ANIMAL research suggests that antioxidants can protect the cochlea from the damaging effects of intense noise exposure. If similar results were found in humans, antioxidants could serve as non-barrier hearing protection, greatly reducing compliance problems associated with wearing ear plugs, muffs, etc. The current study evaluated the effectiveness of one antioxidant, N-acetylcysteine (NAC), on temporary cochlear changes in humans by using both behavioral and physiological measures. Two levels of supplement (900 mg of NAC or placebo) and two levels of noise (60 dB and 102 dB) were used in a full-factorial, within-subjects design. Participants ingested the supplement 60 minutes prior to exposure to a ten minute narrow-band noise centered at 2 kHz (60 dB or 102 dB intensity). The 102 dB exposure was designed to induce a 10–15-dB temporary threshold shift (TTS). Pure-tone thresholds and otoacoustic emissions (OAEs) were measured for 62 minutes after the noise exposure. No significant threshold differences between NAC and placebo occurred. Results from the 102 dB noise conditions showed that OAEs were reduced from baseline, and this reduction was greater with NAC treatment compared to a placebo.

1. INTRODUCTION

The production of reactive oxygen species (ROS) in the inner ear is a normal by-product of cochlear processes, and these free radicals normally are prevented from damaging the cells of the cochlea by a number of antioxidant defense mechanisms. However, these defenses are rapidly overcome by large ROS bursts produced in response to exposure to highly intense sounds. The mitochondria of the outer hair cells (OHCs) produce excess amounts of free radicals which result in hair cell damage. If the endogenous antioxidant glutathione, normally produced by the cell to neutralize free radicals, cannot keep up with the amount of free radicals, apoptosis will occur. The OHCs act as mechanical amplifiers for the motion of the inner hair cell (IHC) cilia, and the IHCs transduce mechanical energy into neural impulses. If there is a permanent alteration or loss of OHC function, IHC action also is reduced or even eliminated, resulting in permanent hearing losses.

Animal research shows that (NAC) and other antioxidants can provide cochlear protection from traumatic noise exposure. For example, Duan et al. (2004) found less hair cell loss in rats exposed to 160 dB impulses if the rats were injected with NAC prior to noise exposure. Permanent threshold shifts, as measured by auditory brainstem responses, also were lessened. Preventing or reducing permanent hearing loss in humans obviously is important, but temporary hearing loss also can be catastrophic for the infantry Soldier. For example, in an urban warfare situation, a sudden, unexpected explosion could lead to an immediate, though temporary, hearing impairment. This temporary hearing loss may not lead to permanent changes in the ear, but without the ability to monitor auditory information in the immediate environment, situational awareness would be reduced dramatically. Considering the potential benefits of NAC in preventing permanent hearing loss, the current study assessed the effects of NAC on temporary hearing loss in humans.

A Bekesy threshold task was used to examine how NAC affected TTS, and OHC function was assessed directly by measuring OAEs. OHCs actively move in response to acoustic stimulation, creating emissions that can be recorded within the ear canal. These OAEs are indicative of OHC activity, where less intense OAEs are associated with low levels of OHC activity. Since previous animal studies found that NAC reduced permanent threshold shifts, it was hypothesized that NAC’s antioxidant action would reduce the level of ROS in the cochlea. Thus, OHCs would be protected and would remain active despite intense noise exposure. Robust OAEs would reflect this OHC activity, and it was expected that OAEs would remain more intense following treatment with NAC than following a placebo.

2. METHOD

The five participants were volunteers from the military community at Fort Rucker, Alabama. The participants were screened for normal pure-tone thresholds, otoacoustic emissions, acoustic reflexes, normal tympanograms, and general good health. Participants were instructed not to take any medication or nutritional supplements for the duration of the study. Thresholds and emissions were measured every day prior
## Effects Of N-Acetylcysteine On Thresholds And Otoacoustic Emissions Following Noise Exposure

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### Distribution/Availability Statement
Approved for public release, distribution unlimited

### Supplementary Notes
See also ADM001736, Proceedings for the Army Science Conference (24th) Held on 29 November - 2 December 2005 in Orlando, Florida., The original document contains color images.

### Security Classification
- Report: unclassified
- Abstract: unclassified
- This Page: unclassified

### Limitation Of Abstract
UU

### Number Of Pages
2

### Form Approved
OMB No. 0704-0188

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to testing to make sure levels had not changed from the screening baseline. In addition, a typanogram was administered every day to insure normal middle ear functioning.

All stimulus presentations and measurements were made through a microphone/speaker combination that was contained within an ear probe. Otodynamics software and hardware controlled OAE measurements, and a Tucker-Davis RP2.1 module controlled the 3 kHz pure-tone threshold stimulus and participant responses. The full-factorial, within-subjects design combined two levels of narrowband noise (centered at 2 kHz; 60 dB and 102 dB intensity) and supplement (900 mg of NAC or a placebo) to create four conditions, the order of which was counterbalanced among participants. Participants completed one condition each day. All conditions followed the same procedure: supplement ingested 60 minutes before noise, 2 baseline OAEs and 2 baseline threshold measurements 4 minutes before noise, 10 minutes of noise presented, OAEs and thresholds measured nineteen times over the course of the next 62 minutes following noise exposure. Pure-tone thresholds were measured using a Bekesy threshold task, where the participant depressed/released a button to maintain the test tone at a barely-audible level.

3. RESULTS AND DISCUSSION

Results were analyzed using a 2 x 2 repeated-measures analysis of variance. As expected, thresholds did not change from baseline in the 60 dB noise conditions (this intensity is equivalent to the level of conversational speech). TTS did occur for NAC and placebo after the 102 dB noise exposure, but the results were highly variable and the differences between NAC and placebo TTS were not statistically significant. Noise and supplement affected OAEs, where NAC and placebo OAEs did not differ with 60 dB noise, but NAC OAEs were significantly reduced compared to placebo OAEs in the 102 dB noise condition. In addition, except for the first six minutes following noise exposure, placebo OAEs did not differ between noise intensities. Figure 1 displays these results over the time course of the experiment. Error bars are included for the 102 dB conditions and represent standard errors of the mean (non-overlapping bars indicate statistically significant differences). If NAC is assumed to function as a free radical scavenger, this finding is somewhat counterintuitive; OHCs should remain active if damaging waste products are removed by NAC. Instead, the OAE differences suggest that NAC may directly influence the OHC structure itself, suppressing activity and reducing the amount of free radicals produced in response to noise.

The reduced emissions after treatment with NAC may indicate that OHC activity is suppressed. Patuzzi (2002) and others have found physiological evidence that suggests TTS is due to the temporary closure of the OHC mechanoelectrical transduction channels, thus eliminating the amplifying action of the cells. While a TTS difference was not found between the NAC and placebo conditions in the current study, the OAE differences suggest that a TTS difference may occur if a different noise condition is used (e.g., a more intense or lengthier exposure, more sensitive behavioral test, etc.). Thus, based on the TTS and OHC work of Patuzzi and others, while NAC may reduce permanent threshold shifts, it could actually increase TTS by facilitating the suppression of OHC activity. Finally, at least one animal study (Miman et al., 2002) has found that antioxidants can actually enhance the negative effects of ototoxic drugs.

Recent research provides exciting evidence that antioxidants may be able to serve as non-barrier hearing protection. However, differential effects on permanent and temporary threshold shifts are not clear, nor is the antioxidant mechanism known (e.g., free radical scavenger vs. OHC suppressor, etc.). In some cases, antioxidants may exacerbate hearing damage. Until these questions are answered, Soldiers should continue to use approved barrier hearing protective devices.

![Figure 1. OAE changes as a function of supplement and noise intensity.](image)

**REFERENCES**

