Journal of the
American Academy of Audiology

Hearing Characteristics of Stroke Patients: Prevalence and Characteristics of Hearing Impairment and Auditory Processing Disorders in Stroke Patients

Journal:	*Journal of the American Academy of Audiology*
Manuscript ID	15-139.R1
Manuscript Type:	Research Article
Date Submitted by the Author:	29-Jul-2016
Complete List of Authors:	Koohi, Nehzat; National Hospital for Neurology and Neurosurgery, Neuro-otology; University College London, The Ear Institute Vickers, Doborah; University College London, The Ear Institute Lakshmanan, Rahul; National Hospital for Neurology and Neurosurgery Chandrashekar, Hoskote; University College London, Institute of Neurology Werring, David; University College London, Institute of Neurology Warren, Jason; University College London, The Institute of Neurology Bamiou, Doris; National Hospital for Neurology and Neurosurgery, Neuro-otology; University College London, The Ear Institute
Keywords:	Auditory processing disorder, Stroke, Hearing impairment, Auditory rehabilitation

Title Page

Date of submission: 29/07/2016

Title: Hearing Characteristics of Stroke Patients: Prevalence and Characteristics of Hearing Impairment and Auditory Processing Disorders in Stroke Patients

Authors: Koohi N[1,2]; Vickers DA[2]; Lakshmanan R[1]; Chandrashekar H[3]; Werring D[3]; Warren J[3], Bamiou DE[1,2]

Institutional affiliations: [1]National Hospital for Neurology and Neurosurgery; [2] UCL Ear Institute, University College London; [3]The Institute of Neurology, University College London

Author address:

4th Floor, Queen Mary Wing

National Hospital for Neurology and Neurosurgery

Queen Square

London

WC1N 3NB

Email: Nehzat.koohi.11@ucl.ac.uk

Financial support: BMA Helen Lawson Grant (British Medical Association) Grant number: 4276892

Background: Stroke survivors may suffer from a range of hearing impairments that may restrict their participation in the post-acute rehabilitation programs. Hearing impairment may have a significant impact on listening, linguistic skills and overall communication of the affected stroke patient. However, no studies sought to systematically characterize auditory function of stroke patients in detail, in order to establish the different types of hearing impairments in this cohort of patients. Such information would be clinically useful in understanding and addressing the hearing needs of stroke survivors.

Purpose: The present study aimed to characterize and classify the hearing impairments, using a detailed audiological assessment test battery, in order to determine the level of clinical need and inform appropriate rehabilitation for this patient population.

Research Design: A case-control study.

Study Sample: Forty-two recruited stroke subjects who were discharged from a stroke unit and 40 control subjects matched for age.

Data Collection and Analysis: All subjects underwent pure-tone audiometry, immitance measurements including acoustic reflex threshold, transient evoked otoacoustic emissions, auditory evoked brainstem response, and a central auditory processing assessment battery, performed in a single session. Hearing impairments were classified as peripheral hearing loss (cochlear and neural type), central auditory processing disorder (CAPD) and as combination of CAPD and peripheral hearing loss.

Results: Overall mean hearing thresholds were not significantly different between the control and stroke groups. The most common type of hearing impairment in stroke subjects was the combination type, “peripheral and CAPD” in the 61–80-years-old subgroup (in 55%), and

auditory processing deficits in the 18–60 year olds (in 40%), which were both significantly higher than in controls.

Conclusions: This is the first study to examine hearing function in detail in stroke patients. Given the importance of hearing for the efficiency of communication, it is essential to identify hearing impairments and differentiate peripheral and central deficits in order to define an appropriate intervention plan.

Key Words: stroke, hearing impairment, auditory processing, rehabilitation

Abbreviations: ABR= auditory-evoked brainstem response; HFA= high-frequency average; NICE=The National Institute for Health and Clinical Excellence; GIN=gaps-in-noise; PTA=pure-tone audiometry; TEOAES=transient evoked otoacoustic emissions; SNHL=sensorineural hearing loss; MRI=magnetic resonance imaging; BSA=British Society of Audiology; TYMP=tympanogram; ART=acoustic reflex thresholds; CAPD=central auditory processing disorder; ASHA=American Speech-Language-Hearing Association Working Group

1 Background

The majority of stroke survivors need rehabilitation (MacDonald et al, 2000), requiring them to be adequately informed of the nature, prognosis, and proposed treatment of their illness. Hearing-impaired stroke survivors have an increased risk of physical decline [odds ratio: 1.83] after discharge to the community (Landi et al, 2006). This may be attributed to restricted participation in post-acute rehabilitation programs due to the hearing impairment (Landi et al, 2006). In addition, it is well known that uncorrected hearing loss may lead to isolation, reduced social activity and reduced quality of life for the hearing impaired and their families (Arlinger, 2003). Stroke can affect all levels of the auditory system (from the inner ear to central tracts), and may result in various types of auditory dysfunctions, such as peripheral hearing loss (cochlea to auditory nerve), disordered auditory processing (brainstem to cortex) and cortical deafness. Some of these presentations such as cortical deafness are rare but quite dramatic and would not go undetected. Other presentations however may be subtler and only be detected by detailed questioning of the patient and by precise psychoacoustic and electrophysiological testing, however, they may still have a significant impact on listening, linguistic skills and overall communication of the affected patient (Hausler and Levine, 2000; Bamiou et al, 2012; Onoue et al, 2014).

Sensorineural hearing loss (SNHL) is highly prevalent in stroke survivors (Formby et al, 1987; Edwards et al, 2006; O'Halloran et al, 2009). Such peripheral type hearing loss may be due to the pathology of the inner ear (Lee, 2012), the auditory nerve, or even the early part of the cochlear nuclei, i.e. the part of the central auditory pathway before the crossing of the auditory fibres at the superior olivary complex brainstem level (Luxon, 1980). Furthermore, stroke-related risk

factors, such as cigarette smoking and atherosclerosis, which have been associated with a more insidious onset of hearing impairment with advancing age (Yamasoba et al, 2013), may directly affect the peripheral hearing organs, or the stroke event itself may damage the auditory pathway up to and including the low brainstem (Lee et al, 2009) thus giving rise to the observed SNHL. Formby et al (1987) assessed hearing in stroke patients between two weeks and one-month post-onset of stroke and reported hearing loss in 61.7% of these patients. Two subsequent longitudinal population-based Australian studies indicated that a past history of stroke increases the likelihood of having hearing loss. Kiely et al (2012) studied 3,526 adults aged 50 years or older and found that a previous history of stroke predicted hearing thresholds, while Gopinath et al (2012) reported that the odds risk of reporting stroke was significantly higher for those with moderate-to-severe hearing loss. The observed association between hearing loss and stroke could be attributed to age-related changes of the inner ear or the auditory nerve (Jacquin et al, 2012), as the risk of both hearing loss and cardiovascular accidents (CVA) increases with age (Hung et al, 2011).

Altogether, the findings from aforementioned studies suggest that the prevalence of hearing impairment in stroke survivors could be higher than hearing impairment that would be expected in the general population. However, none of the few previous studies sought to systematically characterize auditory function of stroke patients in detail, in order to establish the different types of hearing impairments in this cohort of patients. It is well established that if the stroke involves the central auditory pathway in the brain, from the brainstem and beyond, patients may also suffer from auditory processing deficits that are not reflected by their pure-tone hearing thresholds (Bamiou et al, 2006, 2012). Whilst there are a few studies looking

at the auditory processing of highly selected stroke cohorts (e.g. Bamiou et al, 2006; Rey et al, 2007; Bamiou et al, 2012), to date no study has sought to establish the prevalence of auditory processing deficits in the broader stroke population, in the presence or absence of peripheral hearing impairment. Such information would be clinically useful in understanding and addressing the hearing needs of stroke survivors, so that appropriate management can be given to these patients in order to improve their quality of life.

The present study examined hearing in detail and characterized the different types of hearing impairment in stroke patients in a systematic observational case-control study with the ultimate aim to inform a better taxonomy of hearing impairment in stroke patients.

2 Purpose

The aim of the present study was:

1. To assess hearing impairment in detail in stroke patients, in the post-stroke subacute stage, by means of a detailed baseline auditory battery (pure-tone audiometry, acoustic immitance tests, auditory-evoked brainstem responses and transient evoked otoacoustic emissions), and a detailed non-verbal auditory processing battery including the gaps-in-noise test (GIN), i.e. a sensitive test of auditory temporal resolution (Musiek et al, 2005) and the Queen Square Tests of Auditory Cognition (QSTAC) that consists of perceptual spectral property processing, apperceptive processing and semantic processing tests (Goll et al, 2010), and compare to individuals without stroke.
2. To characterize the different types of hearing impairment (peripheral i.e. cochlear and/or neural, and central i.e. arising due to pathology beyond the nerve, or a combination of peripheral and central) in the stroke group in order to identify the prevalence of all types of hearing impairment in this cohort.
3. To examine the prevalence and correlates of different hearing impairments in stroke patients in comparison to those of age-matched controls. On the basis of previous research, it was expected that the type of hearing impairment would be different in the stroke group compared to individuals without stroke.

3 Research Design

3.1 Ethics Approval

The Ethics Committee of the National Hospital for Neurology and Neurosurgery (London) approved the Hearing Evaluation and Auditory Rehabilitation after Stroke (HEARS) study (Project Identification number 11/0469 and REC ref 11/LO/1675). We obtained written informed consent from all the participants.

3.2 Study Design

This case-control study incorporated a stroke group and a control group that were matched for age. All subjects underwent a thorough audiological assessment performed in a single session. Test results were explained to the participants and a report with test results and recommendations for further audiological management, to be taken up by the local services, were provided for every participant tested.

3.3 Inclusion and Exclusion Criteria

The inclusion criteria were: **a.** adults aged between 18 and 80 years old **b.** clinical history of a single stroke verified by magnetic resonance imaging (MRI) of the brain. Exclusion criteria were severe aphasia, cognitive impairment (as shown on the Montreal Cognitive Assessment), significant psychiatric illnesses, other neurological disorders (except stroke) and severe concurrent medical illnesses.

3.4 Participants

3.4.1 Group 1: Stroke Patients

Sixty-five consecutive stroke patients (see the CONSORT flow chart in figure 1) who met the study inclusion criteria recruited from the National Hospital for Neurology and Neurosurgery [NHNN] stroke unit and hyper-acute stroke unit [HASU] at University College London Hospitals [UCLH]. Of these 65, a final fifty stroke patients were recruited. The patients were tested at the department of Neuro-otology, NHNN Queen Square, within three to twelve months post-onset stroke, since at this stage of the stroke, auditory processing deficits if present are likely to become long term (Rey et al 2007).

3.4.2 Group 2: Control Subjects

Forty control subjects were recruited from the hospital staff, colleagues, hospital visitors and friends. The inclusion criteria were: adults aged between 18 and 80 years old, and no history of neurological disorders, stroke, psychiatric disease or cognitive impairment as reported by the volunteers during the initial medical interview.

Figure 1 to be inserted here

Figure 1 The consort diagram showing the flow of participants through the study. KEYS: SRN, stroke research network team; PTA, pure-tone audiometry; TYMP, tympanometry; ART, acoustic reflex threshold; TEOAES, transient evoked optoacoustic emissions; ABR, auditory-evoked brainstem responses; GIN, gaps in noise.

3.5 Assessment

3.5.1 Background Assessment

Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) (Nasreddine et al, 2005) includes sections on visuospatial/executive function (alternating trail-making, cube copy, clock drawing), naming (lion, rhinoceros, camel), attention (forward and backward digit span, tapping to the letter A, subtracting 7s from 100), language (sentence repetition, letter fluency), abstraction (similarities between train and bicycle, watch and ruler), memory (delayed verbal recall of 5 words) and orientation to time and place (6 questions). A qualified neuropsychologist or a stroke specialist nurse (blind to the study) administered the MoCA in the acute stage. If a mild or greater cognitive impairment was detected the test was re-administered 3 months after the stroke in the UCLH stroke follow-up clinic (routine UCLH procedure). The stroke research network (SRN) team only referred those with no impairment or mild cognitive impairment i.e. MoCA< 25 (Pendlebury et al, 2012).

Brain Imaging Acquisition

All participants had a brain MRI performed on a 1.5 Tesla GE Signa scanner (General Electric, Milwaukee, WI) 48 hours after the stroke. The acquisition techniques included diffusion weighted imaging and T1- weighted three-dimensional fast low-angle-shot images for volumetric and morphometric analyses. The scan acquisition parameters for the volumetric T1 weighted imaging were: repetition time = 15 ms; echo time = 5.4 ms; flip angle = 15; inversion time = 650 ms. All scans were reviewed by a consultant stroke neurologist (DW) and a consultant neuro-radiologist (CH) in order to identify and categorize stroke-related structural brain abnormalities.

3.5.2 Baseline Audiological Assessments

We collected information about the patients' hearing status. After otoscopy, wax was removed, if present in the patient's external ear canal, by syringing or microsuction. Patients were then tested in a sound-treated booth with the following test procedures:

Pure-Tone Audiometry

Pure-tone audiometry (PTA) was carried out using a GSI 61 audiometer with TDH-39 headphones (Grason-Stadler, Guymark Uk Limited, Veronica House West Midlands UK). Air-conduction thresholds were measured for each ear at 0.25, 0.5, 1, 2, 4, 6 and 8 kHz following the procedure recommended by the British Society of Audiology [BSA] (2011). Results were averaged in each ear across 0.5, 1, 2, 4, and 8 kHz frequencies for the "PTA average" and at 4, 6, and 8 kHz for the "high-frequency average" (HFA). Normal hearing thresholds were considered < 20 dB across the above frequency range [recommended by the BSA (2011)]. The degree of hearing loss was then classified as mild (20–40 dB HL), moderate (41–70 dB HL), severe (71–95 dB HL), and profound (>95 dB HL) [recommended by the BSA (2011)].

Tympanometry

A tympanogram (TYMP) was obtained with a continuous probe-signal 226-Hz tone at 85 dB sound pressure level using a GSI 33 Middle Ear Analyzer (Grason-Stadler Inc, Milford, New Hampshire). The TYMP results were considered normal if middle-ear pressure was -150 mm H2O or greater and compliance was greater than 0.3 cm.

During otoscopy, tympanosclerosis was detected in three of the stroke patients (all had a history of ear infection) and tympanograms showed high compliance in at least one ear. However, we found no conductive hearing loss in any of the stroke patients with abnormal tympanograms. Only one of the healthy control subjects had an abnormal tympanogram (type

c, negative pressure); this subject had a cold at the time of testing, but no conductive loss was found in the hearing test.

[Stapedial] Acoustic Reflexes Thresholds

The acoustic reflex is the acoustically evoked contraction of the stapedius muscle. The ipsilateral and contralateral acoustic reflex thresholds (ART) were measured on the GSI 33 Middle Ear Analyzer at 0.5, 1, 2, and 4 kHz at levels ranging from 70 dB HL up to a maximum of 120 dB HL, in 5 dB steps, to assess middle-ear, cochlear, VIIIth- nerve, lower brainstem functions. A consistent change in compliance of the middle ear ≥ 0.03ml following stimulation is the criterion for the presence of the acoustic reflex. Acoustic reflexes were considered as abnormal if they exceed 105 dB nHL at two or more adjacent frequencies, or if the interaural threshold difference exceeded 10 dB on at least two adjacent frequencies (Cohen and Prasher, 1988). The patterns interpreted as indicating a brainstem lesion were the "vertical" (abnormal ART by stimulation of one ear only), "horizontal" (ART abnormal by contralateral stimulation of both ears), "inverted-L" (combined vertical and horizontal) and "full house" [all ipsilateral and contralateral reflexes abnormal] (Cohen and Prasher, 1988).

Transient Evoked Otoacoustic Emissions

Transient evoked otoacoustic emissions (TEOAESs) analyse the function of the outer hair cells. Click stimuli are delivered through a probe in the ear canal. The inner ear responses to the click stimuli are recorded automatically. A dual channel analyser was utilised. A linear click at 80 (+/- 3) dB SPL intensity, with 260 averages, was used for ipsilateral stimulation. The repetition rate is 50/s and the post-stimulus recording time is 20 ms. The fast fourier transform (FFT) spectrum analysis and average waveform calculations were performed automatically by the ILO v6 Otodynamic Analyser system. Normal response was considered the finding of overall TEOAESs amplitude >12 dB or amplitude of ≥6 dB in at least three adjacent frequency bands.

Auditory-evoked Brainstem Responses

Auditory-evoked brainstem responses (ABR) are sensitive to brainstem auditory nuclei and tract function abnormalities and thus useful in evaluating undetected damage to the auditory system (Pillion et al, 2008; Jiang et al, 2010).

The ABR were recorded with the Nicolet Spirit 4 channel equipment (Nicolet, Madison, Wisconsin). Electrodes were placed on the forehead (A) and on each mastoid (A1 and A2); the A electrode was used as the ground. Monaural alternating click stimuli of 100 microseconds were presented at a rate of 11.1/second via headphones. Electrode impedance was less than 5 kOhms. The electrical activity was amplified and filtered (range, 100–3000 Hz). A total of 1000 stimuli were given, with a mean window of 10 milliseconds. A standard minimum intensity of 90 dB was used, provided that clear waveforms with waves I, III, and V were observed; 100 dB nHL was used in those with hearing loss. Analysis of ABR was restricted to waves I, III, and V. Waveform morphology, peak latency, and interwave latency and compared with normative departmental data. Peak I broadly corresponds to the distal portion of the VIIIth nerve, peak III to the superior olivary complex, and wave V to the termination of lateral lemniscus axons at the inferior colliculus (Möller, 1998). Subjects were categorized as normal if no deficits in either ear were detected or if absolute latencies were delayed with normal interwave intervals when an audiometric hearing loss was present (Musiek et al, 1996), and abnormal otherwise. The ABR were recorded only in subjects with up to moderate hearing loss (at 2 and 4KHz frequencies).

3.5.3 Selection of Non-verbal Auditory Processing Assessments

Cognitive and language impairments are common after stroke (Tatemichi et al, 1994; Sinanovic et al, 2011), and the presence of such conditions may potentially affect the behavioural auditory processing test battery (Gates et al, 2010). Auditory processing tests in general should include both non-verbal and verbal stimuli to examine different aspects of

auditory processing (e.g., AAA 2010; BSA 2011). However, performance on speech based behavioural tests is heavily influenced by linguistic factors, and cognition (Loo et al, 2013; Gates et al, 2010). The present study thus opted to utilise a non-verbal auditory processing test battery that would place minimal demands upon language, working memory and attention of the stroke patients. Temporal resolution is important to speech perception, and its assessment provides insight into the neural integrity of the central auditory nervous system [CANS] (Gordon-Salant and Fitzgibbons, 1993; Walton et al, 1997). Gaps-in-noise (GIN) is a test of temporal resolution that has a known high sensitivity and specificity to central auditory nervous system (Musiek et al, 2005). The GIN employs non-verbal stimuli and a non-verbal response mode. Goll et al (2010) proposed that the main processing stages of non-verbal auditory cognition could be conceptualised as the early perceptual, apperceptive and semantic levels and developed the Queen Square Tests of Auditory Cognition (QSTC) auditory processing battery.

The QSTAC comprises of individual sound categorisation and sequential comparison tasks that were specifically designed in order to minimise cognitive and linguistic demands on the patient. This battery has been utilized in patients with cognitive disorders (Goll et al, 2010). This test battery probes spectral property processing, apperceptive processing that refers to the perceptual representation of whole "auditory objects" (Nelken & Bar-Yosef, 2008), and semantic auditory processing that refers to the association of stored knowledge (i.e. semantic memory) with the perceptual (apperceptive) object representations (Goll et al., 2010).

.

Gaps-in-Noise

Gaps-in-noise (GIN) provides an estimate of threshold (shortest gap identified), a total percentage correct responses score and an estimate of attention levels (% accuracy at different gap duration levels) (Musiek et al, 2005). The GIN test compact disk was played on a Sony CD player and passed through the GSI 61 diagnostic audiometer. After calibration, the stimuli were presented at 50 dB sensation level re: 1 kHz threshold to each ear independently (Musiek et al, 2005). The GIN is composed of a series of 6-sec segments of broadband noise containing 0–3 silent intervals or gaps per noise segment. The interstimulus interval between successive noise tokens (segments) is 5 seconds and the gap durations presented are 2, 3, 4, 5, 6, 8, 10, 12, 15, and 20 msec. Five practice items preceded the administration of the test items (Musiek et al, 2005).

Perceptual Property Processing

Perceptual property processing involves the cortical analysis of perceptual spectral properties, which contribute to, but are unlikely in isolation to constitute, whole auditory object representations. The patient has to make a judgement of same or different for each of thirty-two same (sixteen) or different (sixteen) spectral shape sounds pairs (Goll et al, 2010).

Apperceptive Processing

The key experimental manipulation here is Spectral Inversion (SI), which flips or exchanges the energy present between higher and lower frequencies in a broadband sound about a user-specified frequency value to create a frequency structure that is 'impossible' in a natural sound (Goll et al, 2010). For this test, forty sounds (twenty non-SI and twenty SI sounds) are presented individually, and for each sound, the participant was asked: 'Is it a real thing or not a real thing?'.

Semantic Processing

Assessments were designed to examine the association of conceptual meaning with environmental sound objects (Goll et al, 2010). Thirty-two individual sounds from a range of human, animal and environmental sounds are paired so that the individual sounds in a pair have dissimilar acoustic characteristics to reduce the availability of perceptual matching cues. All 32 sounds appear once in the 'same' condition (sounds produced by the same source e.g., horse neighing, horse galloping) and once in the 'different' condition (sounds produced by different sources e.g., horse neighing, human coughing).

3.5.4 Patient grouping

Age Groups

Defining a "significant" level of hearing impairment as at least 25 dBHL averaged over the frequencies 0.5, 1, 2, 4 kHz, 16% of the adult population (17–80 years) have a bilateral, and about one in four a unilateral or bilateral, hearing impairment (Davis, 1989). The increase in prevalence of hearing loss is particularly steep after the age of 61 and older. Sixty percent of adults age 61-80 years old in England have hearing impairment of 25 dBHL or greater, whilst the prevalence of hearing impairment in adults, age 18-60 years is only 10% (Davis, 1989). Thus, to minimise the confounding factor of age, we divided the patients into two groups; younger (18-60 years old) and older (61-80 years old).

Audiological Assessment Outcomes

For the purpose of this paper, according to the outcomes of the audiological assessment, each patient was placed into one of four groups (ASHA 2015): 1) Normal 2) Peripheral hearing loss (cochlea to auditory nerve) 3) Central auditory processing disorder (brainstem to cortex and beyond) (ASHA 2015; BSA 2011) 4) combination (peripheral hearing loss and central auditory processing disorder). Below we describe the definition and diagnostic criteria for each category.

- ***Definition of Peripheral Hearing Impairment and Diagnostic Criteria***

Threshold assessment was made at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz and a pure-tone average was calculated. The severity of hearing loss was determined using the British Society of Audiology (BSA) audiometric descriptors (BSA, 2011). Also, high-frequency hearing loss was defined as the air conduction average of frequencies 4, 6, and 8 kHz exceeding 20 dB HL. Mild hearing loss was defined as PTA ≥20 dB HL and ≤40 dB HL, moderate (41–70 dB HL), severe (71–95 dB HL), and profound (>95 dB HL).

The peripheral hearing loss (attributed to pathology in the middle ear, cochlear and/or the distal portion of auditory nerve) was defined as: a) "cochlear type" hearing loss: abnormal PTA average, reduced or absent TEOAESs, present and normal acoustic reflexes and normal ABR or normal interwave interval ABR (Musiek et al, 1996); b) "neural type" hearing loss, i.e. consistent with VIII nerve damage (Starr et al., 1996): normal or raised PTA average, normal TEOAESs, or delayed I–III or I–V interwave interval or absent wave I (showing the damage to the distal portion of auditory nerve) (Musiek et al, 1996) and/or abnormal ART with inverted or vertical pattern (Cohen & Prasher, 1988).

- **Definition of Central Auditory Processing Disorder and Diagnostic Criteria**

According to the technical report of the American Speech-Language-Hearing Association (ASHA) Working Group (2005), deficits in the perceptual processing of auditory information in the Central Nervous System (CNS) and the neurobiological activity that underlies that processing and gives rise to electro-physiological auditory potentials constitute a central auditory processing disorder (CAPD). This was the definition adopted by this study.

A CAPD diagnosis was based on the presence of at least two central auditory nervous system test abnormalities i.e. ABR, ART and GIN, QSTAC (spectral property and apperceptive tests)

in at least one ear, with at least 1 test abnormality being in a behavioural AP test and with the following additional considerations:

i. The electrophysiological test abnormality was not attributable to the presence of hearing loss (see ABR and ART criteria)

ii. A semantic processing abnormality (QSTAC) when found in isolation was not accepted as evidence of disordered auditory processing

- **Definition of Combination Hearing Impairment (Peripheral Hearing Loss and Central Auditory Processing Disorder) Diagnostic Criteria**

For the purpose of this paper, if central auditory processing deficits and/or isolated brainstem type ABR and ART test abnormality was detected in the presence of peripheral hearing loss, we defined the pattern as a combination (peripheral and central) type auditory impairment.

3.6 Data Analysis

Data were initially analyzed using the Statistical Package for the Social Science SPSS 22.0 for descriptive analysis. T-tests or Kruskal-Wallis rank sum Test (for non-normally distributed data) were used to examine differences between the stroke and control groups in continuous variables. Univariate analyses non parametric chi square tests were carried out to examine whether there is any association between the results of a particular hearing test and the stroke status of the participants (with and without age group classification). Prior to conducting the chi-squared analysis, the assumption of adequate cell size was assessed, which requires all cells to have expected values greater than zero and 80% of cells to have expected values of at least five. If the assumptions were not met a Fisher's exact test was used. Logistic regression models were fitted to the binary hearing test results to examine the effects of age (as a dichotomous variable) and stroke status on the outcome of the test. The null

hypothesis that there was no significant difference in distribution across the two groups was rejected when the level of significance of $p<0.05$ was reached.

Multinomial logistic regression models were fitted to the data with the categorical variable “type of hearing" as the dependent variable. Type of hearing could be either “CAPD”, “Normal”, “Peripheral” or both “Peripheral and CAPD”. Group (Stroke/ Control) and age (either as dichotomous or continuous) were the included explanatory variables.

4 Results

The total number of participants in our study from 2012 to 2015 was 90 (50 stroke and 40 controls). Three patients were unable to complete the CAPD test battery due to a hearing loss greater than a moderate degree, and five had cognitive impairment. These patients were excluded and a final 42 out of 50 were selected to determine the difference in abnormality distribution in different audiological tests and the prevalence of different types of hearing impairment in the stroke cohort.

In the final 42 selected stroke patients with complete Audiological testing, the age ranged from 23 to 80 years old, with an average of 58.19 years old (*SD* = 15.06). The most frequently observed category of the age group was older group (*n* = 22, 54%) with the mean age of 70 (SD= 5.4), and the average age of the younger group was 45.4 (SD = 10.6). The most frequently observed category of sex in the stroke group was male, (*n* = 33, 78%). The demographic data on these patients are presented in table 1. The age of the control group ranged from 22 to 80 years old, with an average of 53.08 years old (SD= 15.33). The most frequently observed category of sex in the control group was female, (*n* = 26, 65%). Age was not normally distributed in both stroke and control groups. A Kruskal-Wallis rank sum test was conducted to examine whether there was a significant difference between the age of the stroke patients and controls. The results of the Kruskal-Wallis rank sum test were not significant, $\chi2(1) = 511.5$, $p = .172$. This indicates that the age differences between stroke patients and controls are explainable by random variation. The results of the Kruskal-Wallis test also did not show a significant difference between the age of younger stroke and control groups, $\chi2(1) = 0.34$, $p = .560$, as well as the older stroke and control groups, $\chi2(1) = 0.37$, $p = .545$.

Table 1 to be inserted here

Table 1 Frequencies and percentages for age-groups, auditory vs. non-auditory, sex and side of lesion in the stroke group

4.1 Pure-Tone Audiometry, ART, TEOAES, ABR and CAPD

Figure 2 provides the mean hearing thresholds across frequency categories in the stroke group versus control. Overall mean thresholds for the stroke group were more elevated compared to normal control but there was no statistically significant difference between the control and stroke.

Figure 2 to be inserted here

Figure 2 Hearing thresholds in 42 stroke patients and 40 controls. Results for right and left air conduction are plotted against frequency. KEYS: PTA, pure-tone audiometry; dB, decibel; HL, hearing level. Colour code: red, right ear; blue, left ear

The difference in abnormality distribution (normal, abnormal) in different audiological tests in stroke vs. the control group were analyzed using non-parametric tests. Table 2 shows the distribution of individuals with and without impairment in both stroke and control group.

To eliminate the confounding factor of age, we also divided the age into two subgroups; age group 1 (18–60 years) and age group 2 (61–80 years).

Table 2 to be inserted here

Table 2 Distribution of individuals with and without audiological test abnormalities in the stroke and control groups. KEYS: PTA, pure-tone audiometry; ART, acoustic reflex threshold; TEOAES, transient evoked otoacoustic emissions; ABR, auditory-evoked brainstem responses; GIN, gaps-in-noise; PP, perceptual property processing; AP, apperceptive processing; SP, semantic processing

4.2 Summary of Auditory Impairment Diagnosis

The type of hearing impairment was determined using the criteria described in the methodology section. Summary of the hearing impairment diagnosis in the stroke group are shown in table 3.

Table 3 to be inserted here

Table 3 Age, sex, type of hearing impairment and summary of test results in the stroke group. KEYS: M, male; F, female; Rt, right; Lt, left; CAPD, central auditory processing disorders; PTA, pure-tone audiometry; ART, acoustic reflex threshold, TEOAES, transient evoked otoacoustic emissions; ABR, auditory-evoked brainstem responses; CAP, central auditory processing assessment. + signifies an impairment.

4.3 Types of Hearing Impairment

The most common type of hearing loss in stroke patients was the combination ("peripheral hearing loss and CAPD") in the 61–80-year-old subgroup, and "CAPD" in the 18–60-year-olds. Table 4 summarizes the types of hearing impairment in stroke and controls in both age subgroups. Regardless of type, the percentage of hearing impairment was significantly higher in the 18–60-year-old stroke group than in the controls.

Types of hearing impairment as a function of age group and the side of stroke are shown in figure 3 and 4 respectively.

Figures 3 and 4 to be inserted here

Figure 3 Types of hearing impairment as a function of age group. KEY: CAPD, central auditory processing disorders

Figure 4 Types of hearing impairment as a function of side of lesion. KEY: CAPD, central auditory processing disorders

Table 4 to be inserted about here

Table 4: Type of hearing loss in stroke and controls. Number of patients with different types of hearing impairment.

A multinomial logistic regression is appropriate when the outcome is a polytomous variable. Thus, this model was fitted to the data to model the effect of study group and age group on the probabilities of being "Normal", "CAPD", "Peripheral" or "Peripheral and CAPD". The response (dependent variable) is the type of hearing, which takes the values "Normal", "CAPD", "Peripheral", "Peripheral and CAPD". There are two study groups; stroke patients and controls. The participants are classified into 2 age groups; younger group

(< 61 years old) and older group (≥ 61 years old). Study group and age group are dichotomous variables.

Two models were calculated where "Normal" or "Peripheral" type of hearing were the reference categories for the outcome, while the control group and younger age group (<61 years old) are the reference categories for the independent variables. The overall models were significant ($\chi^2(6) = 64.46$, p-value < 0.001), suggesting that the study group and age group had a significant effect on the odds of observing at least one response category of type of hearing relative to Normal or peripheral hearing.

Stroke is associated with an increase in the relative probability of having "CAPD", and "Peripheral and CAPD" (combination) over "Peripheral" hearing impairment. Older stroke patients were more likely to have combination hearing impairment rather than peripheral hearing loss when compared to the control group and the probability of having a "CAPD" impairment is on average 22% higher for stroke patients than for healthy controls in the same age group. The probability of having "Peripheral and CAPD" hearing impairment is on average 21% higher for older participants than for younger participants in the stroke group (see supplementary material for both coefficient and relative risk estimates).

5 Discussion

5.1 Audiometric Characteristics in Stroke Patients

To our knowledge, this is the first study to examine types of hearing impairment, using detailed audiological assessments, in stroke patients. Although overall mean thresholds (PTA average and HF average) for the stroke group were more elevated compared to healthy controls, there was no statistically significant difference between the control and stroke groups in the overall group and when divided into two age subgroups (18–60 and 61–80-year-olds). In all frequencies, there was no significant difference in pure-tone thresholds between the age subgroup of subjects in the stroke patients and controls. We found that 67% of our older group had a pure-tone average of more than 25 dB HL, very similar to the results of Formby's study (1987). The proportion of our stroke samples with a hearing loss greater than 25 dB HL was also very similar to that in the Davis's UK population study (1989), who found that 61.5% of 61–80-year-olds had a hearing loss of 25 dB or more (mean PTA thresholds). These initial results suggest that the abnormality rate in PTA average in the UK stroke units is similar and comparable to that found among elderly persons in nursing homes (Schow et al, 1980), stroke units in Australia (O'Halloran et al, 2009) and USA (Formby et al, 1987).

Auditory brainstem lesions often damage one or both of the crossed reflex pathways (Jerger and Jerger, 1974), and auditory impairment due to brainstem stroke is well documented in the literature (Jerger and Jerger, 1974; Luxon et al, 1980; Musiek and Pinheiro, 1987; Aharonson et al, 1998; Lee et al, 2002). Abnormal ART is reported in lesions of the auditory nerve, cochlear nuclei and superior olivary complex (Hausler and Levine, 2000; Lee et al, 2002). Only two stroke patients with abnormal ART (patient numbers 17 and 26) had abnormalities on the brainstem auditory pathways (ART patterns were consistent

with intra-axial brainstem pathologies). Overall, the percentage of pathological acoustic reflexes in our cohort were not significantly exceeded that of the age- matched control subjects.

The origin of hearing loss was further investigated by recording TEOAESs. There was no statistically significant difference between the TEOAESs results of stroke patients and the age- -matched controls in both older and younger groups.

Hearing abnormalities in isolated stroke lesions of the auditory brainstem are well documented in the literature (Johnson, 1977; Starr et al, 1996; Hausler and Levine, 2000; Lee et al, 2002; Lee et al, 2008; Pennings et al, 2011) and abnormal ABR have been found in lesions affecting the eighth nerve, medulla (cochlear nuclei), pons (superior olivary complex, trapezoid body, lateral lemniscus) and midbrain (inferior colliculus). Sinanović (2008) analyzed ABR abnormalities in patients with brainstem stroke and reported that 83% of their patients had abnormal ABR. In the present study, we found that 8 (19%) of all our patients had abnormal ABR latencies as compared to 2% of the control subjects. Four of these patients with abnormal ABR had a brainstem stroke. Out of a total of 5 brainstem stroke patients in our sample, i.e. 80% of the brainstem stroke patients had abnormal ABR, similar to Sinanović (2008) findings. The remaining brainstem stroke patient with normal ABR had an upper brainstem stroke lesion in the ventral lateral medulla, which would not be expected to affect the ABR. Four patients with abnormal ABR had cortical lesions, the abnormality in ABR possibly reflecting effects of microvascular ischemia (Mills and Ryals 1985). The difference in normal vs. abnormal ABR in stroke patients vs. controls was significant, however there was no statistically significant difference when the older and younger stroke groups were compared to the same groups in control subjects.

There was a statistically significant difference between the GIN results of stroke patients and the age- -matched controls in both older and younger groups. We found that 74% of our cohort had abnormal unilateral or bilateral GIN. The MRI showed abnormalities in the central auditory pathways in 48% of these but in the remaining 26% non-auditory areas were affected, while two of these had severe small vessel disease. A GIN abnormality could be attributable to specific isolated brain lesions, small vessel disease or simply could be the result of advancing age (Bamiou et al, 2000; Bamiou et al, 2006; John et al, 2012). Strouse et al (1998) found that there are age-related differences in temporal processing. Older listeners, without SNHL, were found to have higher gap detection thresholds (GDTs), which would appear to be an indication of an aging effect in the central auditory systems. A recent study by John et al (2012) provides evidence of significant deleterious effects of advancing age on GIN test performance. Since our study is a cross-sectional study, and we included patients with up to a moderate hearing loss, it is not possible to identify precisely the cause of abnormality on the GIN test performance.

We also found a statistically significant difference between the QSTAC results of stroke patients and the age- -matched controls in both older and younger groups. Results of the non-verbal psychoacoustic battery in the context of their brain lesion will discussed in a separate paper.

5.2 Types of Hearing Impairment and Disordered Auditory Processing in Stroke Patients

Aging is accompanied by a decline in hearing sensitivity due to sensory changes in the ear. Other changes in the central auditory nervous system may contribute to the difficulty for the older adults to understand speech in background noise. Pathological conditions such as stroke can further compromise auditory function. There are many factors that should be

considered for the management of stroke patients with peripheral and central auditory dysfunction. Thus, it is essential to differentiate peripheral and central deficits for the evaluation and rehabilitation of stroke patients. Furthermore, auditory processing disorders and perceptual deficits in stroke patients are less well studied and possibly underdocumented (Polster and Rose, 1998). Patients will not necessarily report such deficits, in their less severe forms, unless they are explicitly questioned (Blaettner et al, 1989; Bamiou et al, 2012). Thus, the prevalence of auditory processing deficit among the wider stroke population is not established. To our knowledge, this is the first study to investigate the prevalence of non-verbal auditory processing deficits in the stroke population, on the basis of a non-verbal auditory psychoacoustic battery (GIN, PP, AP, SP), an electrophysiological test that is sensitive to temporal processing, brainstem abnormalities (ABR) and an electroacoustic test that is sensitive to low brainstem lesions (ART), and to investigate the type of hearing loss in the stroke population. Although the proportion of people with peripheral hearing loss did not significantly differ from the healthy control group, our results indicate that the most common type of hearing impairment in our stroke patients was the combination of peripheral and central hearing impairment in the 61–80-year-olds subgroup (55%), and disordered auditory processing in the 18–60-year-olds (40%), which were both significantly higher than controls. This is of particular significance as none of the younger group with AP deficits were referred for audiological assessments after the onset of stroke. They did not complain of any "hearing problems," which were only identified with the hearing questionnaires that were particularly looking into difficulty hearing speech in background noise and localizing sounds (the results of hearing questionnaires in this patient group will be discussed in a separate paper). Temporal and perceptual property processing are important to speech perception (Gordon–Salant and Fitzgibbons, 1993; Walton et al, 1997), in keeping with a high number of self-reported hearing symptoms of the stroke patients on the Amsterdam inventory for auditory

disability (AIAD) questionnaire (Bamiou et al, 2012). Identification of GIN or other central-type deficits in stroke patients would thus require appropriate management in order to help stroke survivors to cope with the challenges they face during and after recovery period, and to help them to participate as fully as possible in intellectual, social, and family activities.

5.3 Implications for Practice

Our study demonstrates that hearing impairment of any types was present in the majority of stroke patients (86%), none of whom had been previously referred for a hearing assessment. This would suggest that hearing impairment remains a "hidden" disability in this population, which may be overlooked by the neurologists and other healthcare professionals. The current National Institute for Health and Care Excellence (NICE) guidelines (2013) on stroke rehabilitation provide advice on cognitive functions, sensory functions (vision), digestive system function, movement-related functions, communication (speech), mobility, and domestic life. Strategies for identification and management of auditory dysfunction, however, receive significantly less attention, with auditory rehabilitation post-stroke arguably being the "lost dimension" of stroke rehabilitation. Our study findings would suggest that current guidance would benefit from the addition of a hearing assessment, or increasing awareness of possible hearing impairment in stroke patients as such impairment may affect the patients' post-stroke physical outcome and may impact on patient communication in everyday life in the chronic stage of stroke (Bamiou et al, 2012). Conventional hearing aids may be a suitable option for those with peripheral hearing loss, while counselling, directional microphone hearing aids with built-in FM, educating the patients and caregivers may be an appropriate rehabilitation plan to meet the need of older stroke patients with a mixed peripheral and central hearing loss.

Hearing loss is associated with cognitive decline and dementia in older adults (Lin and Yaffe, 2013) and the presence of peripheral hearing loss may lead to an unjustified diagnosis of cognitive impairment (Jorgensen, 2012). There is evidence to suggest that evaluation of peripheral and central auditory function may be important in cases of suspected dementia or other cognitive disorders in older adults (e.g. Gates et al, 1996, 2002, 2008, 2011; Jorgensen, 2012). Because the presence of sensory or perceptual deficit can result in "upstream" effects on memory and related cognitive abilities due to insufficient processing resources (Pichora-Fuller et al, 1995; McCoy et al, 2005), it is critical that audiologists are a part of the multidisciplinary team together with neuro-psychologists, speech therapists, neurologists, and other professionals in the evaluation of stroke patients, in an effort to disentangle the relative effects of peripheral and central auditory dysfunction from higher-level cognitive, language, and other deficits.

Finally, the level of background noise in acute/rehabilitation stroke units is worth noting. Difficulty hearing speech in noise is a common disability experienced by stroke patients with hearing impairment (Bamiou et al, 2012) and therefore it would seem imperative to minimize the level of background noise in hospitals and rehabilitation units in which many patients have hearing impairment.

5.4 Limitations and Future Research

This was a cross-sectional study, and it is challenging to identify precisely the cause of hearing impairment in this population. We used transient evoked otoacoustic emissions rather than distortion product otoacoustic emissions and it is possible subtle cochlear deficits may have been missed. Also, this study has the limitations of small numbers in the older group of controls, exclusion of patients with more than one stroke, those with a greater than moderate

hearing loss and those over 80 years old, and not retesting the changes in hearing thresholds and auditory processing deficits after 12 months. Taking these caveats into account, the evidence presented here should motivate future work in larger patient and control cohorts and the retesting of the patients after 12 months to monitor any auditory changes. Furthermore, the difference in the hearing thresholds might have reached statistical significance with a larger sample size. Finally, structural and functional neuroimaging will be required to be performed at least 24 hours prior to the audiological assessments to correlate AP deficits with patterns of network-specific infarction in stroke patients.

Offering a comprehensive audiological assessment to all stroke patients would be a costly and time-consuming process. Therefore, a preliminary screening program for such patients needs to be identified, e.g. by means of a questionnaire, so that the full audiological assessment could be reserved for those who fail the initial hearing screening.

6 Conclusion

Given the importance of hearing for the efficiency of communication, and to prevent cognitive decline and social isolation, we conclude that audiological evaluation in the stroke population is indispensable as part of the rehabilitation of this population. It is essential to identify hearing loss and differentiate peripheral and central deficits for the evaluation and rehabilitation of stroke patients so that an effective intervention for this population can be reached.

7 References

- Aharonson V, Furst M, Levine RA. (1998) Lateralization and binaural discrimination of patients with pontine lesions. *The Journal of the Acoustical Society of America* 103:2624-33.

- Arlinger S. (2003) Negative consequences of uncorrected hearing loss--a review. *International journal of audiology* 42 Suppl 2:2S17-20.

- American Speech-Language-Hearing Association, 2005. Technical report - (Central) auditory processing disorders. Available at: http://www.asha.org/policy/tr2005-00043.htm Accessed on 07/26/2016

- American Speech Language Hearing Association - ASHA (2015) Type, degree and Configuration of Hearing Loss. Audiology Information Series 10802. Available at:: http://www.asha.org/uploadedFiles/AIS-Hearing-Loss-Types-Degree-Configuration.pdf#search=%22classification%22 Accessed on 07/26/2016

- Bamiou D-E, Liasis A, Boyd S. (2000) Central auditory processing disorder as the presenting manifestation of subtle brain pathology. Audiology. 39:168-72.

- Bamiou D-E, Musiek FE, Stow I. (2006) Auditory temporal processing deficits in patients with insular stroke. *Neurology* 67:614-9.

- Bamiou D-E, Werring D, Cox K. (2012) Patient-Reported Auditory Functions After Stroke of the Central Auditory Pathway. *Stroke; a journal of cerebral circulation* 43:1285-89.

- Blaettner U, Scherg M, Voncramon D. (1989) Diagnosis of unilateral telencephalic hearing disorders *Brain : a journal of neurology* 112:177-95.

- British Society of Audiology, 2011. *Interim position statement on APD*. Available at http://www.thebsa.org.uk/wpcontent/uploads/2014/04/BSA_APD_PositionPaper_31March11_FINAL.pdf [Assessed 5 May 2015]

- Cohen M, Prasher D. (1988) ABR and ART in neuro-otological diagnosis. Scand Audiol 17: 153-162.

- Davis AC. (1989) The prevalence of hearing impairment and reported hearing disability among adults in Great Britain. *Int J Epidemiol* 18:911-7.

- Edwards DF, Hahn MG, Baum CM. (2006) Screening patients with stroke for rehabilitation needs: validation of the post-stroke rehabilitation guidelines. *Neurorehabilitation and neural repair* 20:42-8.

- Formby C, Phillips DE, Thomas RG. (1987) Hearing loss among stroke patients. *Ear and hearing* 8:326-32.

- Gates GA, Anderson ML, Feeney MP. (2008) Central auditory dysfunction in older persons with memory impairment or Alzheimer dementia. *Arch Otolaryngol Head Neck Surg* 134:771-7.

- Gates GA, Anderson ML, McCurry SM. (2011) Central auditory dysfunction as a harbinger of Alzheimer dementia. *Arch Otolaryngol Head Neck Surg* 137:390-5.

- Gates GA, Beiser A, Rees TS. (2002) Central auditory dysfunction may precede the onset of clinical dementia in people with probable Alzheimer's disease. *J Am Geriatr Soc* 50:482-8.

- Gates GA, Cobb JL, Linn RT. (1996) Central auditory dysfunction, cognitive dysfunction, and dementia in older people. *Arch Otolaryngol Head Neck Surg* 122:161-7.

- Gates GA, Gibbons LE, McCurry SM. (2010) Executive dysfunction and presbycusis in older persons with and without memory loss and dementia. *Cogn Behav Neurol* 23:218-23.

- Goll JC, Crutch SJ, Loo JH. 2010. Non-verbal sound processing in the primary progressive aphasias. Brain. 133: 272-285.

- Gopinath B, Hickson L, Schneider J. (2012). Hearing-impaired adults are at increased risk of experiencing emotional distress and social engagement restrictions five years later. *Age Ageing* 41:618-23.

- Gordon-Salant S, Fitzgibbons PJ. (1993) Temporal factors and speech recognition performance in young and elderly listeners. *J Speech Hear Res* 36:1276-85.

- Griffiths TD, Bamiou D-E, and Warren JD. (2010) *The Oxford Handbook of Auditory Science: The Auditory Brain*. pp 509-535. Oxford University Press.

- Hausler R, Levine RA. 2000. Auditory dysfunction in stroke. *Acta Oto-Laryngologica* 120:689-703.

- Hung WW, Ross JS, Boockvar KS. (2011) Recent trends in chronic disease, impairment and disability among older adults in the United States. *BMC Geriatr* 11:47.

- Hurley RM, Musiek FE. Effectiveness of tranbsient-evoked otoacoustic emissions (TEOAESs) in predicting hearing level1 (1994). *J Am Acad Audiol* 5:195-203.

- Jacquin A, Hervieu-Begue M, Daubail B. (2012) Epidemiology of stroke in the elderly : "the silver tsunami". *La Revue du praticien* 62:1221-4.

- Jerger J, Jerger S. (1974) Auditory findings in brain stem disorders. *Arch Otolaryngol* 99:342-50.

- Jiang ZD, Wilkinson AR. (2010) Relationship between brainstem auditory function during the neonatal period and depressed Apgar score. *J Matern Fetal Neonatal Med* 23:973-9.

- John AB, Hall JW, Kreisman BM. (2012) Effects of advancing age and hearing loss on gaps-in-noise test performance. *Am J Audiol* 21:242-50.

- Johnson EW. (1977) Auditory test results in 500 cases of acoustic neuroma. *Arch Otolaryngol* 103:152-8.
- Jorgensen, L (2012). The Potential Impact of Undiagnosed Hearing Loss on the Diagnosis of Dementia (Doctoral dissertation). Retrieved from http://d-scholarship.pitt.edu/.
- Kiely KM, Gopinath B, Mitchell P. (2012) Cognitive, health, and sociodemographic predictors of longitudinal decline in hearing acuity among older adults. *J Gerontol A Biol Sci Med Sci* 67:997-1003.
- Landi F, Onder G, Cesari M. (2006) Functional decline in frail community-dwelling stroke patients. *European journal of neurology : the official journal of the European Federation of Neurological Societies* 13:17-23.
- Lee H, Sohn SI, Cho YW. 2006. Sudden deafness associated with infarction in the territory of the non-anterior inferior cerebellar artery. *J. Neurol.* 253:136-9.
- Lee H, Sohn SI, Jung DK. (2002) Sudden deafness and anterior inferior cerebellar artery infarction. *Stroke; a journal of cerebral circulation* 33:2807-12.
- Lee H, Yi HA. (2008). Sudden deafness related to posterior circulation infarction in the territory of the non-anterior inferior cerebellar artery: frequency, origin and vascular topographical pattern. *Eur. J. Neurol.* 15:380-86.
- Lee H. (2009). Neuro-Otological Aspects of Cerebellar Stroke Syndrome. *J. Clin. Neurol.* 5:65-73.
- Lee H. (2012) Audiovestibular loss in anterior inferior cerebellar artery territory infarction: a window to early detection? *Journal of the neurological sciences* 313:153-9.
- Lin FR, Yaffe K, Xia J. (2013) Hearing loss and cognitive decline in older adults. *JAMA Intern Med* 173:293-9.
- Loo JH, Bamiou DE, Rosen S. (2013) The impacts of language background and language-related disorders in auditory processing assessment. *J Speech Lang Hear Res* 56:1-12.
- Lucertini M, Moleti A, Sisto R. (2002). On the detection of early cochlear damage by otoacoustic emissions analysis. *The Journal of the Acoustical Society of America* 111:972-8.
- Luxon LM. (1980) Hearing loss in brainstem disorders. *Journal of neurology, neurosurgery, and psychiatry* 43:510-5.
- MacDonald BK, Cockerell OC, Sander JW. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain : a journal of neurology. 2000;123 (Pt 4):665-76.

- McCoy SL, Tun PA, Cox LC. (2005). Hearing loss and perceptual effort: downstream effects on older adults' memory for speech. *Q J Exp Psychol A* 58:22-33.
- Mills JA, Ryals BM. (1985) The effects of reduced cerebrovascular circulation on the auditory brain stem response (ABR). *Ear Hear* 6:139-43.
- Möller AR. Neural generators of auditory evoked potentials. (1998) Semin Hear 19:11-27.
- Musiek FE, McCormick CA, Hurley RM (1996) Hit and false alarm rates of selected ABR indices in differentiating cochlear disorders from acoustic tumours. Am J Audiol 5:90-96.
- Musiek FE, Pinheiro ML. (1987) Frequency patterns in cochlear, brainstem, and cerebral lesions. *Audiology* 26:79-88.
- Musiek FE, Shinn JB, Jirsa R. (2005) GIN (Gaps-In-Noise) test performance in subjects with confirmed central auditory nervous system involvement. *Ear Hear* 26:608-18.
- Nasreddine ZS, Phillips NA, Bédirian V. (2005) The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 53:695–9.
- Naufal PM, Schuknecht HF. (1972) Vestibular, facial, and oculomotor neuropathy in diabetes mellitus. *Arch Otolaryngol* 96:468-74.
- Nelken I, Bar-Yosef O. (2008) Neurons and objects: the case of auditory cortex. *Front Neurosci* 2:107-13.
- O'Halloran R, Worrall LE, Hickson L. (2009) The number of patients with communication related impairments in acute hospital stroke units. *International journal of speech-language pathology* 11:438-49.
- Onoue SS, Ortiz KZ, Minett TS. (2014) Audiological findings in aphasic patients after stroke. *Einstein (Sao Paulo)* 12:433-9.
- Pendlebury ST, Mariz J, Bull L. (2012) MoCA, ACE-R, and MMSE versus the National Institute of Neurological Disorders and Stroke-Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards Neuropsychological Battery after TIA and stroke. *Stroke* 43:464-9.
- Pennings RJ, Morris DP, Clarke L. (2011) Natural history of hearing deterioration in intracanalicular vestibular schwannoma. *Neurosurgery* 68:68-77.
- Pichora-Fuller MK, Schneider BA, Daneman M. (1995) How young and old adults listen to and remember speech in noise. *The Journal of the Acoustical Society of America* 97:593-608.
- Pillion JP, Moser HW, Raymond GV. (2008) Auditory function in adrenomyeloneuropathy. *Journal of the neurological sciences* 269:24-9.

- Polster MR, Rose SB. (1998) Disorders of auditory processing: evidence for modularity in audition. *Cortex* 34:47-65.
- Poltl S, Hickson L. (1990) Hearing status of elderly hospital inpatients. *Australian Journal of Audiology* 12:79-83.
- Rey B, Frischknecht R, Maeder P, Clarke S. (2007) Patterns of recovery following focal hemispheric lesions: relationship between lasting deficit and damage to specialized networks. *Restor Neurol Neurosci* 25:285-294.
- Sastry J, Kellie SJ. (2005). Severe neurotoxicity, ototoxicity and nephrotoxicity following high-dose cisplatin and amifostine. *Pediatr Hematol Oncol* 22:441-5.
- Schow RL, Nerbonne MA. (1980) Hearing levels among elderly nursing home residents. *The Journal of speech and hearing disorders* 45:124-32.
- Schwartz DM, Morris MD, Jacobson JT (1994) The normal Auditory Brainstem Response and its variants. In: Jacobson JT, Ed. Principles and applications in auditory evoked potentials, Needham Heights, MA: Allyn and Bacon, 1994;123-153.
- Simoncelli C, Ricci G, Molini E. (1993) Evoked acoustic oto-emissions in patients with diabetes mellitus. Ann Otolaryngol Chir Cervicofac 110:255-8.
- Sinanović O, Raicevic B, Vidovic M. (2008). Brainstem auditory evoked potentials in patients with brainstem stroke. *Eur. J. Neurol.* 15:279-84.
- Sinanović O, Mrkonjić Z, Zukić S. (2011) Post-stroke language disorders. Acta Clin Croat. 50(1):79-94.
- Starr A, Picton TW, Sininger Y. (1996) Auditory neuropathy. *Brain : a journal of neurology* 119 (Pt 3):741-53.
- Strouse A, Ashmead DH, Ohde RN. (1998). Temporal processing in the aging auditory system. *The Journal of the Acoustical Society of America* 104:2385-99.
- Tatemichi T, Desmon D, Stern Y (1994). Cognitive impairment after stroke: frequency, patterns, and relationship to functional abilities. *J Neurol Neurosurg Psychiatry.* 57:202-207.
- Walton JP, Frisina RD, Ison JR. (1997) Neural correlates of behavioral gap detection in the inferior colliculus of the young CBA mouse. *J Comp Physiol A* 181:161-76.
- Yamasoba T, Lin FR, Someya S. (2013) Current concepts in age-related hearing loss: epidemiology and mechanistic pathways. *Hearing research* 303:30-8.

Table 1 Frequencies and percentages for age-groups, auditory vs. non-auditory, sex and side of lesion in the stroke group

Variable	*n*	*%*
Age group		
Younger	20	42
Older	22	58
Auditory vs. Non-auditory		
Non-auditory	18	43
Auditory	14	33
Auditory & Non-auditory	10	24
Sex		
Male	33	78
Female	9	22
Side		
Right	22	52
Left	18	43
Bilateral	2	5

	STROKE	CONTROLS	P-VALUE
PTA			
Total			
Normal	15	26	0.02*
Abnormal	27	14	
Younger			
Normal	14	22	0.69
Abnormal	6	4	
Older			
Normal	1	4	0.06
Abnormal	21	10	
ART			
Total			
Normal	34	35	0.25
Abnormal	8	5	
Younger			
Normal	16	25	0.15
Abnormal	4	1	
Older			
Normal	18	10	0.69
Abnormal	4	4	
TEOAE			
Total			
Normal	29	33	0.2
Abnormal	13	7	
Younger			
Normal	17	25	0.30
Abnormal	3	1	
Older			
Normal	12	8	0.87
Abnormal	10	6	
ABR			
Total			
Normal	34	39	0.02*
Abnormal	8	1	
Younger			
Normal	20	26	0.2
Abnormal	2	0	
Older			
Normal	14	13	0.2
Abnormal	6	1	
GIN			
Total			
Normal	11	38	0.000*
Abnormal	31	2	
Younger			
Normal	8	25	0.000*
Abnormal	12	1	
Older			
Normal	3	13	0.000*
Abnormal	19	1	
QSTAC			
Total			
Normal	16	37	0.000*
Abnormal	26	3	
Younger			
Normal	10	19	0.003*
Abnormal	10	1	
Older			
Normal	6	18	
Abnormal	16	2	0.000*

Table 2 Distribution of individuals with and without audiological test abnormalities in the stroke and control groups. KEYS: PTA, pure-tone audiometry; ART, acoustic reflex threshold; TEOAE, transient evoked otoacoustic emissions; ABR, auditory-evoked brainstem responses; GIN, gaps-in-noise; PP, perceptual property processing; AP, apperceptive processing; SP, semantic processing

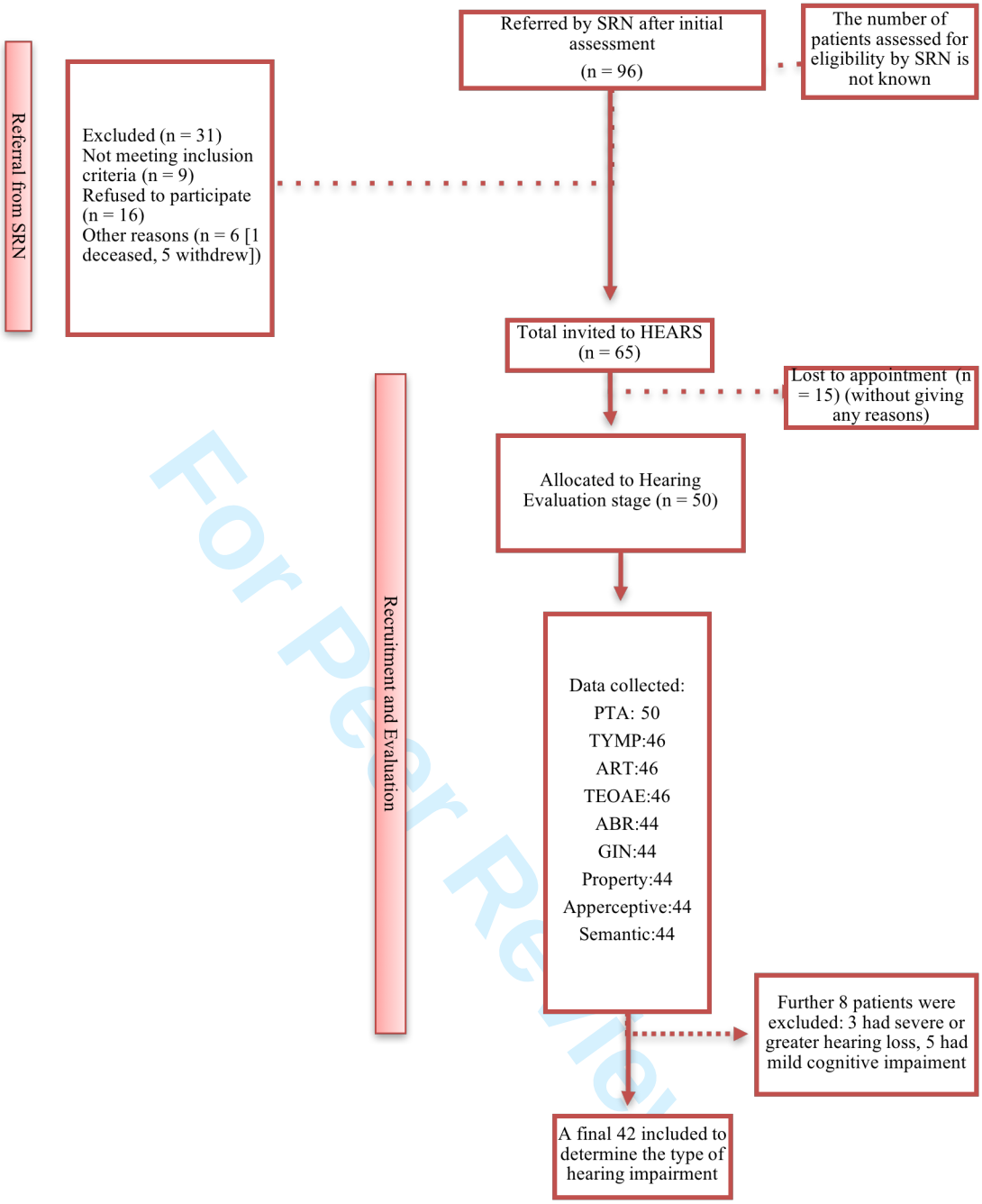
Table 3 Age, sex, type of hearing impairment and summary of test results in the stroke group. KEYS: M, male; F, female; Rt, right; Lt, left; CAPD, central auditory processing disorders; PTA, pure-tone audiometry; ART, acoustic reflex threshold, TEOAE, transient evoked otoacoustic emissions; ABR, auditory brainstem responses; CAP, central auditory processing assessment. + signifies an impairment.

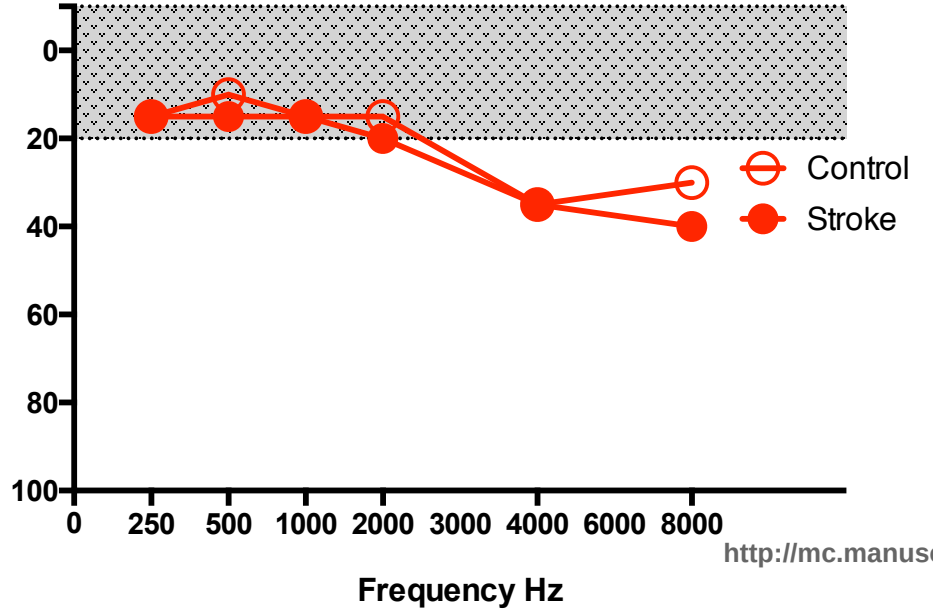
Patient	Age	Sex	Hearing impairment	PTA/ART/TEOAE/ABR/CAP
1	43	M	CAPD	-/-/-/-/+
2	23	M	CAPD	-/-/-/+/+
3	76	M	Peripheral	+/-/+/+/-
4	68	M	Peripheral	+/-/-/-/-
5	76	M	Peripheral and CAPD	+/-/-/+/+
6	63	M	Peripheral and CAPD	+/-/+/-/+
7	53	F	Normal	-/-/-/-/-
8	32	M	Normal	-/-/-/-/-
9	66	M	Peripheral	+/-/-/-/-
10	31	M	CAPD	-/-/-/-/+
11	72	F	Peripheral	+/-/+/-/-
12	60	M	Normal	-/-/-/-/-
13	73	M	Peripheral and CAPD	+/-/+/-/+
14	59	M	Peripheral	+/-/-/-/-
15	44	M	CAPD	-/-/-/-/+
16	67	M	Peripheral and CAPD	+/-/+/+/+
17	57	M	CAPD	-/+/-/-/+
18	75	F	Peripheral	+/+/+/-/-
19	80	F	Peripheral	+/-/-/-/-
20	54	F	Peripheral and CAPD	+/+/+/-/+
21	53	M	Peripheral	+/-/-/-/-
22	77	M	Peripheral and CAPD	+/+/+/-/+
23	63	M	Peripheral	+/-/-/-/-
24	46	M	CAPD	-/-/-/-/+
25	71	M	Peripheral and CAPD	+/+/-/+/+
26	52	M	Peripheral	+/+/-/-/-
27	63	F	Peripheral and CAPD	+/+/+/+/+
28	74	M	Normal	-/-/-/-/-
29	74	M	Peripheral and CAPD	+/-/-/-/+
30	70	M	Peripheral and CAPD	+/-/-/-/+
31	65	M	Peripheral and CAPD	+/-/-/-/+
32	74	M	Peripheral and CAPD	+/-/+/-/+
33	65	M	Peripheral and CAPD	+/-/-/-/+
34	70	M	Peripheral	+/-/+/-/-
35	48	M	Normal	-/-/-/-/-
36	43	F	CAPD	-/-/-/-/+
37	44	M	Peripheral and CAPD	+/+/+/+/+
38	61	M	Peripheral and CAPD	+/-/-/+/+
39	36	M	CAPD	-/-/-/-/+
40	32	M	CAPD	-/-/-/-/+
41	54	F	Peripheral and CAPD	+/-/+/-/+
42	37	F	Normal	-/-/-/-/-

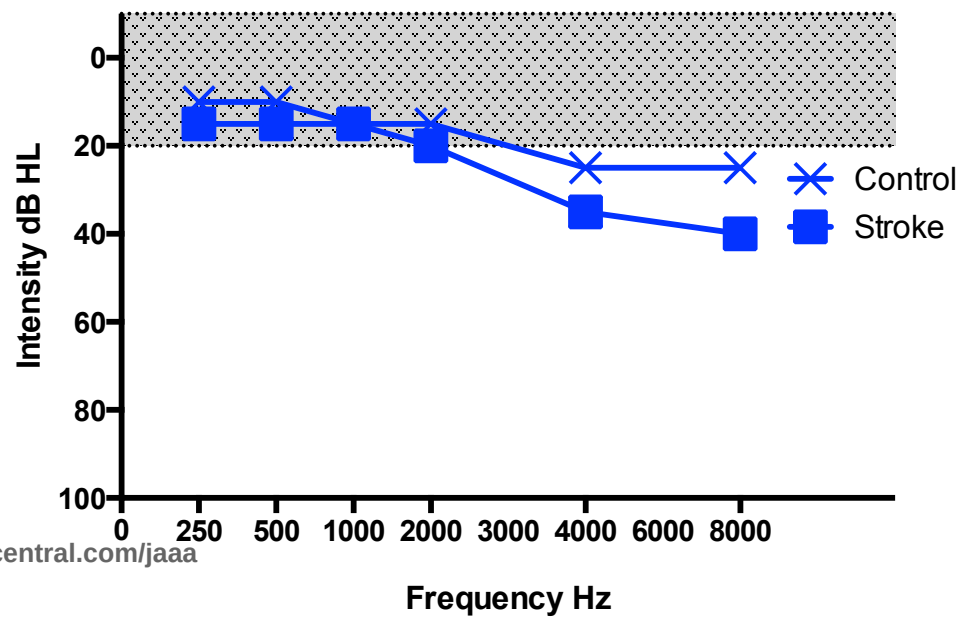
Table 4: Type of hearing loss in stroke and controls. Number of patients with different types of hearing impairment.

	Type of hearing in **control** subjects				
Age group	CAPD	Normal	Peripheral	Peripheral and CAPD	Total
< 61 years old	1(4%)	21(81%)	4(15%)	0(0%)	26(65%)
≥ 61 years old	0(0%)	4(29%)	9(64%)	1(7%)	14(35%)
Total	1(2%)	25(62%)	13(32%)	1(2%)	40

	Type of hearing in **stroke** patients				
Age group	CAPD	Normal	Peripheral	Peripheral and CAPD	Total
< 61 years old	8(40%)	5(25%)	3(15%)	4(20%)	20(48%
≥ 61 years old	1(4%)	1(4%)	8(36%)	12(56%)	22(52%)
Total	9(21%)	6(14%)	11(26%)	16(38%)	42




Right PTA Average 18-80 years old
Intensity dB HL
0
20
40
60
80
100
0
250
500
1000
2000
3000
4000
6000
8000
Frequency Hz
Control
Stroke


Left PTA Average 18-80 years old
Intensity dB HL
0
20
40
60
80
100
0
250
500
1000
2000
3000
4000
6000
8000
Frequency Hz
Control
Stroke

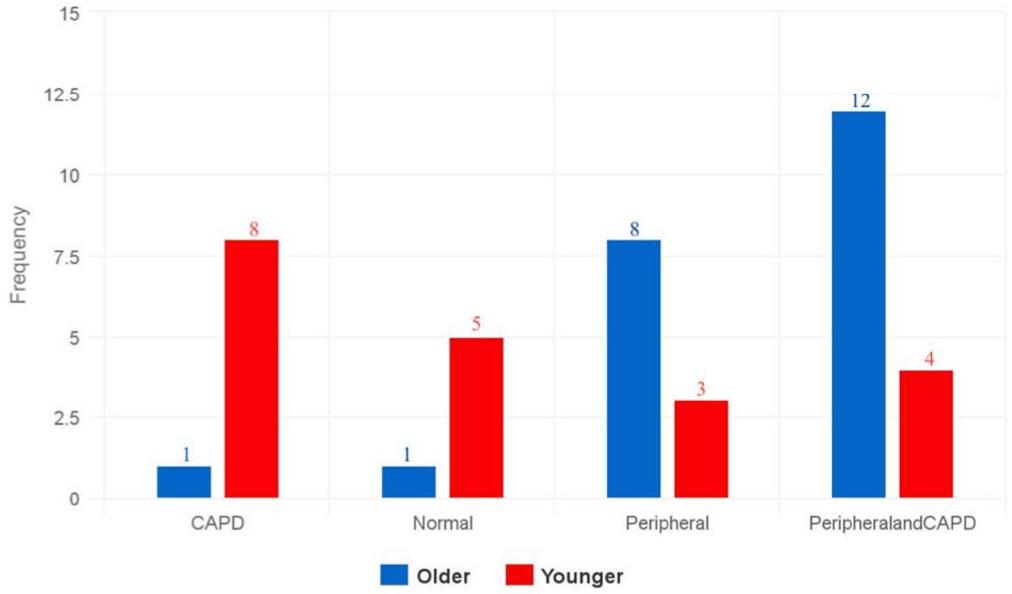


Figure 3 Types of hearing impairment as a function of age group. KEY: CAPD, central auditory processing disorders

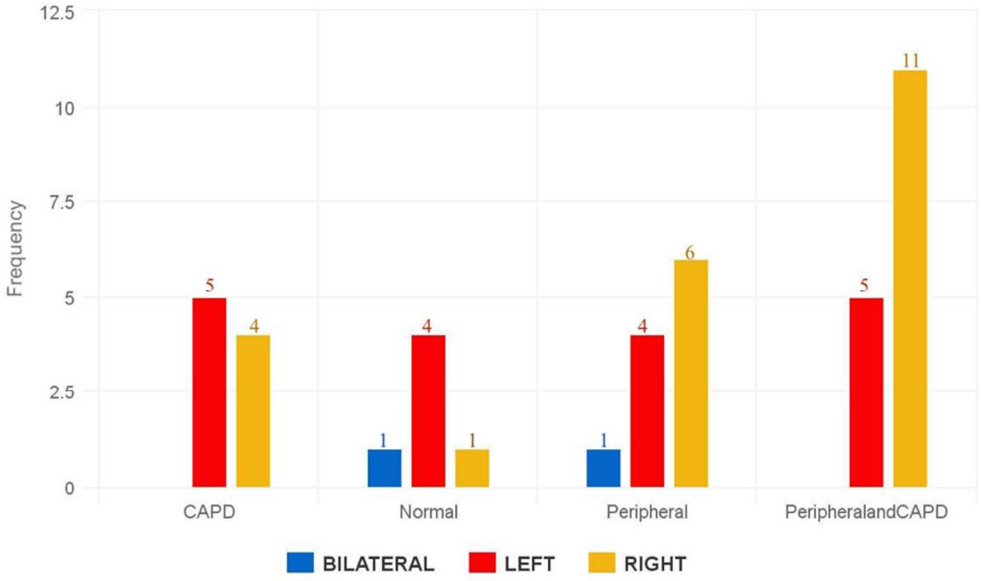


Figure 4 Types of hearing impairment as a function of side of lesion. KEY: CAPD, central auditory processing disorders

Multinomial regression

Multinomial response regression- looking at the conditional distribution of the type of hearing given age (dichotomous; <= 60/ >=61, continuous) and health status (stroke patient/ healthy control). Need to estimate a set of coefficients b^1,b^2,b^3,b^4 corresponding to each response outcome.

$$\Pr(Type\ of\ hearing = CAPD) = \frac{e^{Xb^1}}{e^{Xb^1} + e^{Xb^2} + e^{Xb^3} + e^{Xb^4}}$$

$$\Pr(Type\ of\ hearing = Normal) = \frac{e^{Xb^2}}{e^{Xb^1} + e^{Xb^2} + e^{Xb^3} + e^{Xb^4}}$$

$$\Pr(Type\ of\ hearing = Peripheral) = \frac{e^{Xb^3}}{e^{Xb^1} + e^{Xb^2} + e^{Xb^3} + e^{Xb^4}}$$

$$\Pr(Type\ of\ hearing = Peripheral\ and\ CAPD) = \frac{e^{Xb^4}}{e^{Xb^1} + e^{Xb^2} + e^{Xb^3} + e^{Xb^4}}$$

Model 1: Multinomial logistic regression model with age as a dichotomous variable and 'Normal' as reference category

Table 1. Estimates of the coefficients of the multinomial logistic regression model fitted to the data with Type of hearing as the dependent variable and group and ageGroup as independent variables.

Type of hearing		Coef.	Std. Error	95% Conf. Interval		P-value
				lower	upper	
CAPD						
	group (stroke patients)	3.628	1.149	1.376	5.879	0.002
	ageGroup (>= 61 years old)	-0.583	1.257	-3.005	1.881	0.643
	(Intercept)	-3.146	1.028	-5.161	-1.130	0.002
Normal	(Base outcome)					
Peripheral						
	group (stroke patients)	1.233	0.716	-0.169	2.636	0.085
	ageGroup (>= 61 years old)	2.523	0.686	1.179	3.867	<0.001
	(Intercept)	-1.696	0.511	-2.698	-0.694	0.001
Peripheral and CAPD						
	group (stroke patients)	4.170	1.197	1.825	6.516	<0.001
	ageGroup (>= 61 years old)	2.791	0.906	1.015	4.567	0.002
	(Intercept)	-4.456	1.203	-6.815	-2.098	<0.001

Table 2. Estimated relative risk ratios given by the multinomial logistic regression model which was fitted to the data with type of hearing as the dependent variable and group and ageGroup as independent variables. RRR: Relative Risk Ratio.

Type of hearing		RRR	Std. Error	95% Conf. Interval		P-value
				lower	upper	
CAPD						
	group (stroke patients)	37.620	43.223	3.958	357.588	0.002
	ageGroup (>= 61 years old)	0.558	0.702	0.047	6.560	0.643
	(Intercept)	0.043	0.044	0.006	0.323	0.002
Normal	(Base outcome)					
Peripheral						
	group (stroke patients)	3.432	2.457	0.844	13.957	0.085
	ageGroup (>= 61 years old)	12.468	8.551	3.251	47.815	<0.001
	(Intercept)	0.183	0.094	0.067	0.500	0.001
Peripheral and CAPD						
	group (stroke patients)	64.737	77.470	6.202	675.731	<0.001
	ageGroup (>= 61 years old)	16.293	14.763	2.759	96.219	0.002
	(Intercept)	0.012	0.014	0.001	0.123	<0.001

Model 3: Multinomial logistic regression model with age as a dichotomous variable and 'CAPD' as the reference category

Table 6. Estimates of the coefficients of the multinomial logistic regression model fitted to the data with Type of hearing as the dependent variable and group and ageGroup as independent variables.

Type of hearing		Coef.	Std. Error	95% Conf. Interval		P-value
				lower	upper	
CAPD	(Base outcome)					
Normal						
	group (stroke patients)	-3.628	1.149	-5.879	-1.376	0.002
	ageGroup (>= 61 years old)	0.583	1.257	-1.881	3.048	0.643
	(Intercept)	3.146	1.028	1.130	5.161	0.002
Peripheral						
	group (stroke patients)	-2.394	1.206	-4.757	-0.031	0.047
	ageGroup (>= 61 years old)	3.106	1.186	0.781	5.431	0.009
	(Intercept)	1.450	1.101	-0.708	3.608	0.188
Peripheral and CAPD						
	group (stroke patients)	0.543	1.542	-2.479	3.564	0.725
	ageGroup (>= 61 years old)	3.374	1.199	1.023	5.725	0.005
	(Intercept)	-1.311	1.542	-4.333	1.712	0.395

Table 7. Estimated relative risk ratios given by the multinomial logistic regression model which was fitted to the data with type of hearing as the dependent variable and group and ageGroup as independent variables. RRR: Relative Risk Ratio.

Type of hearing		RRR	Std. Error	95% Conf. Interval		P-value
				lower	upper	
CAPD	(Base outcome)					
Normal						
	group (stroke patients)	0.027	0.031	0.003	0.253	0.002
	ageGroup (>= 61 years old)	1.792	2.253	0.152	21.063	0.643
	(Intercept)	23.232	23.894	3.095	174.400	0.002
Peripheral						
	group (stroke patients)	0.091	0.110	0.009	0.969	0.047
	ageGroup (>= 61 years old)	22.342	26.503	2.185	228.487	0.009
	(Intercept)	4.262	4.692	0.493	36.874	0.188
Peripheral and CAPD						
	group (stroke patients)	1.721	2.653	0.084	35.316	0.725
	ageGroup (>= 61 years old)	29.194	35.017	2.782	306.388	0.005
	(Intercept)	0.270	0.416	0.013	5.540	0.395