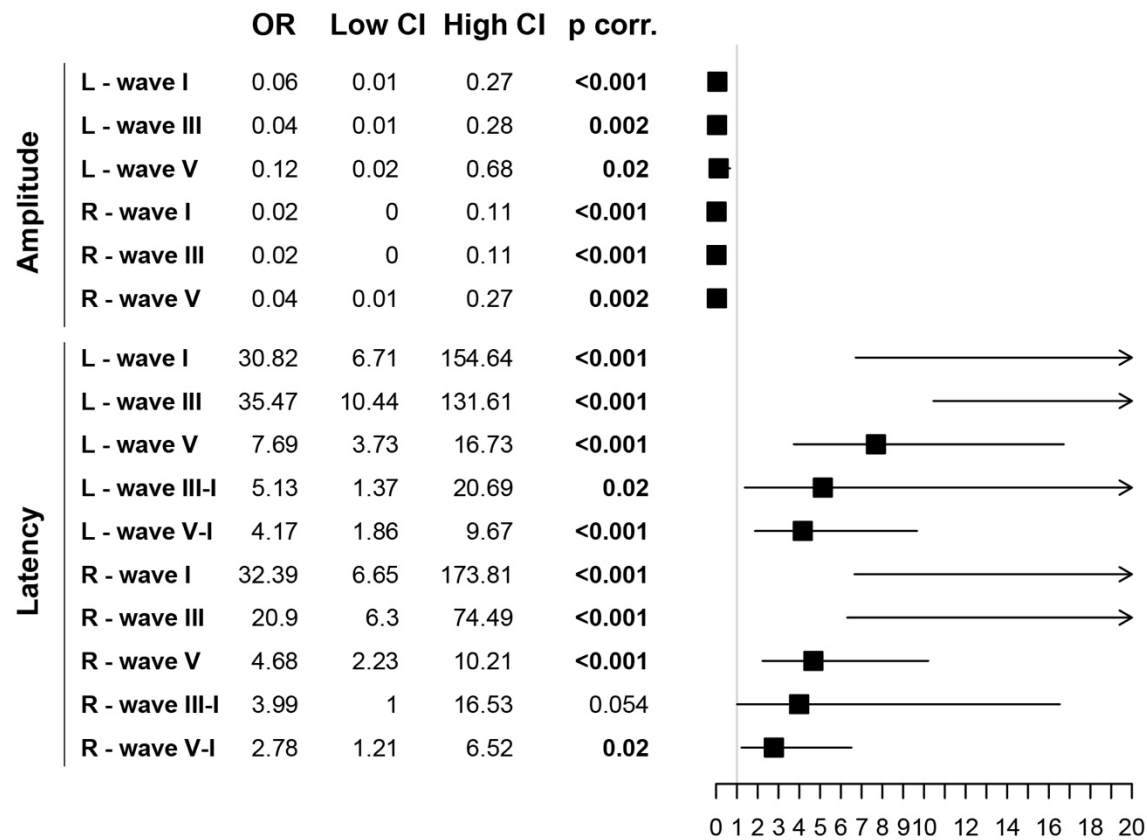


Supplementary Material:

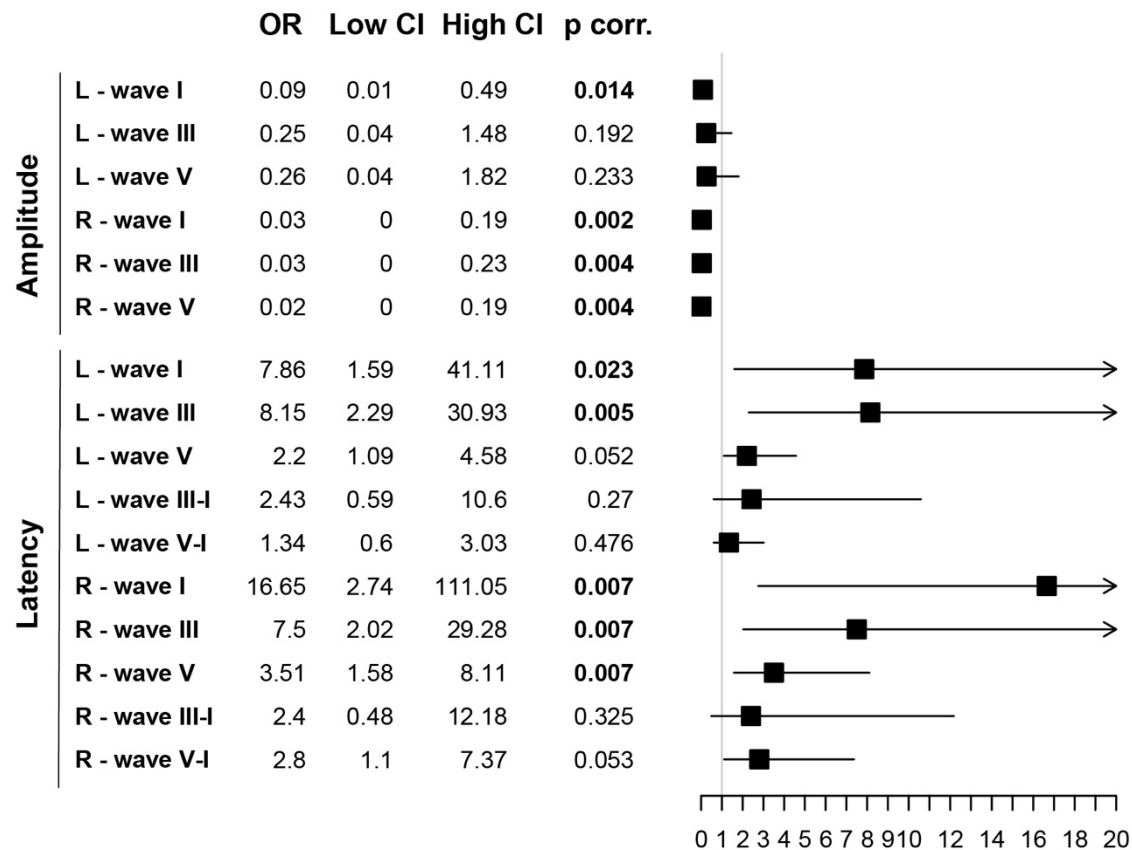
Univariate regression for constant tinnitus vs no tinnitus



**Figure S1.** Forest plot of odds ratios and 95% confidence intervals from univariate logistic regression models of auditory brainstem response variables for constant tinnitus using non-tinnitus controls as a reference.

*Legend:* Arrows indicate an odds ratio and/or upper confidence interval > 20. L: left ear, R: right ear, OR: odds ratio, CI: confidence interval, p corr.: p-value corrected with the method of Benjamini & Hochberg, significant findings ( $p < 0.05$ ) in bold.

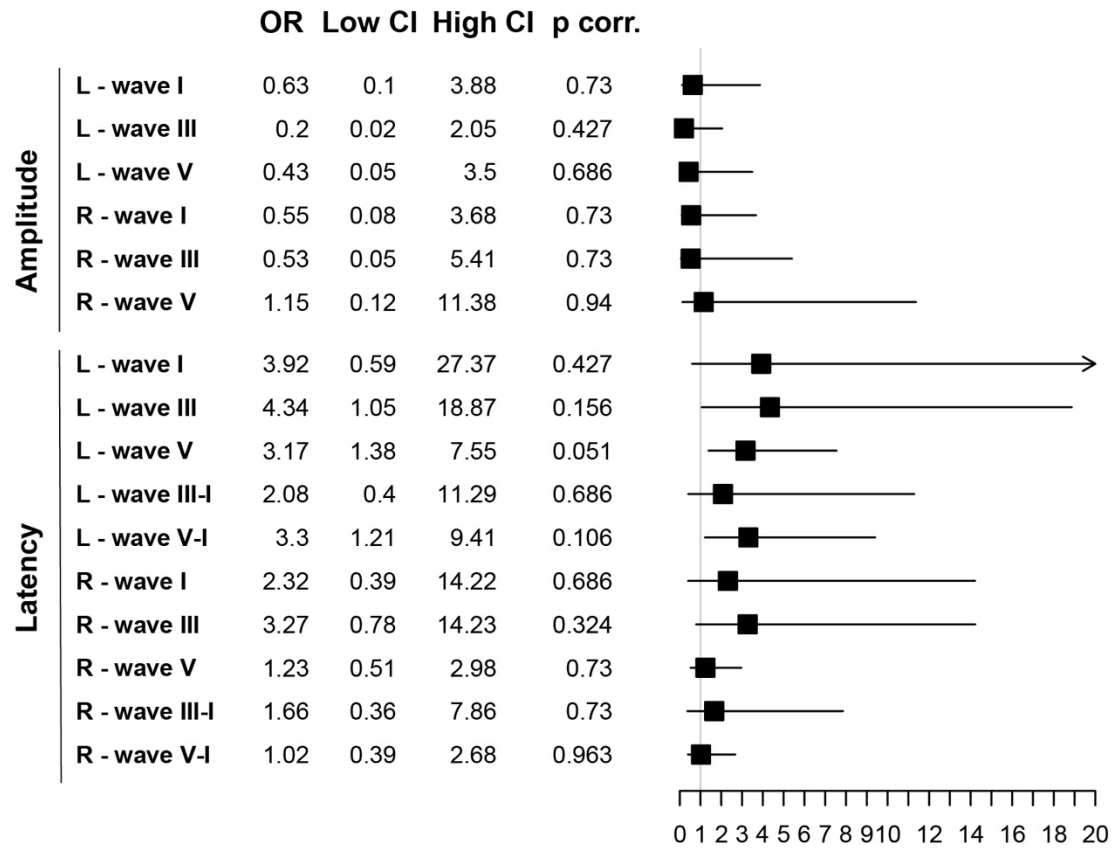
## Univariate regression for occasional tinnitus vs no tinnitus



**Figure S2.** Forest plot of odds ratios and 95% confidence intervals from univariate logistic regression models of auditory brainstem response variables for occasional tinnitus using non-tinnitus controls as a reference.

*Legend:* Arrows indicate an upper confidence interval > 20. L: left ear, R: right ear, OR: odds ratio, CI: confidence interval, p corr.: p-value corrected with the method of Benjamini & Hochberg, significant findings ( $p < 0.05$ ) in bold.

## Univariate regression for constant tinnitus vs occasional tinnitus



**Figure S3.** Forest plot of odds ratios and 95% confidence intervals from univariate logistic regression models of auditory brainstem response variables for constant tinnitus using occasional tinnitus as a reference.

*Legend:* The arrow indicates an upper confidence interval > 20. L: left ear, R: right ear, OR: odds ratio, CI: confidence interval, p corr.: p-value corrected with the method of Benjamini & Hochberg.

|                                        | <b>Wave 3 (2010)</b><br>(n=8,505) |                | <b>Wave 4 (2012)</b><br>(n=7,849) |            | <b>Wave 5 (2014)</b><br>(n=7,363) |                | <b>Wave 6 (2016)</b><br>(n=15,271) |             | <b>Wave 7 (2018)</b><br>(n=14,285) |             |
|----------------------------------------|-----------------------------------|----------------|-----------------------------------|------------|-----------------------------------|----------------|------------------------------------|-------------|------------------------------------|-------------|
|                                        | Occ                               | Const          | Occ                               | Const      | Occ                               | Const          | Occ                                | Const       | Occ                                | Const       |
| Previous wave<br>tinnitus state, n (%) |                                   |                |                                   |            |                                   |                |                                    |             |                                    |             |
| No tinnitus                            | 6,142<br>(72.2)                   | 33 (0.4)       | 5,608<br>(71.5)                   | 45 (0.6)   | 5,257<br>(71.5)                   | 59 (0.8)       | 10,421 (68.2)                      | 102 (0.7)   | 9,533 (66.7)                       | 98 (0.7)    |
| Some tinnitus                          | 1,250<br>(14.7)                   | 50 (0.6)       | 1,158<br>(14.8)                   | 48 (0.6)   | 1,049<br>(14.3)                   | 72 (1.0)       | 2,408 (15.8)                       | 122 (0.8)   | 2,183 (15.3)                       | 135 (1.0)   |
| Often tinnitus                         | 314 (3.7)                         | 69 (0.8)       | 312 (4.0)                         | 81 (1.0)   | 250 (3.4)                         | 85 (1.2)       | 609 (4.0)                          | 206 (1.4)   | 669 (4.7)                          | 203 (1.4)   |
| Constant tinnitus                      | 166 (2.0)                         | 481 (5.7)      | 146 (1.9)                         | 451 (5.8)  | 98 (1.3)                          | 493 (6.7)      | 275 (1.8)                          | 1,128 (7.4) | 278 (2.0)                          | 1,186 (8.3) |
| Gender, n (%)                          |                                   |                |                                   |            |                                   |                |                                    |             |                                    |             |
| Male                                   | 3,267<br>(41.5)                   | 401<br>(63.4)  | 3,002<br>(41.6)                   | 401 (64.2) | 2,720<br>(40.9)                   | 446 (62.9)     | 5,598 (40.8)                       | 928 (59.6)  | 5,146 (40.6)                       | 936 (57.7)  |
| Female                                 | 4,605<br>(58.5)                   | 232<br>(36.7)  | 4,222<br>(58.4)                   | 224 (35.8) | 3,934<br>(59.1)                   | 263 (37.1)     | 8,115 (59.2)                       | 630 (40.4)  | 7,517 (59.4)                       | 686 (42.3)  |
| Age                                    |                                   |                |                                   |            |                                   |                |                                    |             |                                    |             |
| mean (sd)                              | 52.0<br>(11.3)                    | 56.4<br>(10.0) | 54.3 (11.2)                       | 58.2 (9.8) | 56.2 (11.1)                       | 60.2<br>(10.1) | 56.1 (11.4)                        | 59.6 (9.9)  | 58.0 (11.4)                        | 61.3 (9.8)  |
| range                                  | 22 - 72                           | 22 - 71        | 24 - 74                           | 24 - 73    | 27 - 76                           | 26 - 75        | 21 - 78                            | 24 - 77     | 23 - 80                            | 26 - 79     |
| Education, n (%)                       |                                   |                |                                   |            |                                   |                |                                    |             |                                    |             |
| Primary education<br>or lower          | 1,227<br>(15.6)                   | 115<br>(18.2)  | 1,126<br>(15.6)                   | 106 (17.0) | 979 (14.7)                        | 116 (16.4)     | 1,731 (12.6)                       | 221 (14.2)  | 1,504 (11.9)                       | 237 (14.6)  |
| Lower secondary<br>education           | 1,772<br>(22.5)                   | 163<br>(25.8)  | 1,579<br>(21.9)                   | 155 (24.8) | 1,430<br>(21.5)                   | 174 (24.5)     | 2,763 (20.2)                       | 370 (23.8)  | 2,509 (19.8)                       | 377 (23.2)  |
| Upper secondary<br>education           | 1,757<br>(22.3)                   | 129<br>(20.4)  | 1,586<br>(22.0)                   | 131 (21.0) | 1,456<br>(21.9)                   | 150 (21.2)     | 3,015 (22.0)                       | 353 (22.7)  | 2,724 (21.5)                       | 378 (23.3)  |
| First stage of<br>tertiary education   | 1,097<br>(13.9)                   | 80 (12.6)      | 1,018<br>(14.1)                   | 77 (12.3)  | 940 (14.1)                        | 96 (13.5)      | 1,958 (14.3)                       | 198 (12.7)  | 1,861 (14.7)                       | 209 (12.9)  |
| Second stage of<br>tertiary education  | 2,017<br>(25.6)                   | 146<br>(23.0)  | 1,914<br>(26.5)                   | 156 (25.0) | 1,849<br>(27.8)                   | 173 (24.4)     | 4,244 (31.0)                       | 416 (26.7)  | 4,060 (32.1)                       | 421 (26.0)  |

**Table S1.** Characteristics of the SLOSH participants in wave 3 (2010) – wave 7 (2018)

| Flow | Frequency | Percent | Cumulative frequency | Cumulative percent |
|------|-----------|---------|----------------------|--------------------|
| 00   | 33231     | 62.38   | 33231                | 62.38              |
| 01   | 3317      | 6.23    | 36548                | 68.61              |
| 02   | 413       | 0.78    | 36961                | 69.38              |
| 03   | 337       | 0.63    | 37298                | 70.01              |
| 10   | 2998      | 5.63    | 40296                | 75.64              |
| 11   | 4096      | 7.69    | 44392                | 83.33              |
| 12   | 954       | 1.79    | 45346                | 85.12              |
| 13   | 427       | 0.80    | 45773                | 85.92              |
| 20   | 265       | 0.50    | 46038                | 86.42              |
| 21   | 862       | 1.62    | 46900                | 88.04              |
| 22   | 1027      | 1.93    | 47927                | 89.96              |
| 23   | 644       | 1.21    | 48571                | 91.17              |
| 30   | 125       | 0.23    | 48696                | 91.41              |
| 31   | 266       | 0.50    | 48962                | 91.91              |
| 32   | 572       | 1.07    | 49534                | 92.98              |
| 33   | 3739      | 7.02    | 53273                | 100.00             |

**Table S2.** Chart measuring the flow between the tinnitus states for all 53,273 observations in the SLOSH study.

*Legend:* The first digit in the column “Flow” measuring the previous state of tinnitus and the second digit measuring the two year follow up tinnitus state. 0 = no tinnitus, 1 = sometimes tinnitus, 2 = often tinnitus and 3 = constant tinnitus. Hence, “00” measures those who first answered no tinnitus in two waves in a row. “03” measures those who first answered no tinnitus and then constant tinnitus in the next wave

| Parameter                                           | Estimate<br>(SE)  | Z              | P-<br>value | OR     | 95 % CI       | CL<br>range |
|-----------------------------------------------------|-------------------|----------------|-------------|--------|---------------|-------------|
| <b>Model 1 - Unstructured correlation structure</b> |                   |                |             |        |               |             |
| Previous tinnitus (sometimes)                       | 1.727<br>(0.078)  | 22.22          | <.0001      | 5.62   | 4.83-6.55     | 1.72        |
| Previous tinnitus (often)                           | 3.392<br>(0.075)  | 45.48          | <.0001      | 29.74  | 25.69-34.42   | 8.73        |
| Previous tinnitus (constant)                        | 6.402<br>(0.071)  | 90.24          | <.0001      | 603.02 | 524.74-692.98 | 168.24      |
| <b>Model 2 - Exchangeable correlation structure</b> |                   |                |             |        |               |             |
| Previous tinnitus (sometimes)                       | 1.755<br>(0.077)  | 22.68          | <.0001      | 5.78   | 4.97-6.73     | 1.76        |
| Previous tinnitus (often)                           | 3.474<br>(0.074)  | 47.05          | <.0001      | 32.25  | 27.91-37.27   | 9.36        |
| Previous tinnitus (constant)                        | 6.2873<br>(0.073) | 86.37          | <.0001      | 537.72 | 466.22-620.18 | 153.96      |
| Parameter                                           | Estimate<br>(SE)  | Chi-<br>square | P-<br>value | OR     | 95 % CI       | CL<br>range |
| <b>Model 3 - Naïve logistic</b>                     |                   |                |             |        |               |             |
| Previous tinnitus (sometimes)                       | 1.735<br>(0.074)  | 548.68         | <.0001      | 5.67   | 4.90-6.55     | 1.65        |
| Previous tinnitus (often)                           | 3.435<br>(0.072)  | 2297.20        | <.0001      | 31.01  | 26.95-35.69   | 8.74        |
| Previous tinnitus (constant)                        | 6.001<br>(0.067)  | 8132.93        | <.0001      | 403.91 | 354.52-460.17 | 105.65      |

**Table S3.** Results of the generalized estimation equations (GEE) models measuring the effect of previous state of tinnitus on developing/maintain constant tinnitus in SLOSH.

*Legend:* All models are adjusted for age, gender, time and education

| Parameter                              | Estimate<br>(SE) | Z              | P-<br>value | OR     | 95 % CI           | CL range |
|----------------------------------------|------------------|----------------|-------------|--------|-------------------|----------|
| <b><i>Model 1 - Unstructured</i></b>   |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.665 (0.111)    | 15.01          | <.0001      | 5.29   | 4.25-6.57         | 2.32     |
| Previous tinnitus (often)              | 3.301 (0.105)    | 31.57          | <.0001      | 27.14  | 22.11-33.31       | 11.20    |
| Previous tinnitus<br>(constant)        | 6.401 (0.100)    | 64.19          | <.0001      | 602.17 | 495.27-<br>732.14 | 236.87   |
| <b><i>Model 2 - Exchangeable</i></b>   |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.693 (0.111)    | 15.22          | <.0001      | 5.44   | 4.37-6.76         | 2.39     |
| Previous tinnitus (often)              | 3.401 (0.104)    | 32.68          | <.0001      | 30.01  | 24.47-36.80       | 12.33    |
| Previous tinnitus<br>(constant)        | 6.299 (0.103)    | 61.48          | <.0001      | 544.18 | 445.17-665.22     | 220.05   |
| Parameter                              | Estimate<br>(SE) | Chi-<br>square | P-<br>value | OR     | 95 % CI           | CL range |
| <b><i>Model 3 - Naïve logistic</i></b> |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.676 (0.104)    | 260.51         | <.0001      | 5.34   | 4.36-6.55         | 2.19     |
| Previous tinnitus (often)              | 3.374 (0.099)    | 1162.08        | <.0001      | 29.19  | 24.04-35.44       | 11.40    |
| Previous tinnitus<br>(constant)        | 5.895 (0.092)    | 4071.94        | <.0001      | 363.25 | 303.09-435.35     | 132.26   |

**Table S4.** Results of the generalized estimation equations (GEE) models measuring the effect of previous state of tinnitus on developing/maintain constant tinnitus only analyzing males in SLOSH.

*Legend:* All models are adjusted for age, gender, time and education

| Parameter                              | Estimate<br>(SE) | Z              | P-<br>value | OR     | 95 % CI           | CL range |
|----------------------------------------|------------------|----------------|-------------|--------|-------------------|----------|
| <b><i>Model 1 - Unstructured</i></b>   |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.772<br>(0.109) | 16.24          | <.0001      | 5.88   | 4.75-7.28         | 2.53     |
| Previous tinnitus<br>(often)           | 3.455<br>(0.106) | 32.52          | <.0001      | 31.67  | 25.71-39.00       | 13.29    |
| Previous tinnitus<br>(constant)        | 6.400<br>(0.101) | 63.24          | <.0001      | 601.95 | 493.64-<br>734.02 | 240.38   |
| <b><i>Model 2 - Exchangeable</i></b>   |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.798<br>(0.108) | 16.60          | <.0001      | 6.04   | 4.88-7.47         | 2.59     |
| Previous tinnitus<br>(often)           | 3.518<br>(0.105) | 33.43          | <.0001      | 33.70  | 27.42-41.42       | 14.00    |
| Previous tinnitus<br>(constant)        | 6.294<br>(0.104) | 60.82          | <.0001      | 541.55 | 442.12-<br>663.33 | 221.21   |
| Parameter                              | Estimate<br>(SE) | Chi-<br>square | P-<br>value | OR     | 95 % CI           | CL range |
| <b><i>Model 3 - Naïve logistic</i></b> |                  |                |             |        |                   |          |
| Previous tinnitus<br>(sometimes)       | 1.785<br>(0.106) | 285.07         | <.0001      | 5.96   | 4.84-7.33         | 2.49     |
| Previous tinnitus<br>(often)           | 3.485<br>(0.104) | 1115.65        | <.0001      | 32.63  | 26.59-40.03       | 13.44    |
| Previous tinnitus<br>(constant)        | 6.115<br>(0.096) | 4036.66        | <.0001      | 452.44 | 374.66-<br>546.36 | 171.70   |

**Table S5.** Results of the generalized estimation equations (GEE) models measuring the effect of previous state of tinnitus on developing/maintain constant tinnitus only analyzing females in SLOSH.

*Legend:* All models are adjusted for age, gender, time and education



|                         |            | Chartr               |                                |                               |                  | Eclipse             |                                |                              |                  |
|-------------------------|------------|----------------------|--------------------------------|-------------------------------|------------------|---------------------|--------------------------------|------------------------------|------------------|
|                         |            | No tinnitus<br>n=100 | Occasional<br>tinnitus<br>n=80 | Constant<br>tinnitus<br>n=103 | p-value          | No tinnitus<br>n=77 | Occasional<br>tinnitus<br>n=12 | Constant<br>tinnitus<br>n=33 | p-value          |
| Left ear                |            |                      |                                |                               |                  |                     |                                |                              |                  |
| Amplitude<br>( $\mu$ V) | Wave I     | 0.35 (0.15)          | 0.31 (0.13)                    | 0.32 (0.15)                   | 0.159            | 0.44 (0.16)         | 0.46 (0.21)                    | 0.32 (0.16)                  | <b>0.003</b>     |
|                         | Wave III   | 0.20 (0.10)          | 0.20 (0.10)                    | 0.19 (0.09)                   | 0.773            | 0.35 (0.17)         | 0.45 (0.15)                    | 0.29 (0.12)                  | <b>0.017</b>     |
|                         | Wave V     | 0.35 (0.14)          | 0.32 (0.13)                    | 0.31 (0.13)                   | 0.051            | 0.35 (0.14)         | 0.36 (0.11)                    | 0.32 (0.14)                  | 0.652            |
| Latency (ms)            | Wave I     | 1.48 (0.13)          | 1.48 (0.13)                    | 1.51 (0.12)                   | 0.261            | 1.25 (0.12)         | 1.20 (0.08)                    | 1.34 (0.14)                  | <b>0.001</b>     |
|                         | Wave III   | 3.67 (0.19)          | 3.72 (0.17)                    | 3.77 (0.20)                   | <b>0.003</b>     | 3.46 (0.19)         | 3.41 (0.20)                    | 3.60 (0.16)                  | <b>0.001</b>     |
|                         | Wave V     | 5.49 (0.33)          | 5.53 (0.34)                    | 5.67 (0.28)                   | <b>&lt;0.001</b> | 5.18 (0.36)         | 5.04 (0.40)                    | 5.38 (0.30)                  | <b>0.008</b>     |
|                         | Wave I-III | 2.19 (0.21)          | 2.24 (0.18)                    | 2.25 (0.18)                   | 0.123            | 2.21 (0.18)         | 2.21 (0.21)                    | 2.25 (0.16)                  | 0.512            |
|                         | Wave I-V   | 4.00 (0.32)          | 4.04 (0.32)                    | 4.14 (0.25)                   | <b>0.007</b>     | 3.94 (0.34)         | 3.84 (0.37)                    | 4.00 (0.24)                  | 0.381            |
| Right ear               |            |                      |                                |                               |                  |                     |                                |                              |                  |
| Amplitude<br>( $\mu$ V) | Wave I     | 0.35 (0.15)          | 0.29 (0.12)                    | 0.29 (0.15)                   | <b>0.006</b>     | 0.43 (0.18)         | 0.42 (0.23)                    | 0.30 (0.16)                  | <b>0.005</b>     |
|                         | Wave III   | 0.20 (0.10)          | 0.19 (0.10)                    | 0.19 (0.10)                   | 0.656            | 0.40 (0.15)         | 0.40 (0.13)                    | 0.28 (0.15)                  | <b>0.002</b>     |
|                         | Wave V     | 0.34 (0.12)          | 0.30 (0.10)                    | 0.29 (0.13)                   | <b>0.012</b>     | 0.37 (0.12)         | 0.34 (0.12)                    | 0.33 (0.14)                  | 0.325            |
| Latency (ms)            | Wave I     | 1.47 (0.10)          | 1.48 (0.13)                    | 1.49 (0.15)                   | 0.654            | 1.27 (0.12)         | 1.21 (0.12)                    | 1.39 (0.17)                  | <b>&lt;0.001</b> |
|                         | Wave III   | 3.69 (0.17)          | 3.70 (0.17)                    | 3.75 (0.18)                   | 0.093            | 3.45 (0.17)         | 3.43 (0.19)                    | 3.61 (0.21)                  | <b>&lt;0.001</b> |
|                         | Wave V     | 5.51 (0.31)          | 5.55 (0.29)                    | 5.59 (0.28)                   | 0.181            | 5.17 (0.28)         | 5.16 (0.46)                    | 5.33 (0.31)                  | 0.06             |
|                         | Wave I-III | 2.22 (0.16)          | 2.22 (0.18)                    | 2.25 (0.17)                   | 0.406            | 2.17 (0.15)         | 2.22 (0.13)                    | 2.20 (0.24)                  | 0.645            |
|                         | Wave I-V   | 4.03 (0.28)          | 4.07 (0.27)                    | 4.09 (0.27)                   | 0.296            | 3.90 (0.28)         | 3.97 (0.43)                    | 3.95 (0.37)                  | 0.721            |

**Table S6.** Amplitude and latency of auditory brainstem responses Waves in STOP participants.

*Legend:* Mean amplitude (in  $\mu$ V) and latency (in ms) values for the investigated ABR parameters stratified by the two hardwares used. Standard deviation are shown in parenthesis. Reported *p*-values are from ANOVA comparing No, Occasional and Constant tinnitus. Estimates in bold are statistically significant at 0.05 level.

|           |            | Chartr |              | Eclipse |              |
|-----------|------------|--------|--------------|---------|--------------|
|           |            | ICC3   | 95% CI       | ICC3    | 95% CI       |
| Latency   | Wave I     | 0.90   | 0.55 - 0.90  | 0.87    | 0.71 - 0.94  |
|           | Wave III   | 0.96   | 0.81 - 0.96  | 0.92    | 0.81 - 0.97  |
|           | Wave V     | 0.89   | 0.49 - 0.89  | 0.79    | 0.57 - 0.91  |
|           | Wave III-I | 0.92   | 0.82 - 0.97  | 0.87    | 0.70 - 0.94  |
|           | Wave V-I   | 0.77   | 0.52 - 0.90  | 0.82    | 0.62 - 0.92  |
| Amplitude | Wave I     | 0.43   | 0.02 - 0.71  | 0.96    | 0.91 - 0.98  |
|           | Wave III   | 0.26   | -0.17 - 0.61 | 0.18    | -0.25 - 0.55 |
|           | Wave V     | 0.47   | 0.07 - 0.74  | 0.48    | 0.08 - 0.74  |

**Table S7.** Test-retest reliability of the two ABR systems.

*Legend:* To compare the two ABR systems used we performed a test-retest for both systems on eight (50% men) young (mean age 31.6 years, SD: 6.5) healthy participants. This group did not complete the full test battery but were tested using high frequency audiometry and the 9.1 clicks/s at 90 dBnHL ABR condition, 2000 clicks, once per ear, for both systems at two sessions around one week apart. Average ( $\pm$  SD) thresholds were within normal ranges with PTA4 of 2.0 ( $\pm$  8.8) and 2.3 ( $\pm$  9.7) dB HL, for left and right ears respectively and PTAHF of 15.4 ( $\pm$  19.26) and 17.1 ( $\pm$  22.7) dB HL. Latency and amplitude values for ABR waves I, III and V were manually extracted and used to calculate the intraclass correlation coefficient ICC3. The intraclass correlation (ICC3) in a test-retest of the two ABR systems used for this study showed good to excellent reliability (ICC3 > 0.75) for both systems latency measurements. Amplitude measurements generally had poor reliability (ICC3 < 0.5) except for wave I amplitude as measured by the Eclipse system, which showed excellent reliability with ICC3 of 0.96. Reported here are Intraclass correlation coefficients (ICC3) and 95% confidence interval for the studied variables in a test-retest of the two systems used for ABR measurements. Data represents 16 ears from a total of 8 participants.