

## 2 drugs protect hearing better than 1

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Whether on a battlefield, in a factory or at a rock concert, noise-induced hearing loss is one of the most common hazards people face.

Researchers at Washington University School of Medicine in St. Louis have identified a low-dose, two-drug cocktail that reduces <u>hearing loss</u> in mice when given before they are exposed to <u>loud noise</u>. The drugs, already FDA-approved for other conditions, also treat hearing loss after noise exposure.

While both drugs are known to protect hearing on their own, this is the first study to test the two in combination.

"We found they have synergy," says Jianxin Bao, PhD, research associate professor of <u>otolaryngology</u> at the School of Medicine. "Two drugs at lower dosages can block more signaling pathways than one alone, improving results while reducing side effects. We got the idea from cancer and HIV studies that use multiple drugs at lower dosages."

Bao presented the work Feb. 21 in Baltimore at a meeting of the Association for Research in Otolaryngology.

In earlier work, Bao's group found that anticonvulsant drugs for treating <u>epilepsy</u> helped protect hearing in mice after exposure to loud noise. And other groups had determined that glucocorticoids, antiinflammatory drugs often used to treat allergies and asthma, were also protective.



The reasons these drugs reduce noise-induced hearing loss are not well understood. But anticonvulsants are known to block calcium channels in <u>nerve cells</u>, and Bao's group speculates that the drug helps protect neuronal connections between <u>hair cells</u> and auditory <u>neurons</u>.

For this work, Bao and colleagues chose two drugs from the antiepilepsy family and two from the glucocorticoid family.

"We picked drugs that have fewer side effects and that can be chronically used," says Bao, also associate professor of audiology and communication sciences.

To test each drug's ability to prevent hearing loss, they gave various doses to mice two hours before exposing them to noise. To test treatment, they administered the drugs to different groups of mice 24 hours after noise exposure.

Three of the four drugs showed increasing protection with higher doses. And two of the drugs in combination, the anticonvulsant zonisamide and the glucocorticoid methylprednisolone, showed comparable hearing protection at much lower doses than when administered alone.

While the drugs do not prevent all hearing loss following sustained exposure to noise at 110 decibels, or about the sound of a chain saw, they can significantly reduce the loss by about 10 to 30 decibels.

In other words, a mouse with normal hearing might be able to hear a sound at 30 decibels. After exposure to loud noise, that mouse might only hear sounds that reach 50 decibels. But if that mouse were treated, it might be able to hear sounds at 40 decibels. In humans, protecting 5 or 10 decibels makes a difference in being able to hear everyday speech.

Bao says their next step is to test the drugs in animals that model human



hearing more closely.

**More information:** Bao et al. "Development of a combination therapy for noise-induced hearing loss." Presented Feb. 21, 2011 at a meeting of the Association for Research in Otolaryngology.

Provided by Washington University School of Medicine

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