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EFFECTS OF MAGNESIUM ON TEMPORARY THRESHOLD SHIFT

By

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An Audiology Doctoral Project

Submitted to the Graduate Faculty of the Department of Communication Sciences and Disorders in partial fulfillment of the requirements for the degree of Doctor of Audiology

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ABSTRACT


Previous literature has demonstrated that supplemental magnesium may have a prophylactic effect on noise induced hearing loss (NIHL). The purpose of this study was to replicate the findings of a previous investigation concerning the beneficial effects of supplemental magnesium on TTS in humans. Forty participants with normal hearing were divided into two groups, experimental and control. The experimental group received a single, 150 mg dose of supplemental magnesium and the control group received a placebo. After an hour in a quiet environment, all participants were exposed to a narrowband noise centered at 2000 Hz and presented at 105 dB SPL. Audiometric thresholds were measured for the frequency range 250 Hz - 8000 Hz prior to the noise exposure, and then immediately, 30 minutes, and 60 minutes post-noise exposure. Both groups experienced TTS at and above 2000 Hz. The largest TTS was observed immediately following the noise exposure in both groups. There was no significant difference in TTS between the experimental group and the control group. It was concluded that a single dose of 150 mg of supplemental magnesium was not effective in reducing or preventing TTS.
INTRODUCTION

According to the National Institute on Deafness and Other Communication Disorders, over thirty million people in the United States are regularly exposed to hazardous noise levels, both in the workplace and elsewhere. Twenty-eight million Americans have hearing loss, and excessive noise exposure is reported to contribute to the cause of hearing loss in fully one third of those cases (www.nidcd.nih.gov/health/pubs hb/noise.htm#who). The World Health Organization reported in 2001 that 12% of the world population is at risk for developing noise-induced hearing loss (NIHL) (Niu and Canlon, 2001).

The effects of noise on hearing can be measured by examining audiometric thresholds. A baseline test is necessary in order to determine a shift in hearing sensitivity following noise exposure. Noise overexposure causes physical damage to the auditory system and is evidenced by temporary threshold shift (TTS) and permanent threshold shift (PTS), depending on the intensity and duration of exposure. A TTS is a period of decreased hearing sensitivity that may last up to 16 or more hours (Gelfand, 1998). As time passes, hearing sensitivity gradually returns to normal. Long term exposures to excessive noise or single, intense acoustic events may cause a PTS, in which hearing sensitivity does not recover.

According to Liberman (1990) the metabolism inside hair cells in the cochlea is altered by high-level noise. As with the central nervous system, excess excitatory amino acids cause an osmotic imbalance of neurotransmitters within the inner hair cells following acoustic trauma. The excitatory amino acid in the inner hair cells, believed to be glutamate, acts as a neurotransmitter and is excitotoxic during overstimulation. This
excitotoxicity causes extended depolarization of postsynaptic receptors leading to acute swelling and potential cell death, as afferent receptors retract from the synapse with the hair cells. In a TTS, these synapses are thought to repair as the receptors reconnect to the hair cells, and threshold recovery takes place (Puel et al, 1998). Repeated exposure causes the hair cells to die, and results in a PTS (Liberman, 1990).

One of the main safeguards against the hazardous effects of noise overexposure on the auditory system is hearing protection devices (HPDs). Occupational Safety and Health Administration (OSHA) mandates the use of hearing protection devices in the workplace along with a “continuing, effective hearing conservation program” when noise meets or exceeds specified levels. Hearing conservation programs educate employees about noise, noise induced hearing loss, and proper use of hearing protection devices (Lipscomb, 1994). Although hearing protection devices afford some protection from the damaging effects of noise, these methods are only partially effective, since hearing loss still occurs due to noise damage, and no procedures exist for those who work in lower level noise. Furthermore, there is no government regulation of excessive noise exposure from non-occupational sources.

Since hearing loss due to excessive noise exposure continues to account for such a large proportion of overall hearing loss, it is important for researchers and professionals to consider options, in addition to traditional hearing protection devices, as possible methods to decrease the impact of excessive noise. One option that may offer potential to diminish the impact of noise on hearing is the use of supplemental magnesium.

The effects of supplemental magnesium on NIHL were previously investigated by Scheibe, Haupt, & Ising (2000) who studied these effects in guinea pigs. The animals
were divided into two groups. One group was fed a low magnesium diet and the other a high magnesium diet. On each animal, one ear was exposed to 187 dB SPL impulse noise and the other ear to a series of 1000 impulses at 150 dB followed by a series of 2280 impulses at 167 dB. Threshold shifts were measured using auditory brainstem response testing (ABR) at 2 hours post-exposure and at one week post-exposure. For the ears exposed to 187 dB impulse noise, guinea pigs with a high magnesium intake had a significantly lower mean TTS than the animals with a low magnesium intake. No PTS occurred. For the ears exposed to the series of impulse noise, animals with high magnesium intake demonstrated a trend of reduction in mean PTS following the 150 dB exposure. Significantly lower mean TTS and PTS were observed following the 167 dB exposure. This investigation agrees with an earlier study by Joachims, et.al (1983) who found significantly less NIHL in rats fed a magnesium-rich diet versus rats fed a magnesium deficient diet. In this study the magnesium concentration of perilymph was measured and was found to negatively correlate with hearing loss.

Similar results have been reported in humans. Attias et al. (1994) conducted a study on human subjects exposed to high-level impulse noise. Three hundred military recruits exposed to repeated high-level impulse noise during two months of basic training were included in a double-blind study. One hundred fifty participants received a daily supplemental magnesium drink containing 167 mg of magnesium while the other one hundred fifty subjects received a placebo drink. Subjects who received the magnesium supplement had less severe and less frequent noise induced PTS than the subjects who received the placebo. Additionally, no “notable” side effects were observed in any subjects.
According to Attias et al. (1994), intracellular magnesium may contribute to individual susceptibility to NIHL. Magnesium controls energy utilization and cellular membrane permeability and is an essential nutrient (Walden, Henselman, & Morris, 2000). When an increase in energy consumption or a decrease in energy supply occurs, the risk of temporary or permanent decreased cellular function rises. This includes cochlear hair cells (Attias et al, 1994). Because magnesium plays a vital role in regulating cellular energy consumption, an individual with magnesium deficiency may be at an increased risk for NIHL.

The results of Attias et al. (1994) are in agreement with an earlier study by Joachims et al. (1987). In the Joachim et al. study, serum magnesium levels of Israeli military pilots were negatively correlated with audiometric thresholds at 3, 4, and 5 kHz. In other words, lower serum magnesium levels were measured in individuals with poorer audiometric thresholds for frequencies typically affected by NIHL.

Although the results of Attias et al. (1994) and Joachims et al. (1987) support a protective influence of magnesium on the auditory system, the same finding was not observed by Walden et al. (2000). Naturally occurring magnesium levels in sixty-eight soldiers exposed in training to high-level weapon noise were studied. Fasting blood samples were obtained along with pure tone audiometric data. No correlation between natural magnesium levels and audiometric thresholds was observed. It is important to note that Walden et al. (2000) and Joachims et al. (1987) provided no supplemental magnesium to subjects.

Most recently, Gupta (2002) reported a significant difference in TTS for human subjects provided with a single, 150 mg dose of supplemental magnesium when
compared to subjects given a placebo. Both groups of subjects were exposed for 5 minutes to 100 dB SPL of narrowband noise centered at 4000 Hz. Audiometric thresholds were measured pre- and post-exposure. The greatest shifts were observed at threshold frequencies at and above 4000 Hz. Gupta (2002) suggested that magnesium affects the cochlea at the level of the outer hair cells. According to Gupta (2002), this is a prominent site where metabolism of magnesium takes place in the cochlea.

It is clear that the potential prophylactic effects of supplemental magnesium warrant further research. Importantly, in Gupta (2002) a significant effect was observed using a single dose of magnesium provided over a short period of time. In previous studies, significant effects were observed after long-term dosage of supplemental magnesium. To our knowledge, Gupta (2002) is the first report to demonstrate almost immediate prophylactic effects of supplemental magnesium on the effects of noise exposure. Therefore, the purpose of this study was to examine the effects of a single 150 mg dose of supplemental magnesium on TTS by replicating the investigation of Gupta (2002).

METHODS

Participants

Forty volunteers were selected from the Tampa Bay area and University of South Florida (USF) to participate in this investigation. Participants were between the ages of 20 – 39 with a mean age of 26.5 years, and had no history of hearing loss or recent excessive noise exposure. Recent excessive noise exposure was defined as an acoustic event (i.e., concert, car race, etc.) that caused tinnitus, aural pressure, or decreased hearing sensitivity. Participants were also excluded if there was a positive history of
excessive noise exposure. This history was determined through a questionnaire
developed for this study (Appendix). To be eligible for this study, participants had to
demonstrate normal hearing determined by standard audiometric procedures. Normal
hearing was defined as pure tone thresholds \( \leq 20 \text{ dB HL} \) from 250 to 8000 Hz, including
inter-octave frequencies. Normal middle ear function was determined by standard
tympanometry, and acoustic reflex assessment at 1000 Hz.

Participants also presented with normal cochlear function. Cochlear function was
assessed by measuring DPOAEs. Normal function was defined as a signal-to-noise ratio
\( \geq 6 \text{ dB} \), with normal amplitudes at each frequency determined by comparison to
published normative data (Gorga et al, 1997).

Participants were randomly divided into two groups, with one group receiving
supplemental magnesium and the other group receiving a placebo pill. Average
audiometric data for each group is shown in Table 1. Participants were not compensated
financially, but may have received extra credit if taking classes in the Department of
Communication Sciences and Disorders at USF.

Table 1. Average audiometric thresholds (pre-TTS) are shown for each group in dB HL.

<table>
<thead>
<tr>
<th>Group</th>
<th>250</th>
<th>500</th>
<th>750</th>
<th>1000</th>
<th>1500</th>
<th>2000</th>
<th>3000</th>
<th>4000</th>
<th>6000</th>
<th>8000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>7.75</td>
<td>7.75</td>
<td>7.25</td>
<td>8</td>
<td>8.5</td>
<td>9</td>
<td>6.5</td>
<td>5.5</td>
<td>9.25</td>
<td>13.25</td>
</tr>
<tr>
<td>(S.D.)</td>
<td>(2.55)</td>
<td>(3.8 )</td>
<td>(3.8 )</td>
<td>(2.99)</td>
<td>(4.32)</td>
<td>(5.98)</td>
<td>(6.51)</td>
<td>(4.84)</td>
<td>(6.34)</td>
<td>(5.45)</td>
</tr>
<tr>
<td><strong>Experi.</strong></td>
<td>8.5</td>
<td>8.75</td>
<td>8</td>
<td>9.75</td>
<td>9.75</td>
<td>9.25</td>
<td>7.75</td>
<td>7.75</td>
<td>11.75</td>
<td>16.75</td>
</tr>
</tbody>
</table>
**Instrumentation and Stimuli**

All instrumentation for this study was located in the USF Communication Disorders Center (CDC). Tympanometry and acoustic reflex measurements were performed using the GSI TympStar Middle Ear Analyzer. DPOAE measurements were conducted using the Starkey CubDis. Emissions were obtained by varying f2 at the frequencies 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz. A GSI-61 Clinical Audiometer was used for the standard audiometric procedures and to present the noise conditioning as well as the TTS-provoking stimulus. Pure tone air conduction testing via Etymonic ER-3A insert phones was performed using the GSI-61 Clinical Audiometer at the following frequencies: 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz using a modified Hughson-Westlake procedure. The stimulus to elicit the TTS was a narrow band noise centered at 2000 Hz and presented at 105 dB SPL for 5 minutes. Ear canal intensity measurements were performed to ensure that all subjects received the same level of TTS stimulus. These measurements were obtained using the probe microphone of the Audioscan Real Ear Measurement System in Real Ear Unaided Response Mode. The audiometer was adjusted in 1dB steps until the appropriate intensity was achieved.

**Procedures**

All testing was conducted by two third year doctoral students at the USF-Communication Disorders Center (CDC), under the supervision of a certified audiologist. Participants were randomly assigned to the control group or the supplemental magnesium group. The participants in the control group received a placebo instead of magnesium.
This was a double-blind study. That is, neither the participants nor the investigators knew who received the magnesium or the placebo.

Each participant completed appropriate paperwork including case history and noise history, and signed the approved Institutional Review Board (IRB) informed consent document. Baseline audiometric information was measured and each participant was assigned a code number using the next consecutive number in the order in which they were selected.

**Control Group**

Following a baseline audiological evaluation, each participant assigned to this group received a placebo pill and spent one hour in a quiet area. The participant then received 5 minutes of exposure to the TTS stimulus (narrowband noise centered at 2000 Hz and presented at 105 dB SPL).

**Supplemental Magnesium Group**

Following baseline and audiometric evaluation, each participant assigned to this group received a 150 mg magnesium pill and spent one hour in a quiet area. The participant then received 5 minutes of exposure to the TTS stimulus.

For both groups, audiometric data were collected immediately, thirty, and sixty minutes post-TTS exposure. To ensure thresholds returned to baseline results established during the initial visit, each participant was encouraged to return for audiometric and DPOAE testing thirty days after the date of their TTS exposure. Participants were also given the option to waive post-testing if they felt there were no long-term effects of the TTS stimulus on their hearing sensitivity. Twelve participants returned for hearing tests and twenty-eight participants signed waivers. There were no observable differences
between audiometric results at 30 days and pre-TTS results for the 12 participants who chose to return for the tests.

RESULTS

Pre-TTS Audiometric Data

Pre-TTS Audiometric data were analyzed with a two-way (2 X 10) Analysis-of-Variance (ANOVA). This ANOVA was performed to determine if there were any differences between the audiometric data of the control group and experimental group for any of the test frequencies. The effect of frequency was significant \[ F(9, 30)=10.86; \ p<0.01\]. However, neither the effect of group \[ F(1, 38)=3.61; \ p=0.07\], nor the group X frequency interaction was significant \[ F(9, 30)=0.58; \ p=0.81\]. These results indicated that although the participants exhibited different threshold values when test frequencies were compared, both groups had the same thresholds. In other words, there was no difference in terms of hearing sensitivity at the beginning of the study.

Post-TTS Audiometric Data

Audiometric threshold measurements were obtained immediately post-TTS exposure, 30 minutes post-exposure, and 60 minutes post-exposure. The pre-TTS stimulus thresholds were subtracted from the post-TTS stimulus thresholds to determine threshold shift at each frequency. Results from each group were averaged and examined for trends. Threshold shift data for each group is shown in Figures 1 through 3. Threshold shift obtained immediately following the TTS stimulus indicates an average increase in threshold of 13.73 dB (range: 8.75 to 19.25 dB) for the control group and 13.13 dB (range: 8.25 to 18.5 dB) for the experimental group. The greatest shift occurred at
frequencies 2000 - 6000 Hz, with minimal shift at the remaining test frequencies. This is true for both groups. There is a trend in the data for the experimental group to demonstrate a slightly greater threshold shift at all frequencies except 500 Hz and 1500 Hz.

Thresholds obtained 30 minutes post-TTS stimulus indicate an overall decrease in TTS with the greatest shift at 3000 - 6000 Hz, again for both groups. Average TTS at 30 minutes post-TTS was less than 1 dB for both groups and ranged from no TTS to a shift of 4.75 dB. Again, there is a slight tendency for greater threshold shift for the experimental group compared to the control group, but only at 3000 and 4000 Hz. As would be expected from the mostly negligible TTS observed at 30 minutes post-exposure, the thresholds obtained 60 minutes post-TTS stimulus show an average shift of approximately 0.5 dB when all test frequencies are included. The greatest shift continues to occur at 3000 - 4000 Hz, but with both groups exhibiting a TTS less than the 5 dB step-size used to obtain the pure tone thresholds. The tendency for the experimental group to have slightly greater TTS continued to be observed even one hour after TTS stimulus exposure.

TTS data were analyzed with a three-way (2 X 3 X 10) ANOVA. This ANOVA was performed to determine the effects of group (experimental or control), post-exposure time (immediate, 30 minutes, or 60 minutes), and frequency (inter-octave and octave frequencies from 250 – 8000 Hz). The effect of post-exposure time was significant \[ F(2, 37)=68.33; p<0.01 \], as was the effect of frequency \[ F(9, 30)=10.41; p<0.01 \]. The frequency X post-exposure time interaction was also significant \[ F(9, 30)=14.28; p<0.01 \]. The effect of group did not reach statistical significance \[ F(1, 34)=0.45; p>0.05 \].
Figure 1. TTS present immediately post-noise exposure is shown for each group as a function of test frequency.

Figure 2. TTS present 30 minutes post-noise exposure is shown for each group as a function of test frequency.
Figure 3. TTS present 60 minutes post-noise exposure is shown for each group as a function of test frequency.

$p=0.51$. None of the other interactions were significant.

The interaction of post-exposure time and frequency was further evaluated using all pairwise multiple comparison procedures (Tukey Test). Results indicated significantly greater TTS at 3000 Hz and 4000 Hz compared to the other test frequencies ($p<0.05$), but no difference in TTS between them. This difference was only present immediately after the TTS stimulus. There was no difference between TTS measured 30 minutes and 60 minutes post-exposure ($p>0.05$) at any frequency.

**DISCUSSION**

The purpose of this study was to examine the effects of a single dose of magnesium administered over a short period of time on temporary threshold shift. Specifically, the goal was to replicate a study conducted by Gupta (2000). The results of
this study suggest that 150 mg of supplemental magnesium has no protective effect on hearing sensitivity following noise overexposure. The trend in the data actually suggests more TTS present in the experimental group, although this was not statistically significant.

Results of this study indicate an expected frequency effect with regard to TTS. The amount of TTS was greatest at and above the stimulus frequency of 2000 Hz. There was no effect in the lower frequencies of 250 - 1000 Hz. It is often observed that the greatest effects of noise are evident one-half to one octave above the stimulus frequency (Lipscomb, 1994).

Another expected result of this investigation was the effect of post-exposure time. The largest TTS was observed immediately post-exposure. Recovery from TTS was observed as early as 30 minutes post-exposure. Sutton et al. (1994) observed similar TTS recovery in humans, but at 20 minutes post-exposure to a 2000 Hz pure tone presented at 105 dB SPL. In the current study, many participants experienced complete TTS recovery at 60 minutes post-exposure.

The current investigation found no effect of group. This is not in agreement with other studies on supplemental magnesium and TTS (Attias et al, 1994; Gupta, 2002). Gupta (2000) reported a significant difference in TTS between a group of participants given a single dose of supplemental magnesium compared to a group of participants given a placebo. Participants given the magnesium had less of a threshold shift following presentation of an intense narrowband noise than participants in the control group. Further, Attias et al. (1994) has also shown that a dietary magnesium supplement significantly reduced PTS in soldiers exposed to high noise levels. The differences in
results between the current study and the other studies in the literature could be due to several factors including differences in stimuli, magnesium dosage, and study design.

Regarding stimulus differences, the TTS-inducing stimulus in the current study was a narrow-band noise centered on 2000 Hz. Gupta (2002) also used a narrow-band noise but centered on 4000 Hz. In their study, the only observed differences in TTS were for audiometric frequencies at and above 4000 Hz. In the current study, a noise-band stimulus centered on a frequency one octave lower than Gupta (2002) was used to increase the potential range of audiometric frequencies that may reveal a TTS and an effect of magnesium. It is possible that differences in noise spectrum may have led to conflicting results.

Another factor that should be considered was the presentation level of the TTS-stimulus. In this study, the level of the stimulus was carefully monitored using a real ear probe microphone. This monitoring was performed in order to account for individual participant differences in ear canal characteristics that could potentially influence the level of the stimulus. The level of the TTS-stimulus was adjusted to 105 dB SPL for all participants. Since the stimulus was presented from an audiometer, the dB HL had to be adjusted for several participants to maintain this constant level. The actual dB HL values on the audiometer that resulted in a 105 dB SPL stimulus ranged from 92 – 106 dB across the participants. To our knowledge, the stimulus in the Gupta (2002) study was not monitored. It is possible that the actual SPL level in their investigation was higher than intended.

Other studies demonstrating a beneficial effect of supplemental magnesium on noise exposure have used higher levels than the current study. In Attias et al. (1994), the
noise exposure level was 164 dBA. Soldiers in this study did wear earplug hearing protection devices, which reduced the peak noise level by approximately 25 dB. The investigation by Scheibe et al. (2000) utilized stimulus intensity levels of 187 dB SPL and 167 dB SPL. Currently, it is not known whether the intensity of the noise is related to the efficacy of prophylactic magnesium effects, however, this factor is one to consider when comparing the results of this study to the results of previous studies. This may partially account for the discrepancy in results.

Magnesium dosage is also a factor to consider when comparing these investigations. As stated previously, the current study and the study conducted by Gupta (2000) are the only investigations that have examined the effects of a single dose of magnesium over a short period of time. Prior studies with indicating beneficial results used magnesium as a longer term dietary supplement (Attias et al, 1994; Scheibe et al, 2000). If magnesium supplement proves to be an effective preventive measure, the amount of magnesium to achieve a positive effect on threshold needs further investigation.

The design of this study is also a factor that may have affected the results. As previously mentioned, the examiners and the participants were blind as to which received the placebo and which received the supplemental magnesium. The identity of the pills was unknown until after all participants finished the study, and was sealed in an envelope by the compounding pharmacist. This factor allowed for the most control possible regarding investigator bias.
SUMMARY AND CONCLUSIONS

This study investigated the effects of supplemental magnesium on temporary threshold shift. Although the design of this study closely followed that reported by Gupta (2002), we were unable to replicate their results. Specific conclusions were: 1) the greatest TTS occurred for frequencies at and above 2000 Hz, particularly one-half to one octave above the frequency of the noise stimulus; 2) the largest TTS was observed immediately post exposure, with only slight threshold shift present after 30 minutes post-exposure and no difference between 30 minutes and 60 minutes post-exposure; 3) and 150 mg of supplemental magnesium had no apparent protective effect on TTS following intense noise exposure with a narrow band noise centered on 2000 Hz.

The results of this study should not discourage further investigation into the effects of magnesium on NIHL, but should provoke further study. It is clear that more research is needed in this area. Future studies should also use a double-blind design and consider such factors as noise stimulus frequency, duration, and intensity, as well as the important factor of magnesium dosage.
REFERENCES


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Appendix

Noise History Form

Effects of Magnesium on Temporary Threshold Shift:
Distortion Product Otoacoustic Emissions

Co-P.I.s:  Sarah Casey, B.S. and Jenifer Leonard, B.S.
Faculty Advisor:  Richard A. Roberts, Ph.D.

When answering these questions, please consider your past and current history with regard to exposure to loud sounds. Use as much space as you need to answer the questions.

Are you or have you ever been exposed to:

Firearms Where? How Often?

Loud Music Where? How Often?

Recreational Vehicles (i.e., boats, motorcycles, etc.) Where? How Often?

Power Tools Where? How Often?

Heavy Machinery Where? How Often?

Tractor Where? How Often?

Have you ever served in the military? When?

Were you exposed to noise? What?

Is there any other sound exposure that should be disclosed?