación de HL_{CCE} a esa frecuencia. La correlación de Pearson entre HL_{CCE} y la diferencia aérea-ósea fue significativa sólo a 1 kHz e indicó disminución de HL_{CEE} al aumentar la diferencia aérea-ósea. La dirección del efecto fue por lo tanto opuesta al presunto efecto de la pérdida auditiva conductiva en HL_{CCE} y por lo tanto concluimos que la pérdida conductiva es poco probable que afectara las estimaciones HL_{CCE} de la **Figura 6**.

La influencia potencial de las regiones cocleares 'muertas' en los resultados

Una 'región muerta' es "*una zona de la cóclea en la que las CCI y/o las neuronas están funcionando tan mal que un tono que produce vibración máxima de la MB en esa región se detecta a través de una región adyacente donde las CCI y/o neuronas funcionan más eficientemente*" (p. 272 en Moore, 2007). En principio, las regiones muertas podrían afectar a las medidas de las CET ya que la sonda presentada en una región muerta se detectaría en un lugar coclear más alejado del lugar de la sonda: por ejemplo, en un lugar donde la máscara de la CET de la condición en frecuencia podría estar sujeto a un régimen de compresión diferente al del lugar normal de la sonda. Por ejemplo, si la región coclear de 4 kHz estuviera muerta, una sonda de 4 kHz podría estar detectándose con la región coclear de 2 kHz, en la que una máscara de 1.6 kHz, que se consideraría típicamente como una condición de referencia lineal, estaría, en realidad, sujeta a compresión.

Las regiones muertas ocurren casi siempre para pérdidas auditivas por encima de los 60 dB HL (Tabla 1 en Vinay y Moore, 2007). Los participantes del presente estudio fueron seleccionados para tener pérdidas auditivas menores de 80 dB HL para poder medir CETs en el mayor rango de frecuencias posible (**Figura 1**). A pesar de ello, no se pudieron medir CETs para las pérdidas más altas. Del total de 325 curvas de E/S medidas, el número que pueden haber sido afectadas por regiones muertas se puede estimar a partir de los datos de la Tabla 1 de Vinay y Moore (2007) (tenga en cuenta que Vinay y Moore sólo proporcionan datos para 4 kHz y aquí hemos supuesto que la incidencia de las regiones muertas es idéntica a 4 y 6 kHz). Nuestro análisis reveló que la incidencia esperada de las regiones muertas fue de una, dos y dos a las frecuencias de sonda de 2, 4 y 6 kHz, respectivamente. Estos números son tan bajos que es poco probable que hayan sesgado las estimaciones de HL_{CCE} y HL_{CCI}.

Comparación con Estudios Previos

Basado en nuestro análisis de las curvas de E/S con UC, hemos demostrado que HL_{CCE} es en promedio 60-70% de HL_{TOTAL} en el rango de frecuencia de 0.5 a 6 kHz. Este número es más o menos consistente con el reportado por estudios

anteriores para rangos de frecuencia más restringidos, principalmente a 4 kHz (Plack et al., 2004; Lopez-Poveda y Johannesen, 2012). Sin embargo, es ligeramente inferior al valor del 80-90% mostrado en otros estudios basados en modelos de sonoridad (Moore y Glasberg, 1997). Jürgens et al. (2011) mostraron que los dos enfoques (modelo de sonoridad y CETs) deben proporcionar resultados similares. Por lo tanto, la razón de esta diferencia es todavía incierta.

También hemos demostrado que aunque el porcentaje de casos para los cuales HL_{CCI} es igual a HL_{TOTAL} o el porcentaje de casos para los cuales $HL_{CCE} \sim HL_{TOTAL}$ (el porcentaje de disfunción 'pura' de CCE) son pequeños; además, estos porcentajes son mayores para frecuencias ≤1 kHz y disminuyen al aumentar la frecuencia (**Tabla 4**). Hasta donde sabemos, estas tendencias no se han mostrado explícitamente antes, posiblemente debido al menor tamaño de muestra usado en anteriores estudios. Aun así, hay precedentes. De hecho, Moore y Glasberg (1997) estimaron HL_{CCI} usando un modelo de crecimiento de sonoridad y encontraron que aumentaba al disminuir la frecuencia. Asimismo, Jepsen y Dau (2011) reportaron un HL_{CCI} mayor a frecuencias más bajas para algunos sujetos, aunque sus resultados promedio seguían siendo consistentes con la noción común de que el déficit funcional más típico es la pérdida de ganancia mecánica en la base coclear.

Una distinción importante entre los análisis llevados a cabo en el presente estudio y los anteriores es que aquí HL_{CCI} y HL_{CCE} no se han considerado siempre como contribuciones aditivas mutuamente excluyentes a HL_{TOTAL}. Por contra, se ha contemplado la posibilidad de que la Ecuación (1) no sea válida para casos en los que la disfunción de CCI es tan significativa que hace imposible medir un UC. En estos casos, supusimos que HL_{TOTAL} se puede explicar plenamente en términos de HL_{CCI}, aunque todavía es posible que exista una pérdida de ganancia coclear concurrente (véase la parte inferior de la **Figura 7**).

SOBRE LA VALIDEZ DEL MÉTODO DE LAS CET PARA INFERIR LAS CURVAS DE E/S COCLEAR

Un segundo objetivo de la presente tesis fue verificar los supuestos del método psicoacústico de las CET para inferir las curvas de E/S mecánicas cocleares en humanos. Para lograr este objetivo, hemos investigado la velocidad (o tasa) de recuperación de enmascaramiento anterógrado en un subconjunto de ocho oyentes hipoacúsicos cuidadosamente seleccionados en los que sus OEAPDs estuvieran ausentes o casi ausentes sobre un rango de L_2 entre 35 y 70 dB SPL y sobre un rango de f_2 entre 500 y 4000 Hz (**Tabla 5**). Los principales hallazgos fueron:

1. En la mayoría de los casos, la velocidad de recuperación de enmascaramiento anterógrado fue constante a través de frecuencias y niveles; Sin embargo, en algunos casos, la recuperación del enmascaramiento anterógrado disminuyó al aumentar la frecuencia y al aumentar del nivel (**Figura 11** y **Figura 12**).
2. Para aquellos casos en los que la velocidad de recuperación de enmascaramiento anterógrado disminuyó con el aumento de la frecuencia, la recuperación de enmascaramiento anterógrado también disminuyó con el aumento del nivel (**Figura 13**).
3. En promedio, sin embargo, la velocidad de recuperación de enmascaramiento no cambió significativamente en el rango de frecuencias de sonda (500-6000 Hz) o niveles (70-100 dB SPL) probado.
4. Para algunos individuos, la velocidad de recuperación del enmascaramiento medido con una sonda fija de alta frecuencia fue más lenta para las máscaras de baja frecuencia en las CET fuera de frecuencia que para las máscaras de igual-frecuencia, mientras que para otros la recuperación de enmascaramiento fue comparable para las máscaras de igual-frecuencia y fuera de frecuencia (**Figura 15**).
5. En promedio, sin embargo, la velocidad de recuperación del enmascaramiento anterógrado no fue significativamente diferente para ambos tipos de máscaras (igual-frecuencia y fuera de frecuencia).

LIMITACIONES DE LOS PRESENTES DATOS

Suponiendo que la ausencia de OEAPDs para niveles L_2 < 70 dB SPL indica que la respuesta coclear es lineal, los presentes resultados sugieren que la velocidad de recuperación del enmascaramiento anterógrado es independiente de la frecuencia y del nivel sonoro en promedio y para una mayoría de individuos, pero no para todos y cada uno de los individuos. Sin embargo, se podría argumentar que la ausencia de OEAPDs por debajo de 70 dB SPL no implica necesariamente respuestas lineales a los niveles más altos involucrados en las CETs actuales (70-100 dB SPL, **Figura 10**). En otras palabras, se podría argumentar que las CETs actuales podrían estar afectadas por la compresión. No pudimos descartar esta posibilidad experimentalmente porque la distorsión generada por nuestro sistema de medición de OEAPD era demasiado alta a niveles L_2 > 70 dB SPL como para evaluar de forma fiable la presencia o ausencia de OEAPDs generadas por la cóclea en esos niveles. En los primates, sin embargo, la ganancia coclear, definida como la sensibilidad coclear en la FC pre-mortem menos la post-mortem, es de aproximadamente 40 dB a 6.5 a 8 kHz (véase la Tabla 1 de Robles y Ruggero, 2001). El subconjunto de participantes utilizado para verificar las suposiciones del método de CET tenía pérdidas de audición de al menos 40 dB y normalmente mayor en todas las frecuencias testadas (**Figura 11** y **Figura 12**). Por lo tanto, es razonable suponer que las respuestas cocleares fueron lineales para la mayoría de los participantes y para la mayoría de las condiciones.

Por otro lado, cualquier compresión residual produciría CETs anormalmente abruptas (Nelson et al., 2001). La **Figura 17** muestra un histograma de las pendientes de las CETs de la condición de igual-frecuencia para el subconjunto de participantes sin EAOPDs. La figura sugiere claramente dos grupos de CETs: un grupo normalmente distribuido con pendientes ≤0.35 dB/ms y un grupo con pendientes más altas. Es tentador especular que el primer grupo (con pendientes menos pronunciadas) corresponde posiblemente a CETs no afectadas por compresión coclear, mientras que el segundo grupo (con pendientes más pronunciadas) corresponde a las CETs que podrían estar afectadas por la compresión residual. Este último grupo incluye las CETs más pronunciadas para los participantes S054, S116 y S121. Estos tres participantes tenían audiogramas con mucha pendiente; esto decir, mayor pérdida en altas

frecuencias que en las bajas (véanse los paneles a la izquierda de la **Figura 11** y **Figura 12**). Casualmente, S054 y S121 son dos de los tres casos para los cuales las pendientes de las CET disminuyeron al aumentar la frecuencia (S012, S054, y S121). Si los datos actuales se reanalizaran omitiendo las pendientes >0.35 dB/ms, sólo quedaría un caso (S012) para el que la pendiente de las CET seguiría cambiando con la frecuencia o el nivel. Para todos los demás casos, la pendiente de las CET sería aproximadamente constante a lo largo de la frecuencia y del nivel. Por lo tanto, es tentador concluir que la pendiente de las CETs disminuyó al aumentar la frecuencia o el nivel sonoro de algunos de los participantes porque estos participantes tenían compresión residual y que, en ausencia de compresión, la velocidad de recuperación del enmascaramiento anterógrado sería constante para todas las frecuencias y niveles sonoros.

Hemos supuesto que las pendientes de las CETs dependen simultáneamente de compresión de la MB y de la tasa de recuperación del efecto 'interno' de la máscara (es decir, del efecto post-MB) (Nelson et al., 2001). Estudios fisiológicos, psicofísicos y de simulación recientes, han mostrado o sugerido fuentes de no linealidad post-MB. Por ejemplo, se ha demostrado que la vibración de la lámina reticular muestra más compresión que la vibración correspondiente de la MB (Chen et al., 2011), lo que indica que el movimiento de la célula ciliada interna (CCI) no está directamente acoplado al movimiento MB como se suele pensar (Guinan, 2012). Además, Lopez-Poveda et al. (2005) observaron que las pendientes de las CETs de referencia son más bajas para algunas personas hipoacúsicas que para las normoyentes y argumentaron que esto podría deberse a la compresión inespecífica de frecuencia en las CCIs que está presente en los normoyentes pero reducida o ausente en los oyentes hipoacúsicos. Esta idea de que las no linealidades de las CCIs podrían estar incrementando la pendiente de las CET ha sido avalada posteriormente por simulaciones de modelos de potenciales de CCI (Lopez-Poveda y Eustaquio-Martin, 2006) y por otros estudios psicoacústicos (Plack y Arifianto, 2010). Esta evidencia sugiere que, además de la compresión de MB, la pendiente de una CET también puede verse afectada (acentuada) por la compresión añadida por la lámina reticular o la CCI. En el presente contexto, esto implica que incluso si las presentes CETs no se vieron afectadas por la compresión de la MB, todavía podrían verse afectadas por la compresión post-MB. En ese caso, el

presente análisis seguiría siendo correcto si la compresión post-MB fuese comparable en todas las condiciones mostradas aquí, algo incierto.

Por supuesto, el método de las CETs fue específicamente diseñado para inferir compresión en la MB. Debido a que consiste en la comparación de las pendientes de dos CET medidas con diferentes frecuencias y que no hay evidencia (que sepamos) de que la compresión post-MB sea diferente para diferentes frecuencia, cualquier efecto de una posible compresión post-MB sobre las CETs sería cancelado en la comparación y, por lo tanto, el método CET todavía resultaría útil al propósito para el que fue diseñado.

RELACIÓN CON ESTUDIOS PREVIOS

Utilizando un enfoque similar al aquí empleado, Stainsby y Moore (2006) concluyeron que la velocidad de recuperación del enmascaramiento anterógrado disminuye al aumentar la frecuencia. El presente estudio utiliza una muestra de sujetos más grande (N=8 frente a N=3), seleccionados con criterios más rigurosos de OEAPD y un análisis diferente. Los resultados de nuestro análisis sugieren que la tendencia reportada por Stainsby y Moore podría deberse a que, al contrario de lo que supusieron y a pesar de sus esfuerzos, sus participantes sí tenían compresión residual a bajas frecuencias.

IMPLICACIONES DE ESTIMAR LA COMPRESIÓN A PARTIR DE CETS

Al inferir la compresión coclear periférica a partir de las CETs, hemos supuesto que la tasa post-mecánica (es decir, 'libre de compresión') de la recuperación del efecto enmascarador es independiente de la frecuencia de la sonda y del nivel de la máscara (Lopez-Poveda et al., 2003; Nelson et al., 2001). En promedio, los presentes datos apoyan estos supuestos. Esto no quiere decir, sin embargo, que los supuestos se cumplan en todos y cada uno de los individuos. Los efectos eferentes pueden afectar a la recuperación del enmascaramiento anterógrado tanto en las personas normoyentes como en las hipoacúsicas con función residual de las CCEs (Jennings, Strickland y Heinz, 2009; Wojtczak y Oxenham, 2010; Yasin et al., 2013). Por lo tanto, que la recuperación post-mecánica del enmascaramiento anterógrado sea independiente de la frecuencia y del nivel para personas sin compresión coclear mecánica no implica que las estimaciones de compresión inferidas con el método CET estándar sean

exactas. Wojtczak y Oxenham (2009) demostraron que para personas normoyentes, la recuperación del enmascaramiento anterógrado es más lenta para niveles por encima de 83 dB SPL. Es decir, Wojtczak y Oxenham mostraron que el método de CET puede sobreestimar la compresión aproximadamente en un factor de dos cuando las CETs de referencia contienen niveles por encima de 83 dB SPL (es decir, en esos casos, el exponente de compresión real podría ser la mitad del valor inferido). Wojtczak y Oxenham argumentaron que esto era posiblemente debido a que las máscaras activan el MEMR.

Los presentes resultados sugieren que algo similar puede ocurrir también para las personas hipoacúsicas. Las CETs de referencia tenían pendientes menos pronunciadas que las CETs de en frecuencia medidas con la misma frecuencia de sonda (**Figura 15**). Una explicación de este resultado podría ser que, a pesar de nuestras precauciones, el subconjunto de participantes utilizados en nuestro análisis todavía tenía compresión residual en frecuencias altas a pesar de nuestros esfuerzos para utilizar participantes con respuestas cocleares lineales. Por otro lado, las CETs de referencia para los participantes siempre implicaron valores superiores a entre 90 y 95 dB SPL, que son comparables con los umbrales de activación de MEMR de los participantes (véase la **Tabla 2**). De hecho, el umbral de activación real del MEMR puede ser de entre 8 y 14 dB más bajo que el estimado con métodos clínicos similares a los empleados aquí (Feeney, Keefe y Marryott, 2003; Neumann, Uppenkamp y Kollmeier, 1996). El MEMR puede ser provocado por sonidos con una duración de 116 ms (Keefe, Fitzpatrick, Liu, Sanford, y Gorga, 2010), que es aproximadamente la mitad de la duración de las máscaras empleadas para medir las CETs. El MEMR dificulta la transmisión de frecuencias entre 300 y 1000 Hz y no tiene un efecto significativo en la transmisión de frecuencias superiores a 2000 Hz, pero facilita la transmisión de frecuencias entre 1000 y 2000 Hz. Las máscaras usadas para medir las CETs de referencia eran suficientemente largas como para activar el MEMR durante el transcurso del enmascaramiento y el rango de frecuencias (800-2000 Hz) se encontraba dentro del rango del efecto facilitador de MEMR. Por lo tanto, es concebible que el MEMR facilite la transmisión de la máscara de la condición de referencia, reduciendo de este modo el nivel de la máscara en el umbral de enmascaramiento de la sonda. El MEMR tendría un efecto mucho menor para las correspondientes CETs de

igual-frecuencia porque las frecuencias de la máscara implicadas eran mayores que 2000 kHz, donde el efecto MEMR es insignificante. Por lo tanto, una explicación alternativa para las pendientes más planas de las CETs de referencia podría ser que la recuperación del enmascaramiento anterógrado depende del nivel del enmascarador posiblemente debido a la activación del MEMR. Si esta última explicación fuera correcta, los datos de la **Figura 15** indicarían que la compresión deducida de comparar las pendientes de las CETs de igual-frecuencia y de referencia podría parecer el doble de la compresión real para aquellos oyentes hipoacúsicos cuyas CETs de referencia impliquen niveles de máscara por encima del umbral individual de activación del MEMR.

LA INFLUENCIA DE LA DISFUNCIÓN MECÁNICA COCLEAR EN LA INTELIGIBILIDAD DEL HABLA EN RUIDO

El objetivo principal de la presente tesis fue evaluar la importancia relativa de la disfunción mecánica coclear sobre la capacidad de los oyentes hipoacúsicos para entender el habla (supraliminar o amplificada) en dos ruidos de fondo diferentes SSN (URV_{SSN}) y R2TM (URV_{R2TM}). En relación con este objetivo, los principales resultados encontrados fueron:

1. Para la presente muestra de oyentes hipoacúsicos, la edad, el audiométrico de tonos puros (UATPs) y la compresión coclear residual (cuantificado por el exponente de compresión de la MB, o ECMB) prácticamente no se correlacionaron entre sí (**Tabla 7**) y, sin embargo, fueron predictores significativos de URVs en entornos ruidosos (**Tabla 8**).
2. El ECMB fue el predictor más importante del URV_{SSN}, mientras que el UATPs fue el predictor más importante de URV_{R2TM} (**Figura 16** y **Tabla 8**).
3. La pérdida de ganancia mecánica coclear (HL_{CCE}) se correlacionó con URV_{SSN} y URV_{R2TM} (**Tabla 7**), pero no mejoró los modelos de Regresión Lineal Múltiple (MLR) del URV_{SSN} o del URV_{R2TM} una vez que los predictores anteriormente mencionados se incluyeron en los modelos.
4. La edad también fue un predictor significativo de URV_{SSN} y URV_{R2TM}, y fue prácticamente independiente de ECMB (**Tabla 7**).

La ausencia de una correlación entre la edad y el UATP en la presente muestra de oyentes hipoacúsicos fue sorprendente, dada la conocida relación entre esas dos variables (revisado por Gordon-Salant, Frisina, Popper, y Fay, 2010). Una posible explicación es que exigimos que los participantes fueran candidatos a audífonos (requisito necesario para un aspecto del estudio no reportado aquí) y que, a la vez, tuvieran pérdidas auditivas de leve a moderada en el rango de frecuencia de 0.5 a 6 kHz, algo necesario para inferir la HL_{CCE} utilizando métodos psicoacústicos de enmascaramiento. Por lo tanto, es posible que sus pérdidas auditivas abarcasen un rango más estrecho de lo que se observaría en nuestra misma franja de edad en una muestra verdaderamente aleatoria.

El hallazgo de que el UATP y el ECMB se correlacionaran con la inteligibilidad del habla en el ruido era esperable (**Tabla 7**). Sin embargo, un aspecto significativo, aunque incidental, de nuestros datos es que estos factores no estaban correlacionados o apenas correlacionaban entre sí (**Tabla 7**) y, sin embargo, todos ellos afectaron a la inteligibilidad en diferente proporción para los dos tipos de ruidos enmascaradores (**Tabla 8**).

De los dos indicadores utilizados para caracterizar la disfunción mecánica coclear, la pérdida de ganancia coclear (HL_{CCE}) se correlacionó con la inteligibilidad del habla en los dos tipos de ruido empleados (SSN y R2TM), mientras que la compresión residual (ECMB) se correlacionó sólo con la inteligibilidad del habla en SSN. Los dos indicadores (HL_{CCE} y ECMB) se correlacionaron entre sí (**Tabla 7**). Sin embargo, HL_{CCE} no se mantuvo como predictor significativo de inteligibilidad para ninguno de los dos ruidos cuando se incluyeron otras variables en el modelo estadístico de regresión lineal múltiple. Por otro lado, el ECMB fue el predictor más significativo de inteligibilidad en ruido SSN (**Tabla 8**). Ciertamente, nuestras estimaciones de HL_{CCE} y ECMB son indirectas y se basan en numerosos supuestos. Sin embargo, suponiendo que estas estimaciones son razonables, los presentes hallazgos sugieren que la pérdida de ganancia mecánica coclear (HL_{CCE}) y la compresión residual (ECMB) no son predictores equivalentes del impacto de la disfunción mecánica coclear en la inteligibilidad en SSN. Nuestros hallazgos sugieren, además, que la compresión residual podría ser más significativa que la pérdida de ganancia coclear, tal vez porque el impacto de HL_{CCE} sobre la inteligibilidad

puede compensarse con amplificación lineal mientras que el impacto de ECMB puede que no lo sea.

Nuestro hallazgo sobre la importancia de la compresión coclear para la inteligibilidad en SSN parece inconsistente con los resultados de otros estudios. Por ejemplo, Noordhoek, Houtgast y Festen (2001) encontraron poca influencia de la compresión residual sobre la inteligibilidad del habla de banda estrecha centrada en 1 kHz. Asimismo, Summers, Makashay, Theodoroff y Leek (2013) mostraron que la compresión no estaba claramente asociada con la comprensión del habla intensa (a un nivel fijo de 92 dB SPL) en ruido estacionario. Esta inconsistencia puede deberse, al menos en parte, a las diferencias metodológicas entre los estudios. En primer lugar, Summers et al. evaluaron la inteligibilidad utilizando el porcentaje de frases reconocidas correctamente para una RSR fija en lugar del URV (en dB RSR). En segundo lugar, y quizás lo más importante, aunque Summers et al. infirieron la compresión a partir de las CETs, como hicimos nosotros, no adoptaron precauciones importantes para inferir la compresión con exactitud mediante el método de las CETs. Como se explica en la Introducción, el método de las CETs se basa en la suposición de que la compresión coclear se puede deducir comparando las pendientes de las CETs que no están afectadas por compresión (referencias lineales) con las de las CETs afectadas por compresión. Summers et al. utilizaron diferentes CETs de referencia lineal para diferentes frecuencias de sonda y sus referencias lineales fueron CETs para una frecuencia de máscara igual a 0.55 veces la frecuencia de la sonda. Se ha demostrado que esto, casi con toda certeza, subestima la compresión, particularmente a frecuencias más bajas (véase, por ejemplo, Lopez-Poveda y Alves-Pinto, 2008; Lopez-Poveda, Plack, y Meddis, 2003). Como resultado, es casi seguro que Summers et al. subestimaron la compresión, especialmente para sus normoyentes, algo que pudo contribuir a ocultar diferencias de compresión entre oyentes con distingos umbrales audiométricos.

Para nuestra muestra de oyentes hipoacúsicos, el ECMB fue el predictor más significativo de la inteligibilidad del habla en SSN, mientras que el UATP fue el predictor más significativo de la inteligibilidad en R2TM (**Tabla 8**). Hopkins y Moore (2011) investigaron los efectos de la edad y la pérdida auditiva coclear sobre la sensibilidad a la estructura temporal fina (TFS), la selectividad frecuencial y la percepción del habla en ruido para una muestra de

normoyentes e hipoacúsicos. Mostraron que, una vez descartado el umbral absoluto (al menos, parcialmente), la sensibilidad a la TFS era el único predictor significativo de la inteligibilidad del habla en ruido modulado en amplitud, mientras que el ancho de banda del filtro auditivo era el único predictor significativo de inteligibilidad en ruido estacionario SSN. Aunque no se muestra aquí, la capacidad de nuestros participantes para procesar los aspectos temporales del sonido fue el predictor más significativo de inteligibilidad en un ruido tipo R2TM (véase Johannesen et al., 2014). Los presentes resultados combinados con los de Johannesen et al. (2014) parecen coherentes con los de Hopkins y Moore, considerando que el ancho de banda del filtro auditivo es un correlato psicoacústico de la selectividad de la frecuencia coclear (Evans, 2001; Shera, Guinan y Oxenham, 2002) y, por tanto, un indicador de disfunción coclear.

Por supuesto, la compresión periférica (ECMB) y el ancho de banda del filtro auditivo son indicadores psicoacústicos indirectos y diferentes de la disfunción coclear pero aun así están relacionados. Se ha demostrado mediante técnicas psicoacústicas que el ancho de banda del filtro auditivo aumenta a medida que disminuye la compresión coclear (Moore, Vickers, Plack, y Oxenham, 1999). Por otro lado, estudios fisiológicos han demostrado que la disfunción de las CCE reduce la selectividad frecuencial y la compresión mecánica de la cóclea (Ruggero et al., 1996). A la luz de esta evidencia, es tentador pensar que la relación entre la compresión (ECMB) y la inteligibilidad en SSN se deba a que la inteligibilidad empeora al aumentar la interacción espectral de las señales del habla y del ruido debido al aumento del ancho de banda de los filtros auditivos (Moore, 2007). Sin embargo, resulta desconcertante, que el mismo mecanismo no esté al menos ligeramente involucrado en la inteligibilidad del habla en ruido modulado (Hopkins y Moore, 2011) o del tipo R2TM.

El hallazgo de que la edad fue un predictor significativo de inteligibilidad tras descontar los efectos de ECMB en URV_{SSN} y de UATP en URV_{R2TM}, sugiere que la edad *per se* afecta a la inteligibilidad del habla en el ruido. Este resultado es consistente con el de Füllgrabe, Moore y Stone (2015), quienes demostraron que para ancianos y jóvenes emparejados por audiometría, la edad empeoraba significativamente la inteligibilidad en varios tipos de ruidos, incluso después

tenido en cuenta el efecto de la edad sobre la sensibilidad para detectar cambios en la estructura temporal fina de los sonidos.

CONCLUSIONES

1. Para oyentes hipoacúsicos con curvas de entrada/salida cocleares que muestran un umbral de compresión, la disfunción de las células ciliadas internas y externas contribuye, en promedio, en un 30-40 y un 60-70% a la pérdida auditiva total, respectivamente, y estas contribuciones son aproximadamente constantes en el rango de frecuencias de 0,5 a 6 kHz.
2. No obstante, la variabilidad individual de ambas contribuciones es grande, particularmente a bajas frecuencias y para pérdidas auditivas de leves a moderadas.
3. La gran mayoría de los oyentes con deficiencia auditiva sufren de disfunción mixta de células ciliadas internas y de células ciliadas externas, aunque en casos con una disfunción sustancial de las células ciliadas internas, cualquier disfunción concurrente de las células ciliadas externas no contribuye a la pérdida auditiva.
4. El porcentaje de casos en los que la pérdida auditiva puede ser explicada exclusivamente bien en términos de pérdida de ganancia coclear, o bien de procesos ineficaces de células ciliadas internas (es decir, el porcentaje de casos con disfunción exclusiva de células ciliadas externas o internas, respectivamente), es mayor a frecuencias ≤1 kHz y disminuye gradualmente al aumentar la frecuencia.
5. El porcentaje de casos que sufren pérdida total de ganancia coclear (es decir, casos que muestran curvas de entrada/salida cocleares lineales) aumenta gradualmente al aumentar la frecuencia.
6. De acuerdo con el análisis de las curvas de enmascaramiento temporal para los oyentes con pérdida auditiva con respuestas de membrana basilar presuntamente lineales, concluimos que la velocidad de recuperación del enmascaramiento anterógrado es independiente de la

frecuencia del tono sonda y del nivel de la máscara, por lo que es razonable utilizar una referencia lineal en el método de las curvas de enmascaramiento temporal para tonos sonda de alta frecuencia para inferir la compresión coclear a frecuencias más bajas.

7. La referencia lineal de las curvas de enmascaramiento temporal pueden ser a veces más planas que las correspondientes curvas de enmascaramiento temporal de frecuencia para frecuencias de sonda idénticas. La razón es incierta. Podría ocurrir cuando la máscara usada para medir la curva de enmascaramiento temporal de referencia es de suficiente duración e intensidad para activar el reflejo acústico del oído medio. Cualquiera que sea la razón, la compresión de la membrana basilar podría sobreestimarse en estos casos hasta en un factor de dos.
8. La disfunción estimada de las células ciliadas externas (pérdida de la ganancia coclear) no está relacionada con la capacidad de comprender el habla audible en ambientes de ruido estacionario.
9. La compresión coclear residual se relaciona con la comprensión del habla en un ruido estacionario, pero no en un ruido fluctuantes de dos hablantes (invertido en el tiempo).
10. La edad *per se* reduce la inteligibilidad del habla, independientemente de los umbrales absolutos o de la disfunción coclear mecánica.