Central Auditory Gain Modulation in the Rehabilitation of Workers with Tinnitus

Sylvie Hébert
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SUMMARY

Tinnitus is sound perceived in the absence of an external sound source. This abnormal auditory sensation, which can be in the form of buzzing, ringing or whistling, affects one or both ears. For a significant number of people with hearing loss, it can cause considerable deterioration in the quality of life and ability to work. In the two studies described in this report, a recent model, referred to as central auditory gain, has been used to integrate normal and pathological data into the same conceptual framework. It has been speculated that “central auditory gain” is a normal mechanism by which the auditory system modulates its response when acoustic conditions change. For example, auditory sensitivity increases with auditory deprivation, while it decreases with auditory stimulation. This phenomenon has been documented in adults with normal hearing. However, mainly subjective assessments of intensity have been measured, leaving questions about the existence and the localization of this central auditory gain mechanism unaddressed.

The objective of the first study was to demonstrate the existence of central auditory gain and to localize it functionally. Two groups of adults with normal hearing wore earplugs or noise generators for one week. They underwent tests before and after deprivation (earplugs) or stimulation (noise generators) with a hearing assessment battery that included measurements from the cochlea to the auditory cortex. The results demonstrate that the auditory system effectively modulates its response according to acoustic conditions (deprivation or stimulation, although less so for the latter), and that this modulation does not occur at the peripheral level (i.e., in the cochlea), but within the auditory cortex, i.e., in the highest level of the auditory system. In fact, in our study no change was observed below this level. Thus, the presence of auditory gain modulation of purely central origin is supported by our data.

The objective of the second study was to examine whether the central auditory gain could be modulated among adults with tinnitus. In fact, in this population, it has been suggested that the central auditory gain mechanism is maladaptive (in that it overreacts to stimuli), and that it could be responsible for tinnitus and hyperacusis, which are defined as auditory hypersensitivity. The model suggests that tinnitus reflects spontaneous neural hyperactivity, while hyperacusis reflects hyperactivity caused by external sounds. Essentially, the central auditory gain appears to be chronically altered among people with tinnitus and hyperacusis and constitutes the principal pathophysiological mechanism in hearing disorders. If such is the case, a return to normal of the gain adaptation mechanisms should be reflected by a decrease in the sensitivity observed in appraisals of loudness and even a decrease in the intensity of the tinnitus. In the second study, participants with or without hearing loss, and who had tinnitus, used noise generators for three weeks. Auditory and psychometric measurements were taken before the test, after one week of wearing the generators, after three weeks, and then one month after the end of the tests.

Our laboratory results suggest that wearing noise generators decreases sensitivity to external sounds and reduces the loudness of tinnitus. This decrease was more significant in the group without hearing loss. The subjective intensity of the tinnitus and the disturbance that it causes in daily life, as measured by visual analogue scales, also declines with treatment. The preliminary findings are the first resulting from a joint examination of two different tasks (the loudness of tinnitus and loudness functions) that involve a modulation of intensity (external sounds and tinnitus) possibly originating from a common mechanism, normal in one case and pathological in the other. Overall, our data suggest that the central auditory gain mechanism, present among
the participants with normal hearing, could be used successfully to objectively measure improvement after the use of noise generators in people suffering from tinnitus and hyperacusis.
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1. INTRODUCTION

Chronic tinnitus is a buzzing or whistling noise perceived in the ears or the head without there being any external sound source. This phantom sound can have devastating effects on the quality of life and ability to work. Tinnitus is associated with sleeping disorders (Hébert and Carrier 2007, Hébert, Fullum et al. 2011), physiological dysfunction similar to that present in stress-related illnesses (Hébert, Paiement et al. 2004, Hébert and Lupien 2007, Hébert and Lupien 2009, Simoens and Hébert 2012), anxiety, depression (Shargorodsky, Curhan et al. 2010) and auditory hypersensitivity (Hébert, Fournier et al. 2013). Sensorineural hearing loss is a known risk factor for tinnitus. As noise exposure is the second greatest cause of sensorineural hearing loss (Rabinowitz 2000), people who work in noisy environments are highly at risk for tinnitus. The results of studies vary with respect to the prevalence of tinnitus among workers who have hearing loss caused by noise. For example, a recent study conducted among military personnel exposed to high impact noises (and likely high stress levels) reported a prevalence of tinnitus of 80% (Yankaskas 2013). Conversely, in various targeted populations of workers exposed to noise, a lower prevalence rate of permanent tinnitus was reported; between 4.6% and 51.3% (Axelsson and Sandh 1985, Mrena, Ylikoski et al. 2007). A population study carried out in Great Britain with 23,000 adults, and thus less subject to selection bias, reported a prevalence rate of persistent tinnitus of 2.6 (95% CI: 2.0 to 3.4) among men over 35 who had been exposed to noise for more than 10 years in their workplace (Palmer, Griffin et al. 2002). In other words, a worker exposed to noise for a long period is approximately 2.6 times more likely to have persistent tinnitus than a worker not exposed to noise or exposed over a shorter period of time. The definition of persistent or permanent tinnitus does not make it possible to know whether this type of disorder was troublesome in the studies. However in Québec, the Institut national de santé publique du Québec (INSPQ) database showed that 13.7% of workers in noisy environments (>80 dBA) reported annoying tinnitus between 2000 and 2011, which is about 10 times higher than the proportion among the general population (Axelsson and Ringdahl 1989).

Because of its subjective nature, a clinical diagnosis of tinnitus is often based solely on the patient’s reporting. Few audiology clinics do psychoacoustic pitch and loudness match tests for tinnitus, despite the fact that they are the minimum assessment recommended by international experts (Langguth, Goodey et al. 2007). The costs, both human (such as the time and energy invested to find health professionals and to consult them about the symptoms they have noted) and economic (such as absence from work), of this lack of tinnitus assessment are enormous and workers and employers would benefit by having this type of hearing disorder assessed with appropriate measures and according to objective and explicit criteria. These measures exist, and include those developed by the Tinnitus and Hyperacusis Research Laboratory at the Université de Montréal, such as a touchscreen to perform precise psychoacoustic matches of the tinnitus. These new measures show exceptional test-retest reliability over a four to eight month period (Basile, Fournier et al. 2013, Fournier and Hebert 2013). Moreover, recent scientific data (Kujawa and Liberman 2009, Schaette and McAlpine 2011, Shi, Chang et al. 2016) have shed light on factors other than measurable hearing loss from an audiogram that may react to the presence of and, above all, the severity of tinnitus. In particular, hearing loss can be hidden and impossible to assess with standard clinical measurements. Determining a hidden loss can guide clinicians and prevent greater decline. Moreover, auditory hypersensitivity is a significant symptom associated with tinnitus, and one on which this study suggests that it is possible to act. Finally, some non-hearing-related risk factors, such as depression and burnout,
also play an important role with respect to tinnitus and should be investigated (Hébert, Canlon et al. 2012, Hébert, Canlon et al. 2012).

The long-term objective of this study was to validate the most relevant and sensitive tinnitus assessment tools in order to develop a pragmatic clinical protocol and to implement it with workers suffering from tinnitus. With that in mind, this study aims to show that the normal hearing system adapts to acoustic changes (deprivation, stimulation), to locate the origin of this physiological mechanism, and to show that these changes can be modulated among people with tinnitus.
2. STATE OF SCIENTIFIC KNOWLEDGE

Loudness, or the perceived intensity of a sound measured in decibels (dB), is a major perceptual attribute of ambient sound. While the relationship between loudness and dB level is obvious, i.e., the more the dB level increases, the more loudness increases, the latter may vary a great deal, depending on hearing function or acoustic conditions. In a worker whose hearing is normal, the hearing system modifies its response according to the level of surrounding noise. Thus, after wearing earplugs for a few days, hearing sensitivity increases: sounds that were comfortably previously now feel too loud (Formby, Sherlock et al. 2003). The stapedius reflex, which is regulated by subcortical structures situated in the brainstem and which reflects sound intolerance thresholds, also reacts at a lower dB level after hearing deprivation (Munro and Blount 2009). Conversely, after wearing noise generators for a certain time, hearing sensitivity decreases: normally comfortable sounds are now perceived as soft (Formby, Sherlock et al. 2003). A pilot study from the laboratory at the Université de Montréal (unpublished data), assessed several components of the hearing system in adults with normal hearing: wearing earplugs for one week increased sensitivity and loudness functions at frequencies of 1 kHz and 4 kHz and stapedius reflexes, but did not change the growth of acoustic distortion products that are generated at the cochlear level. This supports the idea that the gain appears to be initiated centrally in the brainstem or later in the hearing process. To summarize, hearing sensitivity adjusts itself upward (after deprivation) or downward (after stimulation), according to the average level of sound input, possibly by an adaptation mechanism of the central gain. However, a review of animal and human studies shows that the exact nature and location of this gain is unclear (Fournier, Schonwiesner et al. 2014).

Recently, it has been suggested that tinnitus and auditory hypersensitivity, two pathologies related to loudness, are the result of a maladapted central gain (Norena 2011). In fact, there is consensus around the idea that peripheral damage, even slight, is required for tinnitus to occur (Weisz, Hartmann et al. 2006, Norena 2011, Schaeette and McAlpine 2011). Thus, tinnitus may be the result of an increase in spontaneous neuronal activity, while hypersensitivity is the result of increased neural activity induced by external sounds.¹ For the first time, it was demonstrated that hearing sensitivity increases in people with tinnitus (Hébert, Fournier et al. 2013). Compared to people without tinnitus but with comparable hearing, loudness functions, closely measured for comfortable to overly loud levels, were less than 10 dB on average among listeners with tinnitus, which is equivalent to approximately 10 times the sound pressure.

Modulation of the central gain is a potentially powerful paradigm for rehabilitation. For example, if stimulation using a noise generator reduces the auditory hypersensitivity associated with tinnitus, specific improvement objectives (e.g., in numbers of dB) could guide the return to work process and confirm whether there is less hypersensitivity during follow-up. To corroborate this hypothesis, a study of young participants (~42 years) with hearing loss and hyperacusis reported a reduction in discomfort thresholds of 5 to 15 dB (after 2 to 15 weeks, respectively) after wearing a noise generator (Norena and Chery-Croze 2007). The measurement of loudness functions before and after wearing noise generators could thus quantify loudness modulation.

In our laboratory, we had previously developed a precise and robust method to assess tinnitus (Basile, Fournier et al. 2013, Fournier and Hébert 2013). In this study, it helped us test the hypothesis that noise generators can decrease the intensity of tinnitus. At the same time,

¹ Note that increased neural activity is a possible mechanism, but it is not the only one. In fact, tonotopic reorganization and increased neural synchrony could also be involved.
psychometric scales will also make it possible to verify whether the subjective intensity of tinnitus decreases as the loudness of the tinnitus lessens.
3. DESCRIPTION OF THE STUDIES

The long-term objective of the program will be to implement a clinical protocol for audiological assessment in order to diagnose, set the therapeutic course, and care for workers with tinnitus. To achieve this objective, two preliminary studies were necessary. They are presented in this report.

3.1 Study 1

The objective of Study 1 was to functionally demonstrate the bidirectional modulation of the central gain through the wearing of earplugs and noise generators by people with normal hearing, to examine these potential changes at every level of the hearing system, from the cochlea to behaviour, including the auditory cortex, and to locate these changes through the spatial and temporal precision of magnetoencephalography (MEG) (Parkkonen, Fujiki et al. 2009).

Some studies of the central gain have only used loudness judgments and the stapedius reflexes (Formby and Gold 2002, Formby, Sherlock et al. 2003, Sherlock and Formby 2005). The judgment of loudness is an interesting behavioural measurement because it reflects perception, but it remains a general measurement that does not detect the location of changes. The stapedius reflex is an objective measurement, reflecting the contribution of the brainstem, but it is incomplete, because it is only an intermediate structure of the auditory system that reflects both afferent and efferent pathways. Moreover, if the gain is central, cochlear contribution must be completely excluded, in particular, because the paradigm will be used to study people with cochlear hearing loss. It is crucial to assess the contribution of the cerebral cortex and the location of changes to verify whether there is a link between increased hearing sensitivity and cortical hyperactivity (Gu, Halpin et al. 2010), on the one hand, and, on the other, decreased hearing sensitivity and cortical activity.

The primary hypothesis is that earplug use will increase hearing sensitivity, while noise generator use will reduce it, and that these modulations of sensitivity levels are observed from the brainstem to the cortex, but are absent in the cochlea.

3.1.1 Methodology

Participants

Thirty-one adults were recruited by word-of-mouth and through posters. They were assigned to the earplug group (n=16, 7 F, 9 M) or to the noise generator group (n=15, 9 F, 6 M) according to their preference. There was no significant difference in age (26.1 for the earplug group and 24 for the noise generator group, \( p = .13 \)) or education level (17.9 and 17.7 years, respectively \( p = .80 \)). There was no difference in the number of women and men in the two groups (\( p = .29 \) using an \( X^2 \) test). The demographic and audiological characteristics of the two groups are presented in Table 1.
**Table 1.** Sociodemographic (standard deviation) and audiological characteristics of the participants in the earplug and noise generator groups (n.s. = not significant)

<table>
<thead>
<tr>
<th></th>
<th>Earplugs (N=16)</th>
<th>Range (Min/Max)</th>
<th>Noise generators (N=15)</th>
<th>Range (Min/Max)</th>
<th>Value p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26.1 (4.6)</td>
<td>20–35</td>
<td>24 (2.5)</td>
<td>21–29</td>
<td>n.s.</td>
</tr>
<tr>
<td>Number of men/women</td>
<td>9/7</td>
<td></td>
<td>6/9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of education</td>
<td>17.9 (2.5)</td>
<td>14–23</td>
<td>17.7 (2.0)</td>
<td>15–21</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Tympanometry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Volume (mL)</td>
<td>1.2 (.32)</td>
<td>0.6/1.6</td>
<td>1.3 (0.31)</td>
<td>0.9/2.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>- Compliance (mL)</td>
<td>0.80 (.44)</td>
<td>0.13/2.3</td>
<td>0.71 (0.43)</td>
<td>0.3/1.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>- Pressure (daPa)</td>
<td>-8.4 (14)</td>
<td>-33/10</td>
<td>-3.1 (13)</td>
<td>-</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Stapedius reflexes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ipsi (dB HL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1000 Hz</td>
<td>86.3 (5.6)</td>
<td>80/100</td>
<td>88.7 (5.4)</td>
<td>80/100</td>
<td>n.s.</td>
</tr>
<tr>
<td>- 4000 Hz</td>
<td>85.0 (7.2)</td>
<td>80/100</td>
<td>91.3 (6.6)</td>
<td>80/105</td>
<td>=0.017</td>
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<tr>
<td><strong>Audiometry</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>- PTA, low frequencies</td>
<td>3.3 (3.8)</td>
<td>-1.2/13.7</td>
<td>5.9 (3.4)</td>
<td>1.2/12.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>(dB HL)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PTA, mid-frequencies</td>
<td>3.1 (5.0)</td>
<td>-3.3/16.7</td>
<td>2.8 (3.7)</td>
<td>-1.7/14.2</td>
<td>n.s.</td>
</tr>
<tr>
<td>(dB HL)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PTA, high frequencies</td>
<td>4.9 (5.3)</td>
<td>-4.2/14.2</td>
<td>5.0 (4.0)</td>
<td>-.8/13.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>(dB HL)*</td>
<td></td>
<td></td>
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</table>

*Pure tone audiometry (PTA) at low (250, 500 Hz), mid (1, 2, 3 kHz) and high (4, 6, 8 kHz) frequencies for both ears.

The inclusion criteria were normal air-conduction thresholds (<15 dB HL for frequencies between 250 and 8 kHz), normal tympanometry, stapedius reflexes at 1 and 4 kHz (< 100 dB SPL), and the presence of otoacoustic emissions (1 to 8 kHz, the groups did not differ, all Fs < 1) (see Figure 1). Exclusion criteria were the presence of an outer, middle or inner ear disorder, chronic tinnitus, neurological disorder, the presence of metal in the body, many fillings or tattoos (the presence of metal is contraindicated for magnetoencephalograms, because it interferes with signal capture).
Figure 1. Mean of otoacoustic emission levels (standard error of the mean) for the earplug group (blue) and the noise generator group (green), from 1000 to 8000 Hz for both ears.

Experimental material and protocols: The eligible participants obtained Starkey made-to-measure moulded earplugs (earplug group) or two Siemans Pure Life noise generators (noise generator group).

The attenuation and stimulation levels were symmetrical, i.e., 18.6 dB attenuation and 19.8 dB of stimulation for frequencies from 1 kHz to 4 kHz, as measured in situ by an electroacoustic analysis device (Affinity, Interacoustics) (see Figure 2).
Figure 2. Mean of attenuation levels (standard error of the mean) of earplugs (green) and stimulation from noise generators (blue) according to frequency

All the participants were tested as follows:

Tonal audiometry: Classic tonal audiometry and high-frequency tonal audiometry by half-octave steps (250 Hz–16 kHz) was carried out with an AC40 audiometer (Interacoustics) and Telephonics TDH-39P earphones for conventional frequencies (250 Hz to 8000 Hz), and Sennheiser HDA 200 earphones (Sennheiser Electronic GmbH & Co., Wedemark, Germany) for high frequencies.

Distortion product otoacoustic emission growth (DP growth) was evaluated from 45 to 75 dB with the ILO292 USB-II system (Otodynamics Ltd.).

Contralateral suppression of distortion product otoacoustic emissions (with and without contralateral noise) was measured with the IL0292 USB-II system (Otodynamics Ltd.). The stimuli used to generate transitory-type otoacoustic emissions were clicks at 70 dB SPL and the stimulus suppressor was white noise at 75 dB SPL.

The ipsilateral and contralateral stapedius reflexes were measured with the Interacoustics Titan system, using ER3-A insert earphones. The presentation level began at 70 dB HL and increased by steps of 1 dB until a compliance change equal to or more than 0.2 mL was obtained. When it was obtained, the program measured the compliance change again at the same value in dB to verify the stability of the measurement. If the compliance change was confirmed at the same value, the frequency was changed and the procedure continued until all the reflex thresholds for all the frequencies was obtained.

Otherwise, it continued to increase the intensity level until a compliance change of 0.2 mL or more was obtained twice in a row.
The amplitude and latency of brainstem auditory evoked potentials (ABR, waves I to V) were recorded with four electrodes: one on each mastoid, one at the vertex (Cz) and one grounded electrode on the forehead. The impedance reading had to be the same between the electrodes and below 5 kOhm to begin the experiment. The evoked responses were recorded using a BIOSEMI system and the width of the response filter was 100 to 1500 Hz. The stimuli used were clicks of 0.6 ms. punctuated by an inter-click interval of 70 ms. at 60, 70, 80, and 90 dB SPL levels with reversed polarity. The number of tests was 2500 per condition, which were presented pseudo-randomly in blocks of 1000 ms. ER-3A insert earphones were used to present the sounds.

The amplitude and latency of the auditory cortex evoked magnetic potentials (mNa, N100 and P200) were measured with 100 ms. of white noise, with 1000 ms. between clicks, under four conditions: 60, 70, 80, and 90 dB SPL. The conditions were presented pseudo-randomly in two blocks of nine minutes.

Recordings were done with a 275-channel Meg system (CTF 275 from VSM MedTech Ltd., Vancouver, Canada) with continuous sampling at a rate of 1200 Hz and a low-pass filter at 300 Hz. The head position was determined with coils attached to the nasion and the preauricular points.

The loudness functions were measured at 4 kHz with an adaptive automated method modified from the “loudness growth in half-octave bands” (LGOB [35]) procedure. The stimuli were chains of three frequency-modulated (FM) sounds of 300 ms. separated by 300 ms. of silence. In short, the program sought to determine the six limits between seven loudness categories (inaudible, very soft, soft, OK, loud, very loud, too loud). The limit between “inaudible” and “very soft” represents the hearing threshold; the limit between “very loud” and “too loud” represents the pain threshold. The listeners’ task was to choose into which category of loudness they would rank each stimulus presented by pressing one of the seven buttons on the response box. The task was programmed with MATLAB R2006a and automated with a Tucker-Davis Technologies System 3 (real-time signal processing system). The stimuli were calibrated with an SE SoundPro DL 1/3 octave level meter (Quest Technologies, WI, USA) coupled with an artificial EC-9A ear (Quest Electronics, Oconomowoc, WI, USA).

Sequence

The selection session lasted about two hours. All the participants were first informed about the study and had to read and sign the consent form before beginning any experimental procedure. If the individual was eligible and willing to participate in the study, a second session was scheduled approximately one week later. For the earplug group, impressions were taken of their ears at the end of the selection visit.

During the pretest session, the order of the tests was determined by the availability of rooms. The instructions given to participants consisted of wearing earplugs or noise generators from the time they woke up to when they went to bed. Foam earplugs (earplug group) and a table noise generator (noise generator group) were provided for the night. A second session was scheduled one week later. At this session, the magnetoencephalography task was generally carried out first, for logistical reasons. The participants arrived at the laboratory wearing their earplugs or noise generators and did not take them off until they started the experiment. The participants had to put their earplugs or noise generators back on between the various tasks and were not to remove them until just before the experiment began. The duration of each pre- and post-experimentation session was approximately four hours, interspersed with breaks. The
participants received $60 for their participation. Moreover, the participants in the earplug group were able to keep their earplugs and the participants in the noise generator group had the possibility of obtaining moulded earplugs at the end of the study.

**Statistical analyses**

Variance analyses (ANOVA) were carried out separately for each group.

More specifically, for distortion product otoacoustic emission growth (DP growth) an ANOVA (25 X 2) was conducted on the mean levels of distortion products, with stimulation levels (51 to 75) and time (pre-, post-experimentation) as repeated measurements.

For the contralateral suppression of distortion product otoacoustic emissions, an ANOVA (5 X 2 X 2 X 2) was conducted on the mean levels of otoacoustic emissions, with frequencies (1 to 4 kHz), condition (silence, with masking), ears (left, right) and time (pre-, post-experimentation) as repeated measurements.

For the stapedius reflexes, an ANOVA (2 X 2 X 2) was conducted on the threshold triggering levels, with frequencies (1 and 4 kHz), condition (ipsilateral, contralateral) and time (pre-, post-experimentation) as repeated measurements.

For the brainstem auditory evoked potentials (ABR, waves I to V) ANOVAs (2 X 3) were conducted on the values of amplitudes and latencies, with condition (pre-, post-experimentation) and waves (I, III and V) as repeated measurements.

For auditory cortex evoked magnetic potentials (N100m and P200m), ANOVAs (2 X 2 X 2 X 4) were conducted on the values of amplitudes and latencies, with the factors of session (pre-, post-experimentation), type of response (N100m, P200m), hemisphere (right, left), and levels (60, 70, 80, 90) as repeated measurements.

For loudness functions, ANOVAs (6 X 2 X 2) were conducted on the intensity levels of the limits of loudness categories, with categories (threshold to too loud), ears (left, right) and time (pre-, post-experimentation) as repeated measurements.

All the analyses were carried out with SPSS 22.0.0 software (SPSS Products, IBM Corp. 1989, 2013).

### 3.1.2 Results

Table 2 summarizes the results obtained for all of the variables analyzed. The main effect of experimentation (deprivation for the earplug group, stimulation for the noise generator group) was only observed for the amplitudes of cortical evoked potentials. The following sections describe the other effects observed.
Table 2. Summary of all the pre- and post-experimentation effects for each test

<table>
<thead>
<tr>
<th>Experimental Tests</th>
<th>Earplug Group</th>
<th>ANOVA</th>
<th>p Value</th>
<th>Noise Generator Group</th>
<th>ANOVA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth of distortion product otoacoustic emissions (dB SPL)</td>
<td>Pre-</td>
<td>5.9</td>
<td>.21</td>
<td>Pre-</td>
<td>3.5</td>
<td>.16</td>
</tr>
<tr>
<td></td>
<td>Post-</td>
<td>5.6</td>
<td>0.65</td>
<td>Post-</td>
<td>3.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Contra-lateral suppression of distortion product otoacoustic emissions (dB SPL)</td>
<td>Pre-</td>
<td>2.4</td>
<td>.56</td>
<td>Pre-</td>
<td>2.5</td>
<td>.00</td>
</tr>
<tr>
<td>loudness (dB SPL)</td>
<td>Post-</td>
<td>2.6</td>
<td>2.5</td>
<td>Post-</td>
<td>2.5</td>
<td>2.6</td>
</tr>
<tr>
<td>- Silence (dB SPL)</td>
<td>Pre-</td>
<td>3.3</td>
<td>0.56</td>
<td>Pre-</td>
<td>3.0</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Post-</td>
<td>3.2</td>
<td>2.5</td>
<td>Post-</td>
<td>2.6</td>
<td>2.5</td>
</tr>
<tr>
<td>- With masking noise (dB SPL)</td>
<td>Pre-</td>
<td>1.5</td>
<td>2.9</td>
<td>Pre-</td>
<td>3.6</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>Post-</td>
<td>2</td>
<td>2.5</td>
<td>Post-</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Triggering thresholds for stapedius reflexes (dB HL)</td>
<td>Pre-</td>
<td>88.2</td>
<td>2.9</td>
<td>Pre-</td>
<td>93.1</td>
<td>2.9</td>
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<tr>
<td></td>
<td>Post-</td>
<td>86.3</td>
<td>3.1</td>
<td>Post-</td>
<td>93.6</td>
<td>3.1</td>
</tr>
<tr>
<td>Brainstem auditory evoked potentials at 90 dB SPL (mean wave I, III, V)</td>
<td>Pre-</td>
<td>0.32</td>
<td>1.0</td>
<td>Pre-</td>
<td>0.31</td>
<td>2.4</td>
</tr>
<tr>
<td>- Amplitude (mV)</td>
<td>Post-</td>
<td>0.33</td>
<td>.31</td>
<td>Post-</td>
<td>0.32</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>F(1.10) = 1.0</td>
<td>F(1.10) =</td>
<td></td>
<td>F(1.12) = 2.4</td>
<td>F(1.12) =</td>
<td></td>
</tr>
<tr>
<td>- Latency (ms.)</td>
<td>Pre-</td>
<td>3.51</td>
<td>0.5</td>
<td>Pre-</td>
<td>3.61</td>
<td>3.59</td>
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<tr>
<td></td>
<td>Post-</td>
<td>3.52</td>
<td>0.5</td>
<td>Post-</td>
<td>3.59</td>
<td>3.59</td>
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<tr>
<td></td>
<td>F(1.10) = .5</td>
<td>F(1.10) =</td>
<td></td>
<td>F(1.12) = .5</td>
<td>F(1.12) =</td>
<td></td>
</tr>
<tr>
<td>Auditory cortex evoked magnetic potentials, averaged for all the levels (Score Z)</td>
<td>Pre-</td>
<td>11.7</td>
<td>7.8</td>
<td>Pre-</td>
<td>12.8</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Post-</td>
<td>13.3</td>
<td>7.8</td>
<td>Post-</td>
<td>11.5</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>F(1.12) = 0.016</td>
<td>F(1.12) =</td>
<td></td>
<td>F(1.13) = 3.2</td>
<td>F(1.13) =</td>
<td></td>
</tr>
<tr>
<td>Loudness function (dB SPL)</td>
<td>Pre-</td>
<td>72.6</td>
<td>5.6</td>
<td>Pre-</td>
<td>77</td>
<td>77.9</td>
</tr>
<tr>
<td></td>
<td>Post-</td>
<td>69.6</td>
<td>5.6</td>
<td>Post-</td>
<td>77</td>
<td>77.9</td>
</tr>
<tr>
<td></td>
<td>F(1.15) = 0.032</td>
<td>F(1.15) =</td>
<td></td>
<td>F(1.13) = .48</td>
<td>F(1.13) =</td>
<td></td>
</tr>
</tbody>
</table>
**Distortion product otoacoustic emission growth (DP growth)**

For both groups, there is a mean effect of sound level, with a higher level of otoacoustic emissions for higher levels of stimulation, $F(24.360) = 111.45, p < .001$, $F(24.336) = 84.93, p < .001$, for the earplug and the noise generator group, respectively (Figure 3).

![Graph showing distortion product otoacoustic emissions growth](image)

**Figure 3.** Mean level of distortion product otoacoustic emissions (standard error of the mean) for each level of stimulation in pre- (black) and post-experimentation (red) for the earplug (A) and noise generator (B) groups
Contralateral suppression of distortion-product otoacoustic emissions

For both groups, there is a main effect of condition (with or without contralateral noise), $F(1.14) = 48.1, p < .001$, $F(1.13) = 80.9, p < .001$ for the earplug and noise generator groups, respectively. This confirms that in the presence of contralateral noise, otoacoustic emissions in both groups were suppressed (Figure 4).

Figure 4. Mean level of transitory otoacoustic emissions (standard error of the mean) measured in silence and with contralateral noise (suppression), pre- (black) and post-experimentation (red), for the earplug (A) and noise generator (B) groups.
Stapedius and contralateral reflexes

For both groups, there is a main effect of condition (ipsilateral compared to contralateral) with the triggering threshold of the stapedius reflexes being higher contralaterally than ipsilaterally, $F(24.360) = 111.45$, $p < .001$ (84 dB HL ipsilaterally compared to 90 dB HL contralaterally), for the earplug group, and $F(24.336) = 84.93$, $p < .001$ for the noise generator group (89 dB HL ipsilaterally compared to 97 dB HL contralaterally) (Figure 5).

![Figure 5](image)

Figure 5. Mean triggering level of the stapedius reflex (standard error of the mean) for the averaged ipsilateral and contralateral condition, pre- and post-experimentation, at frequencies of 1 kHz (purple) and 4 kHz (orange), for the earplug (A) and noise generator (B) groups.

The brainstem auditory evoked potentials (ABR, waves I to V)

For both groups, there is a main effect of waves, $F(2.20) = 75.6$, $p < .001$ and $F(2.24) = 80.7$, $p < .001$, for the earplug and noise generator groups, respectively (Figure 6). As expected, the amplitudes of the three waves differed: that of wave V is the highest and that of wave I is the weakest.
For both groups, there is a primary effect of waves, $F(2.20) = 3163, p < .01$ et $F(2.24) = 2921, p < .001$, for the earplug and noise generator groups, respectively (Figure 6). As expected, the latency of the three waves differed: that of wave V is the longest and that of wave I, the shortest.

*The auditory cortex evoked magnetic potentials (N100m and P200m)*

The responses evoked were observed among all the participants in all sessions and for all conditions. The topography of responses is consistent with the bilateral sources of auditory cortices.

The analyses revealed that the amplitudes increase in the post-experimental session compared to the pre-experimental session for the earplug group ($p = .02$), and inversely for the noise generator group (amplitudes decreased in the post-session compared to the pre-session, $p = .05$) (Figure 7A). A significant effect of intensity was also observed, $F(3.75) = 3.17, p = .02$: the amplitude of 90 and 80 dB stimulations is greater than those of 70 and 60 dB stimulations (all the $ps < .014$, see Figure 7B).

**Figure 6.** Amplitude (A, B) and latency mean (C, D) of brainstem auditory evoked potentials (standard error of the mean), pre- and post-experimentation, for the earplug (A, C) and noise generator (B, D) groups, for stimulation at 90 dB SPL only.
Figure 7. Amplitude of N100m and P200m responses
(A) Mean amplitudes for conditions 90, 80, 70, and 60 dB, according to group and session
(B) Main effect of mean intensity for both groups and sessions (standard error of the mean)

Loudness functions

For the earplug group, loudness functions shift considerably to the left (sensitization) for all the limits of the loudness categories after one week of deprivation, $F(1.15) = 5.6, p = .032$ (on average 72.6 dB HL in pre-experimentation compared to 69.6 dB HL in post-experimentation).

For the noise generator group, although the data point to less sensitivity, the difference is not significant, $F<1$, (on average, 77 dB HL in pre-experimentation compared to 77.9 dB HL in post-experimentation) (Figure 8).

Figure 8. Mean of intensity level for each of the loudness categorization limits (standard error of the mean) in pre- (black) and post-experimentation (red) (average of right and left ears) for the earplug (A) and noise generator (B) groups
3.1.3 Discussion

The results of the first study show that after one week of temporary hearing deprivation or stimulation at comparable levels, the auditory system compensates by amplifying sound after deprivation and by lowering it after stimulation. This change takes place at the highest level of the auditory system, in the cortex. In fact, no change was observable in the lower levels of the auditory pathways, i.e., the cochlea (by the growth of distortion product otoacoustic emissions), the brainstem (by stapedius reflexes) and auditory nerve evoked responses (by waves I, III, and V).

The results are consistent with those from a study that documented changes in loudness judgments (Formby, Sherlock et al. 2003) for similar deprivation durations, i.e., when sensitivity to sounds sharpens after deprivation so that sounds become louder than before it. However, while there is a tendency towards less sensitivity after a week of stimulation, the results of the loudness judgment task were not significant. The reason for this result is not clear, because the task used is adaptive and thus should be very sensitive. It may be that the hearing sensitivity of the participants in the noise generator group was already at a maximum level in each category and that additional stimulation changed nothing since a ceiling effect was already present. This appears plausible, given that the participants chose which group they wanted to be in (noise generators or earplugs). It is also compatible with the results of their stapedius reflexes, which were higher than those of the earplug group, even in the pretest. Along the same lines, weaker stapedius reflexes in the earplug group may have prompted the participants to choose the “protection” group instead of the stimulation group. Given that group assignment was one of convenience and not random, this possibility cannot be ruled out.

This is the first time that a study has exhaustively and systematically examined human auditory pathways, which makes it original and novel. Indeed, a number of studies have documented behavioural effects or effects (sometimes mixed) on the stapedius reflexes (Formby, Sherlock et al. 2003, Sherlock and Formby 2005, Formby, Gold et al. 2007, Munro, Walker et al. 2007, Munro and Merrett 2013), but none have explored all of the auditory pathways in the same participants. A recent animal study (Chambers, Resnik et al. 2016) reported that almost complete destruction of the auditory nerve (95% of the related synapses, but preservation of the hair cells), which eliminated brainstem responses and the acoustic startle reflex, kept sound detection intact. This response is associated with increased cortical activity that compensates for the peripheral damage. Although the study caused permanent and non-transitory loss, the results described are consistent with this one.

The concept of central auditory gain is thus partially supported by these data gathered from normal subjects, as well as by the animal data. A maladjusted central gain is suggested as being the origin of tinnitus and hyperacusis.

However, could this gain be modulated in people with cochlear damage? The second study examined this question by having participants with tinnitus wear noise generators.
3.2 Study 2

The objective of Study 2 was to demonstrate gain modulation through the use of noise generators by workers with tinnitus and to examine whether a potential modulation is associated with subjective improvement. Some studies (Munro and Trotter 2006, Munro, Walker et al. 2007, Munro and Merrett 2013, Munro, Turtle et al. 2014) suggest that central gain modulation is functional in cases of deafness and hyperacusis. However, it is not known whether the central gain can be modulated in cases of tinnitus, and whether this modulation is visible on the psychoacoustic parameters of tinnitus, hearing sensitivity, and subjective intensity (distress related to the tinnitus, visual analogue scales).

The primary hypothesis is that wearing noise generators will reduce hearing sensitivity and the subjective intensity of tinnitus, and, consequently, psychological distress. The workers will be monitored over time to examine whether the modulation is stable and whether it varies with the degree of hearing loss.

3.2.1 Methodology

Participants

Fourteen workers (4 women, 10 men) with chronic unilateral (n= 4) or bilateral (n= 10) tinnitus were recruited by word-of-mouth or by using posters. The average age was 53.6 (range: 41 to 66 years) with an average of 16.9 years of education (range: 11 to 24 years). The participants had tinnitus for 10 years on average (range: 6 months to 23 years). In order to examine the contribution of hearing loss, the participants were separated into two groups of seven, i.e., a group without hearing loss and a group with hearing loss. The group without hearing loss had to have thresholds ≤ 40 dB HL at all frequencies between 250 Hz and 8 kHz in both ears. The participants with hearing loss had thresholds of > 40 dB at least one frequency between 250 Hz and 8 kHz, in at least one ear. The averages of hearing thresholds by frequency for each ear, in each of the groups, is presented in Figure 9.
Figure 9. Hearing threshold means of the right and left ears (standard deviation) in the group without hearing loss and the group with hearing loss.
The inclusion criteria were having chronic tinnitus (≥ 6 months) and stapedius reflexes present in ipsilateral condition at the frequencies of 1 k and 4 kHz (≤100 dB SPL), and not having more than 10 dB of difference between the thresholds in both ears. The exclusion criteria were having a disorder of the outer, middle or inner ears (e.g., agenesis of the ear canals, earwax plug, tympanic membrane perforation, otitis), or a neurological disorder (e.g., neuroma, multiple sclerosis).

**Experimental material and protocols**

Tonal audiometry: Classic tonal audiometry and high-frequency audiometry by half octave steps (250 Hz–16 kHz) was carried out with an AC40 audiometer (Interacoustics) and Telephonics TDH-39P earphones for conventional frequencies (250 Hz to 8000 Hz), and Sennheiser HDA 200 earphones (Sennheiser Electronic GmbH & Co., Wedemark, Germany) for high frequencies.

The participants were also assessed using our tinnitus assessment battery. The battery is described in detail in a previously published article (Basile, Fournier et al. 2013). Briefly, the participant sits in front of a touchscreen and must rate how closely each pure sound, presented binaurally, resembles their tinnitus, on a scale of 0 to 10 (0 = “does not match my tinnitus at all” and 10 = “perfectly matches my tinnitus”). The subject must also adjust the sound level with a visual gauge so that it is at the same volume as the tinnitus. All frequencies from 250 Hz to 16 kHz are presented, by half octave. The participants were also tested on loudness functions (see Study 1, page 5 for the description of the task).

Finally, the following questionnaires (for more details, see the appendices) were used:

**Satisfaction with Life Scale** (Diener, Emmons et al. 1985): The “Satisfaction with Life Scale” is a five item instrument to assess satisfaction with life. For each statement, the participants must determine on a scale of 1 (strongly disagree) to 7 (strongly agree) their level of agreement or disagreement. The total score in this questionnaire is between 5 and 35 points. The degree of satisfaction with life is categorized as follows: extremely dissatisfied (5-9), dissatisfied (10-14), slightly dissatisfied (15-19), neutral (20-24), satisfied (25-29), and extremely satisfied (30-35).

**Hyperacusis Questionnaire** (Khalfa, Dubal et al. 2002): The “Hyperacusis Questionnaire” consists of 14 items rated from 0 to 3, where 0 = no; 1 = yes, a little; 2 = yes, quite a lot; and 3 = yes a lot. The total score, which is obtained by adding all the items, is between 0 and 42 (maximum sensitivity).

**Tinnitus Handicap Questionnaire (THQ)** (Kuk, Tyler et al. 1990): This questionnaire reflects the degree to which the patient feels handicapped because of the tinnitus. Patient must rate each of the 27 phrases in the questionnaire from 0 to 100. This score represents the degree to which the patient agrees with the statement. The total score is calculated in percentages and a high percentage corresponds to a major handicap.

**V.A.S.**: Visual analogue scales (VAS) measure subjective characteristics and are widely used in intervention studies. The subject must indicate, on a continuous 10-cm line, his or her level of agreement with a statement. The calculation is made using a ruler to measure the distance between the far left of the line and the line drawn by the participant. Five scales were used: (1) current intensity of the tinnitus, (2) intensity of the tinnitus in the past week, (3) current annoyance level, (4) annoyance level last week, and 5) hearing sensitivity. High scores designate a high level of intensity and annoyance.
Adjustment of noise generators: the level of white noise of the generators was adjusted by using the following algorithm (Figure 10):

**Figure 10. Algorithm to adjust noise generators in Study 2**
The levels of stimulation measured at the eardrum for both groups are presented in Figure 11.

![Figure 11](image)

Figure 11. Mean of the stimulation levels measured at the eardrum according to frequency (standard error of the mean) for each of the groups

**Sequence**

The selection session lasted about two hours. All the participants were first informed about the study and had to read and sign the consent form before beginning any experimental procedure. If the individual was eligible and willing to participate in the study, a second session was scheduled approximately one week later, or at the participant’s convenience. During the pretest session, the order of the tests was determined by the availability of rooms. The instructions given to participants consisted of wearing noise generators for as long as possible, from the time they woke up to when they went to bed. A summary of tasks for the experimentation sessions is illustrated in Figure 12.
3.2.2 Results

**Audiometry:** The aerial thresholds for frequencies from 250 Hz to 8 kHz were 10±7.9 and 13.3±8.8 dB HL for the right and left ears, respectively, in the “without loss” group. For frequencies from 9 to 16 kHz, the thresholds were 34.5±21.1 and 38.5±19.1 dB HL for the right and left ears, respectively. For the “with loss” group, the aerial thresholds for the frequencies from 250 Hz to 8 kHz were 32.2±13.0 and 34.8±13.4 dB HL for the right and left ears, respectively. For frequencies from 9 to 16 kHz, the thresholds were 67.5±13.3 and 66.0±15.0 dB HL for the right and left ears, respectively (Figure 9).

**Tinnitus assessment battery:** For the “without loss” group, a decrease in the overall tinnitus loudness (all frequencies combined) was observed, ranging from 29.6±22.1 dB HL before the activity to 25.9±7.3 dB HL at 1 week post-experimentation, to 21.9±17.3 dB HL at 3 weeks post-experimentation, and reverting to 24.7±19.7 dB HL after one month. For the “with loss” group, a lesser decrease was also observed, with 35.4 ±17.0 dB HL before the activity, to 36.2±14.7 dB HL at 1 week post-experimentation, to 31.0±20.7 dB HL at 3 weeks post-experimentation, and to 34.8±16.0 dB HL after one month. Figure 13 shows the loudness for each frequency in the four measurement periods for each group.
Figure 13. Mean of tinnitus intensity level for each frequency in the four measurement periods for each group

_Loudness function_: For loudness functions, a slight increase in the levels in each category was observed, especially in the last categories. For example, for the “without loss” group, the
average level in the “OK/Loud” category rose from 98.95 dB at pre-experimentation to 100.3 dB at 3 weeks post-experimentation, from 105.3 to 106.5 in the “Loud/Very Loud” category, and from 109.7 to 110.3 in the “Very Loud/Too Loud” category. For the “with loss” group, the average level in the “OK/Loud” category went from 96.4 at pre-experimentation to 97.9 at 3 weeks post-experimentation, from 102.3 to 104.3 in the “Loud/Very Loud” category, and from 107.4 to 108.2 in the “Very Loud/Too Loud” category. Figure 14 illustrates the 3 week pre- and post-experimentation loudness functions for both groups.

Figure 14. Intensity level mean for each of the loudness categorization limits in pre- and post-experimentation at the three week period for the “without hearing loss” and “with hearing loss” groups

Loudness functions and tinnitus loudness: Figure 15 illustrates the increase in levels of the higher categories of loudness functions (Very Loud/Too Loud, Loud/Very Loud, and OK/Loud) in conjunction with the decrease in tinnitus loudness for 1 week pre-and post-experimentation, and 3 weeks post-experimentation sessions, with a slight return towards the pre-experimentation values 1 month post-experimentation for both groups. The effect is more pronounced for the “without loss” group.
Figure 15. Mean of the upper levels of loudness categories and mean of tinnitus intensity (standard error of the mean) for both groups in the four measurement periods.
Questionnaires:

*Satisfaction with Life:* No improvement was observed in the responses to the *Satisfaction with Life* questionnaire from both groups (see Table 3).

*Hyperacusis Questionnaire:* No improvement was observed in the responses to the *Hyperacusis Questionnaire* from both groups (see Table 3).

*Tinnitus Handicap Questionnaire:* A slight improvement was observed for the “without loss” group, but no improvement was noted for the “with loss” group (see Table 3).

| Table 3. Results from the questionnaires for the “without loss” and “with loss” groups |
|---------------------------------|-------------|-------------|
| Satisfaction with Life          | Without loss| With loss   |
| Pre-exp.                        | 29          | 29          |
| 3 weeks post-exp.               | 30          | 29          |
| 1 month post-exp.               | 29          | 30          |
| Hyperacusis Questionnaire       |             |             |
| Pre-exp.                        | 17          | 19          |
| 3 weeks post-exp.               | 16          | 19          |
| 1 month post-exp.               | 18          | 21          |
| Tinnitus Handicap Questionnaire |             |             |
| Pre-exp.                        | 31.2        | 38.7        |
| 3 weeks post-exp.               | 26.2        | 36.3        |
| 1 month post-exp.               | 26.7        | 39.9        |

*VAS:* On the visual analogue scales, an improvement was observed between the measurement periods (overall values of 5.0, 3.4, 3.1 at pre-experimentation, 1 week post-experimentation, and 3 weeks post-experimentation) and a return to the pre-experimentation level (4.8) at the 1 month post-experimentation follow-up for the “without loss” group, but not for the “with loss” group (overall values of 5.2, 5.3, 5.7 and 6.1 at pre-experimentation, 1 week post-experimentation, 3 weeks post-experimentation, and 1 month post-experimentation), (see Figure 16).
The data from the second study, although it included only a limited number of participants, suggest that wearing noise generators for three weeks can modulate both tinnitus loudness and loudness functions. This study is the first ever to have jointly examined two different tasks (tinnitus loudness and loudness functions) that use intensity modulation possibly originating from a common mechanism, the central auditory gain. Most studies (Hobson, Chisholm et al. 2010) have examined subjective loudness scales and therefore cannot draw conclusions about the potential mechanism. In addition, the improvement appears to be greater among participants without hearing loss at standard frequencies and is subjective (at least in the short term), as measured by the visual analogue scales. However, among participants with hearing loss, despite a slight improvement with respect to tinnitus loudness overall, the first four visual scales suggest deterioration over time, a somewhat surprising result. One possible explanation is that for participants with hearing loss, adding noise without adequate amplification may be harmful in the long term, and becomes annoying over time. A recent study that compared two groups of participants with hearing loss and tinnitus (dos Santos, Bento et al. 2014), one with a
combination of amplification and noise generators and the other with amplification only, revealed similar improvement in reducing the annoyance caused by tinnitus. However, the single effect of a noise generator was not examined in that study, which limits a direct comparison with ours. Another study (Schaette, Konig et al. 2010) compared participants with tinnitus who were wearing noise generators or devices on the basis of the frequency of their tinnitus. The group that had tinnitus at < 6 kHz experienced a drop in the intensity of their tinnitus (visual analogue scale), while those with tinnitus at ≥ 6 kHz had a slight increase (insignificant) in its intensity. However, in this study, hearing loss was a confounding variable, because the participants were not divided into groups according to that variable. Because the frequency spectrum of tinnitus is in the hearing loss, the group of participants with tinnitus below 6 kHz could have had greater hearing loss at the frequencies targeted by the devices and thus benefit from a greater amplification effect, while those with tinnitus above 6 kHz, with slight loss and little stimulation, would not have benefited from amplification or stimulation. The absence of amplification in this study was deliberate because adding amplification to the sound generators would have compared two activities with one. A future study could address this issue.

The scores on the standard Satisfaction with Life Questionnaire, already very high at baseline, were not sensitive to the effects of the activity. Also, the scores on the Tinnitus Handicap Questionnaire and the Hyperacusis Questionnaire showed slight drops as the activity progressed. As the questions on these scales are very general (e.g., “Do you feel frustrated because of your tinnitus?”), they may not be ideal for this type of activity, or the activity may not have been long enough to measure an overall change in the impact of tinnitus on all aspects of daily life.

Since no changes were noted in the peripheral auditory structures in the first study, we can assume that the change in gain observed in the second study is located in the auditory cortex of participants with tinnitus. However, it is also possible that for patients with tinnitus, other cortical and subcortical structures are involved in gain modulation. Given that the protocol did not include data from the cortical and subcortical areas, such as brainstem auditory evoked potentials or the magnetoencephalography, this was not possible to confirm.

These ground-breaking and very encouraging data suggest that the number of participants per group should be increased in order to perform inferential statistics in addition to the descriptive statistics carried out here.
3.2.4 Limits of Study 2

The manner in which Study 2 was conducted deviates somewhat from the original project, mainly in terms of sample size and participant profiles. These differences in the samples represent the contrast between theory and reality in the field, with respect to recruitment. In fact, despite sustained recruiting efforts (several ads in targeted journals, use of audiology clinics and the university clinic database where more than 200 files were reviewed), we were unable to recruit the targeted number of 30 workers, and were only able to recruit 14. These workers were then divided into two groups based on hearing condition (with and without loss) because, although more than 80 people were contacted, it was not possible to find workers with tinnitus and without hearing loss who met the strict inclusion/exclusion criteria and who wanted to participate in such a busy protocol, which required a great deal of time and participation in several laboratory sessions. The pre-experimentation, one week post- experimentation, three weeks post-experimentation and one month post-experimentation selection sessions, which were to take place on specific dates over a minimum period of two months, represented a total of approximately 18 hours of participation, in addition to the requirement of wearing noise generators for 3 weeks, 24 hours a day (using table generators at night). It was therefore decided along the way to include workers with slight to moderate hearing loss, who represent a substantial subgroup of people suffering from tinnitus, and thus not to deprive the volunteers of a potentially beneficial activity. This addition of a “with loss” subgroup appeared to be largely offset by the finding that noise generators may not be a solution for workers with hearing loss, but they are likely to be for workers without hearing loss. In addition, this group served as a control group for multiple repetitions of the same tests over time. Indeed, the improvement experienced by the “without loss” group could not be attributed to a task-learning effect, because the “with loss” group improved very little or not at all. These two points were unanticipated positive additions to this study.

It is important to note that recruitment difficulties are common. A recent study (Bauer, Berry et al. 2016) reports that the difficulty of recruiting participants with tinnitus in intervention studies is considerable and surprising, given the severity and the distress reported by that population. For example, 21% of participants who responded to the recruitment ads subsequently indicated that they were not interested because they did not want to wear the hearing aids provided free of charge and be obliged to travel for treatment and follow-ups. The enrolment rate in the study varied from 3.5 to 11.9% depending on the study sites, for a total of 36 people out of 568 (6.3%) over a 17-month recruitment period. Another intervention study (Piccirillo, Finnell et al. 2007) reported that out of 1028 participants with tinnitus who were recruited, 259 came for screening, and 135 eventually participated, representing a rate of 13%. Thus, the 17.5% rate for this study, with a recruitment period of approximately eight months compares favourably with other studies.
4. CONCLUSION

To conclude, the two studies described in this report are consistent with the idea that the central gain mechanism is present and functional among people with normal hearing, and among people suffering from tinnitus, especially when the latter do not have hearing loss according to clinical standards. These studies are the first to suggest (1) the existence and functional location of the central gain in humans, and (2) that the loudness of external sounds and of tinnitus can be jointly modulated by the use of noise generators by people with chronic tinnitus. This last observation, unprecedented in current scientific literature, is a promising prospect for patients with chronic tinnitus.

Of course, a number of questions remain unanswered, both for people with normal hearing and those with tinnitus. For example, would a longer period of deprivation or stimulation increase cortical compensation and therefore a modulation in the gain? Among people with tinnitus, would prolonging stimulation be even more beneficial or would the gain modulation be limited in their case? How long do the effects last? Can we observe central gain modulation in the auditory cortex of people with tinnitus? As well, since the amplification function was not activated in this study to avoid introducing two elements instead of one (amplification plus noise generator stimulation), could people with hearing loss benefit more from amplification or from amplification coupled with noise generators?

Finally, several new studies could arise from this one. For example, the next step could be to vary the time frame of the activity to determine the ideal duration and to examine cortical responses based on it. At the same time, a clinical protocol could be established to determine whether objective and subjective loudness measurements could improve the quality of life of people suffering from tinnitus.


APPENDICES

Satisfaction with Life

Below are five statements that you may agree or disagree with. Using the 1 to 7 scale below, indicate your agreement with each item by placing the appropriate number on the line to the right of that item. Please be open and honest in your responses.

7 – Strongly agree
6 – Agree
5 – Slightly agree
4 – Neither agree or disagree
3 – Slightly disagree
2 – Disagree
1 – Strongly disagree

1. In most ways, my life is close to my ideal. _____
2. The conditions of my life are excellent. _____
3. I am satisfied with my life. _____
4. So far I have gotten the important things I want in life. _____
5. If I could live my life over, I would change almost nothing. _____
HYPERACUSIS QUESTIONNAIRE

Surname, first name: 
SEX: ☐ Male ☐ Female

*Do you tolerate noise less well than most people?  
*Do you tolerate noise less well compared to a few years ago?  
*Have you ever had hearing problems? If so, of what kind?

*In the following questionnaire, put a cross in the box corresponding to the answer which best applies to you (no; yes, a little; yes, quite a lot; yes, a lot).

1. Do you ever use earplugs or earmuffs to reduce your noise perception?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

2. Do you find it harder to ignore sounds around you in everyday situations?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

3. Do you have trouble reading in a noisy or loud environment?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

4. Do you have trouble concentrating in noisy surroundings?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

5. Do you have difficulty listening to conversations in noisy places?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

6. Has anyone you know ever told you that you tolerate noise or certain kinds of sound badly?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

7. Are you particularly sensitive to or bothered by street noise?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

8. Do you find the noise unpleasant in certain social situations (e.g., night clubs, pubs or bars, concerts, cocktail receptions)?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

9. When someone suggests doing something (going out, to the cinema, to a concert, etc.) do you immediately think about the noise that you are going to have to put up with?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

10. Do you ever turn down an invitation or not go out because of the noise you would have to face?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

11. Do noises or particular sounds bother you more in a quiet place than in a slightly noisy room?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

12. Do stress and tiredness reduce your ability to concentrate in noise?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

13. Are you less able to concentrate in noise towards the end of the day?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot

14. Do noise and certain sounds cause you stress and irritation?  
□ No □ Yes, a little □ Yes, quite a lot □ Yes, a lot
**Tinnitus Handicap Questionnaire**  
*(Kuk et al., 1990)*

Instructions: Please indicate your degree of agreement with each statement by scoring them between 0 (strongly disagree) and 100 (strongly agree).

1. I have support from my friends regarding my tinnitus. _____
2. Tinnitus creates family problems. _____
3. My tinnitus has gotten worse over the years. _____
4. I do not enjoy life because of tinnitus. _____
5. The general public does not know about the devastating nature of tinnitus. _____
6. I am unable to follow conversation during meetings because of tinnitus. _____
7. Tinnitus affects the quality of my relationships. _____
8. I think I have a healthy outlook on tinnitus. _____
9. I cannot concentrate because of tinnitus. _____
10. Tinnitus causes me to avoid noisy situations. _____
11. Tinnitus contributes to feeling of general ill health. _____
12. Tinnitus interferes with my ability to tell where sounds are coming from. _____
13. Tinnitus makes me feel annoyed. _____
14. I am unable to relax because of tinnitus. _____
15. Tinnitus makes me feel insecure. _____
16. Tinnitus makes me anxious. _____
17. I feel frustrated frequently because of tinnitus. _____
18. Tinnitus makes me feel tired. _____
19. Tinnitus causes me to feel depressed. _____
20. Tinnitus interferes with my speech understanding when listening to the television. _____
21. Tinnitus has caused a reduction in my speech understanding ability. _____
22. Tinnitus interferes with my speech understanding when talking to someone in a noisy room. _____
23. I find it difficult to explain what tinnitus is to others. _____
24. I complain more because of tinnitus. _____
25. I have trouble falling asleep at night because of tinnitus. _____
26. I feel uneasy in social situations because of tinnitus. _____
27. Tinnitus causes stress. _____
**My tinnitus on a visual analogue scale.**

1. On a scale from “not annoying” to “very annoying,” mark a cross on the line at the location that best corresponds to your tinnitus **over the past week**.

   - ______________________ +

   Not annoying               Very annoying

2. On a scale from “not annoying” to “very annoying,” mark a cross on the line at the location that best corresponds to your tinnitus **now**.

   - ______________________ +

   Not annoying               Very annoying

3. On a scale from “very soft” to “very loud,” mark a cross on the line at the location that best corresponds to the sound level of your tinnitus **over the past week**.

   - ______________________ +

   Very soft                  Very loud

4. On a scale from “very soft” to “very loud,” mark a cross on the line at the location that best corresponds to the sound level of your tinnitus **now**.

   - ______________________ +

   Very soft                  Very loud

5. On a scale from “not at all sensitive to loud sounds” to “very sensitive to loud sounds,” mark a cross on the line at the location that best corresponds to your hearing sensitivity **over the past week**.

   - ______________________ +

   Not at all sensitive to loud sounds               Very sensitive to loud sounds