Army Tests Hearing Drug at the Rifle Range

Medicine might prevent noise-induced hearing damage, a persistent problem for soldiers repeatedly firing loud weapons


THIS WE'LL DEFEND

of *fullscreen*

Soldiers in the drill-sergeant school at the shooting range in Fort Jackson. The training involves repeated firing of an M16 rifle, shots from which can register at around 155 decibels. *Andy McMillan for The Wall Street Journal*

Juan Ospina, a soldier at Fort Jackson, S.C., swallows a liquid in the clinical trial of an experimental drug to prevent hearing loss, conducted among soldiers who repeatedly fire a loud weapon during their training. *Andy McMillan for The Wall Street ...*

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64 COMMENTS

FORT JACKSON, S.C.—Staff Sgt. Tyler Durden and his fellow soldiers have been at the shooting range since 3 a.m. Every few seconds, a piercing shot from an M16 rifle rings out. With sunrise still an hour away, shell casings litter the ground.

The M16 is one of the U.S. Army's quieter weapons, but that isn't saying much. For the shooter, shots from the rifle, even if muffled by Army-issue earplugs, register above the noise level hearing experts consider safe. Over 11 days at the range as the soldiers train to become drill sergeants, each will fire an M16 at least 500 times. The Army is worried about hearing loss.

That is why, when the troops line up for breakfast under a tent, Sgt. Durden steps away to see two civilian nurses waiting at the side, who hand him a small bottle. He downs the liquid in one gulp before hurrying back to the breakfast line.

Sgt. Durden is a participant in a clinical trial, one tackling an issue that is both costly and garnering greater awareness in the military: hearing damage. Such damage traces not just to explosive sounds such as an M16 shot—a momentary 155 decibels, far louder than a jackhammer—but also to constant exposure to lesser noise such as that of engines. The trial is testing an experimental drug that might prevent noise-induced hearing loss, in a collaboration between an academic scientist and the military.

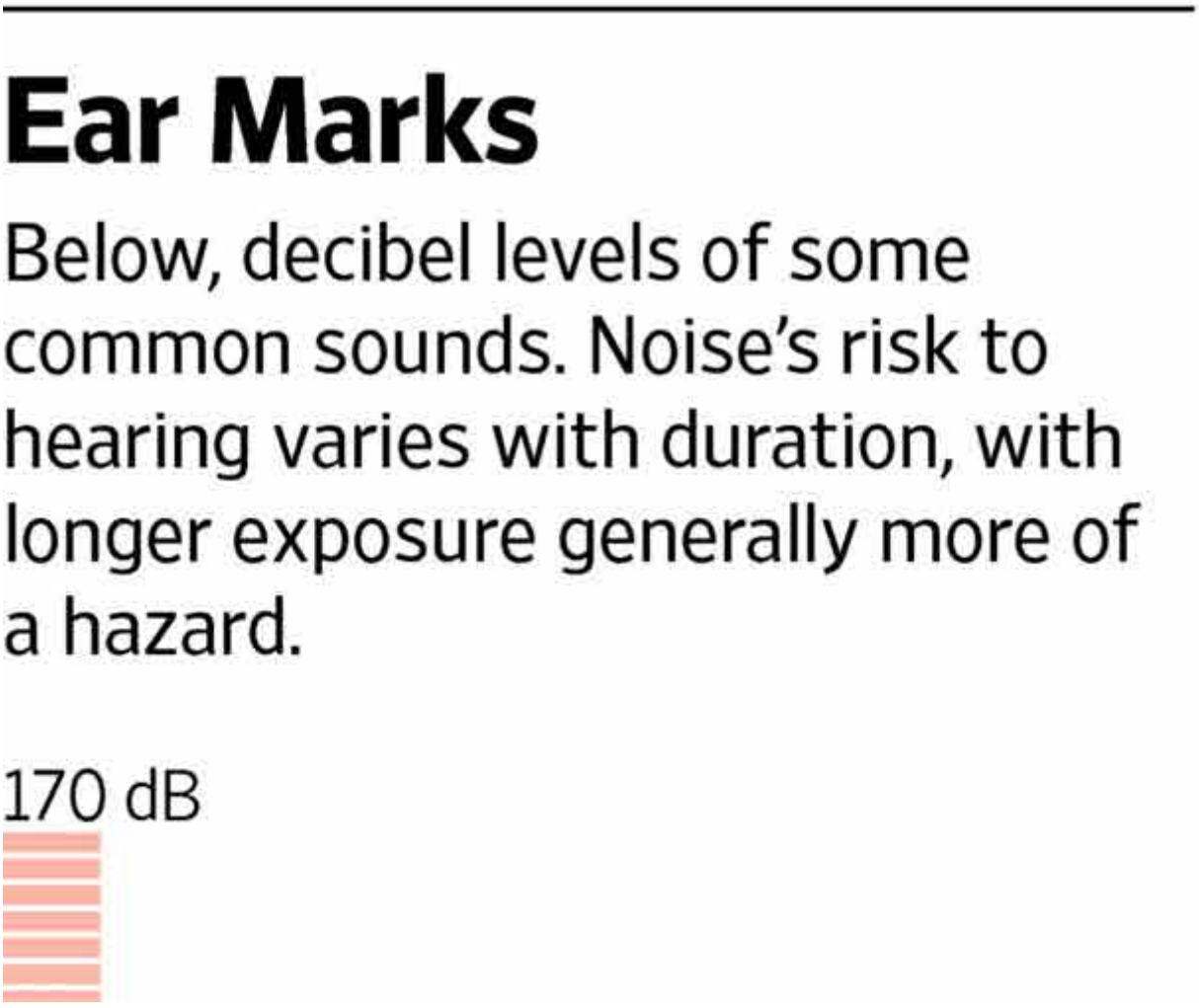
If ultimately endorsed by federal regulators, the drug would be the first approved to prevent hearing loss. It could have benefits far beyond the military. Factory workers, miners, loggers, musicians, pilots and others who work in noisy industries face high rates of hearing damage. Globally, a billion teenagers are putting themselves at risk through the din of clubs, concerts and even some sports events, the World Health Organization estimates.

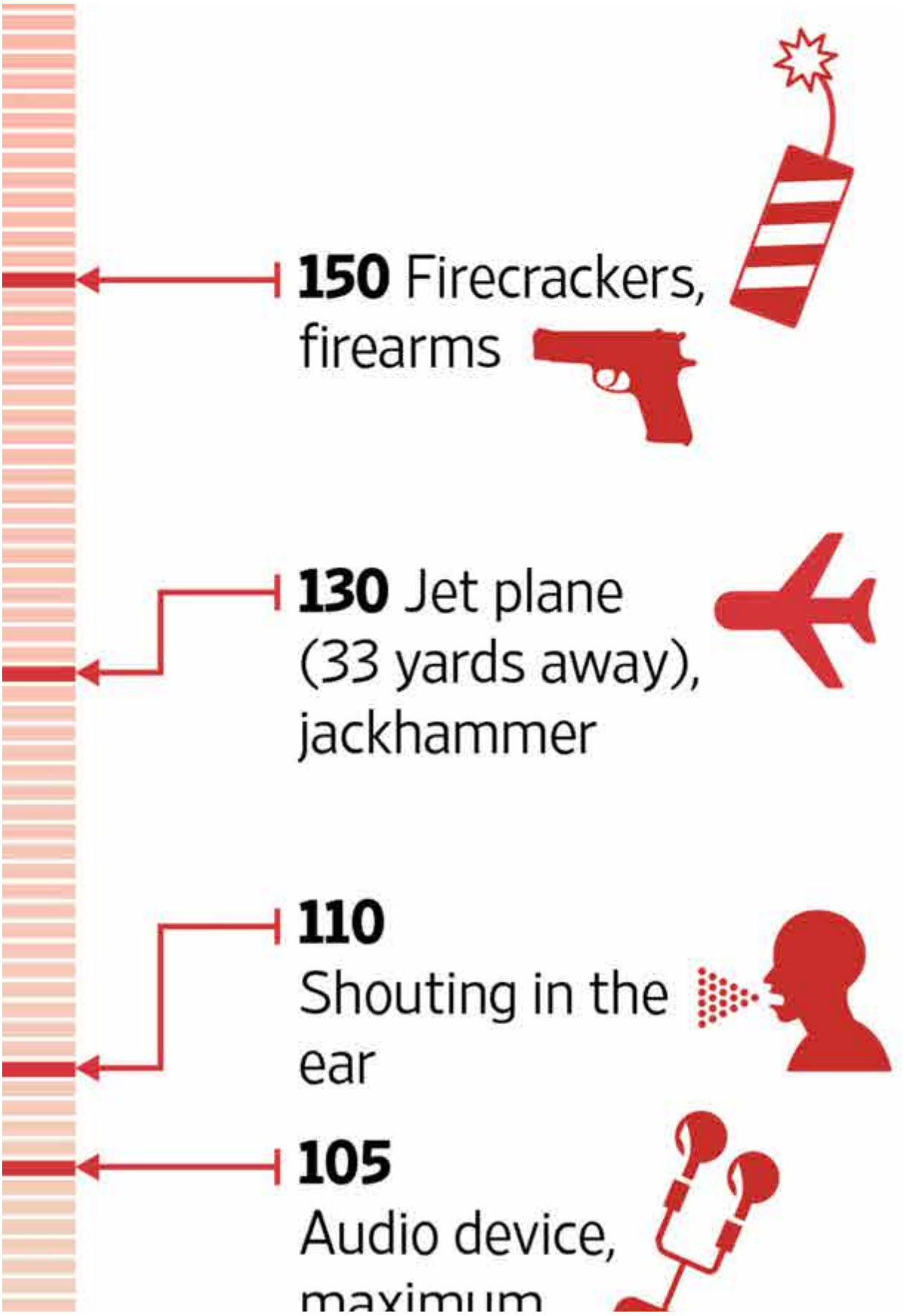
The compound being tested, a liquid form of a micronutrient called d-methionine that is found in cheese and other foods, was developed into a drug by Kathleen C.M.

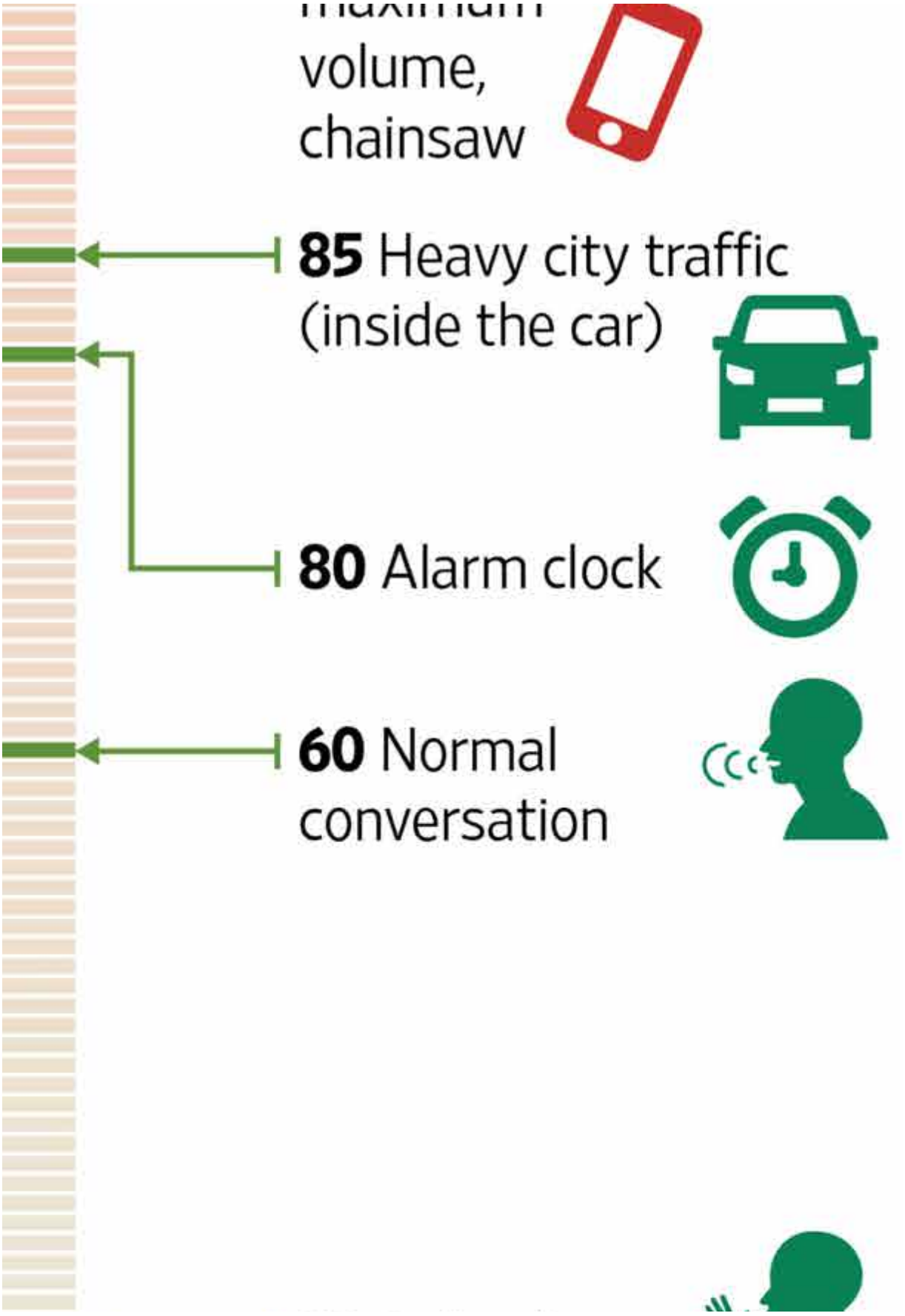
Campbell, an audiologist and professor at Southern Illinois University School of Medicine.

Clinical trials of drug candidates are normally the province of pharmaceutical or biotechnology companies, and she did work with a small biotech at one point. But the arrangement collapsed, leaving Dr. Campbell without a partner. She continued pursuing development on her own, but it wasn't easy to find a large test population of people who are repeatedly exposed to loud noises.

The military offered a solution. An officer at Fort Jackson approached Dr. Campbell after a lecture she gave to a military audience and suggested the Army base as a clinical-trial site. Fort Jackson trains tens of thousands of soldiers, including about 16 classes every year of those taking intense training to become drill sergeants, during which they fire many rifle rounds in a short time.




150 Firecrackers, firearms
130 Jet plane (33 yards away), jackhammer
110 Shouting in the ear
105 Audio device, maximum


volume,
chainsaw
85 Heavy city traffic
(inside the car)
80 Alarm clock
60 Normal
conversation

ENLARGE

After decades of war, there is increasing awareness of the need to address hearing damage. Modern weapons systems are noisier. The number of auditory disability claims continues to grow. Tinnitus, or constant ringing in the ears, and hearing loss were the most prevalent of the new service-connected disabilities for which the U.S. Department of Veterans Affairs paid compensation in fiscal 2013.

The Army sometimes needs to remove soldiers with known hearing loss from war zones because of worries their situational awareness is diminished. Other soldiers, who might have a lesser hearing impairment that hasn't been diagnosed, could also pose a danger to themselves or others, by being less quick to identify a threat, according to the Department of Defense Hearing Center of Excellence.

"Noise is ubiquitous in the military," says Rebecca Ludwig, a former hearing-program manager at Fort Jackson, citing not just shots and explosions but also generators,

ship engines and certain vehicles such as Humvees.

Sgt. Cody Brunet and Sgt. Ryan Cope, both 29 years old, say they have noticed changes in their hearing after about nine years each in the Army. "I say 'What?' a lot more," says Sgt. Brunet. Sgt. Cope says he has to turn up the volume when he watches television, prompting complaints from his wife. In the din of meal time at the Army mess hall, "People turn their good ear to you" to hear, Sgt. Brunet says.

Phase 3 Trial

It took Dr. Campbell two years to get all the permissions she needed to launch a clinical trial at Fort Jackson, including statements from various commanders that the process wouldn't interfere with their operations. She needed approval from a military institutional review board that makes sure soldiers' rights are protected. An ombudsman is required to sit in when soldiers are told about the trial, to be certain they aren't pressured by superior officers to participate. Ultimately, the Department of Defense put up about $2.9 million in funding.

Working with a military audiologist, Dr. Campbell designed a randomized Food and Drug Administration-sanctioned Phase 3 study, the late-stage test of efficacy that can lead to drug marketing approval. The trial began in late 2013 and is spread over three years, designed to enroll up to 600 subjects.

Each soldier gets a hearing test, and then, over 18 days that include stints at the rifle range, drinks a liquid containing either the drug or a placebo twice a day. Another hearing test at the end measures any change in the soldiers' threshold of hearing or ability to detect high- or low-frequency tones. Although some noise-caused hearing damage doesn't appear until many years later, more-subtle changes can show up swiftly, including some that can be measured but aren't necessarily noticed by the person.

Dr. Campbell quickly discovered that military personnel are transferred a lot. Several times, she has had to replace members of the trial team, such as audiologists or the site physician, when they were deployed abroad or sent to other bases.

Because the South Carolina base sprawls over miles, she considered doing the

required hearing tests in an RV, but scrapped the idea because of noise in the parking lot from military vehicles going in and out all day. Finally, a commander offered to give up one of the base's break rooms, and the hearing tests are done there.

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Army Staff Sgt. Tyler Durden is part of the trial of the drug, which if cleared by regulators would be the first approved to prevent hearing loss. Photo: Andy McMillan for The Wall Street Journal

The biggest challenge has been keeping up with soldiers whose schedules begin very early in the day and change unexpectedly. One morning in June, Elizabeth Bullock, a registered nurse and the trial's project manager, was at her usual spot in the mess hall with bottles of medication but discovered several soldiers enrolled in the trial weren't there. She scrambled to determine where they might go next, then raced to find them, pulling a roller bag behind her. She caught up with them just as they were headed into a shooting session.

"We spend a lot of time chasing them," she says. "It is our biggest challenge."

The trial isn't the military's first attempt to deal with hearing loss. Efforts to help World War II veterans with hearing problems triggered interest in the issue and led to the first professional audiology training programs at universities. Things have come a long way since soldiers stuffed crumpled-up cigarette filters in their ears. But more-sophisticated prevention efforts haven't solved the problem.

Modern earplugs go unused by many soldiers, who worry that the plugs decrease awareness and make it harder to hear commands. Ear muffs can be unwieldy or uncomfortable in the heat. Efforts to develop better hearing protection devices are under way, but sophisticated protection built into military helmets isn't yet available to all soldiers.

Earlier this year, researchers published the results of a study in Marines of a compound called N-acetylcysteine. The trial found no significant effect on overall hearing loss. But there were indications the substance has promise, according to Richard Kopke, principal investigator and CEO of Hough Ear Institute in Oklahoma City, and he hopes to test it in combination with a second one.

A Seattle biotech called Sound Pharmaceuticals Inc. received Defense Department support to run a trial of another compound in soldiers, but the study was never enrolled because of logistics concerns.

Free radicals

That means that farthest along, in the quest for a drug to prevent hearing damage, are d-methionine and the Fort Jackson clinical trial.

Researchers believe excessive noise causes the body to produce large numbers of highly reactive molecules that can harm tissues such as the hair cells of the inner ear. The theory behind d-methionine is that, being an antioxidant, it can neutralize some of these damaging molecules, while at the same time bolstering the body's innate defenses against them.

Should d-methionine someday become an approved drug, soldiers going into combat or beginning weapons training might take it in advance of expected exposure to extreme sounds such as gunshots or blasts.

But Dr. Campbell believes it could be helpful if taken after the exposure, too. The idea is that the body's production of the damaging molecules, which are called free radicals, continues for several days after an exposure to extreme noise, so that the drug could still have time to mop some of them up.

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The compound being tested, a liquid form of a micronutrient called d-methionine that is found in cheese and other foods, was developed into a drug by Kathleen C.M. Campbell, an audiologist and professor at Southern Illinois University School of Medicine. Photo: Andy McMillan for The Wall Street Journal

Recruitment of soldiers to her trial at Fort Jackson is steady but going more slowly than hoped. So far, 210 participants have enrolled.

Many want to know whether Dr. Campbell ever served in the military. She didn't, although her father and two in-laws did.

Other soldiers have expressed curiosity about her motives, asking if she has a

financial interest in the drug. She tells them the medical school owns the patent, but she would stand to benefit if the drug reached the market. She would receive half the profits the school gets, which she says would likely be just a fraction of the money earned by a corporate partner.

Although this is a Phase 3 trial, turning the compound into a marketable drug would require working with a company to produce, market and distribute it, the university and the military agree. The U.S. Army Medical Research and Materiel Command, which oversees Dr. Campbell's grant, is assessing the potential commercial market.

Col. Mark Packer, executive director of the DOD Hearing Center of Excellence, says the center is creating a database of reported cases of hearing loss to foster more research and aid companies that want to better understand what kind of market might exist for a drug. The center is also trying to make it easier for researchers and companies to run hearing-loss trials at bases, including navigating the extra paperwork and military culture, he says.

Sgt. Durden, the soldier who broke away from the breakfast line at the shooting range to gulp down his clinical-trial dose, joined the Army as a teenager. Now 32, the Tennessee native says his entire career has involved noise exposure. He has been in combat. And while parachuting, he has sat in and jumped out of noisy planes. Although his hearing was good enough to qualify for the drug trial, he suffers from tinnitus.

Sgt. Durden's duties sometimes include training other soldiers to shoot. He wears earplugs when he does so, yet he takes them out if he can't hear responses to his instructions. Deployed in Iraq a decade ago, he says, he would take out his earplugs whenever he grew worried he might miss a threat.

That is why he joined the trial, he says: A drug for hearing loss is needed, because earplugs alone won't solve the problem.

There is always going to be the next young soldier like him who considers the threat and asks himself, "Is protecting another soldier's life worth losing my hearing?" says Sgt. Durden. "Yes, it is. All day, every day."

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