Insulin injections could one day be replaced with rock music, research in mice suggests

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More than 37 million people in the U.S. have diabetes. According to the American Diabetes Association, 8.4 million Americans needed to take insulin in 2022 to lower their blood sugar. Insulin, however, is tricky to

deliver into the body orally because it is a protein easily destroyed in the stomach.

While researchers are developing pills that resist digestion in the stomach and skin patches that monitor blood sugar and automatically release insulin, the most reliable way currently to take insulin is through frequent injections.

I am a professor of pharmacology and toxicology at Indiana University School of Medicine, where my colleagues and I study drug delivery systems. Researching innovative new ways to get medications into the body can improve how well patients respond to and comply with treatments. An easier way to take insulin would be music to the ears of many people with diabetes, especially those who aren't fans of needles.

In a recent study in *The Lancet Diabetes & Endocrinology*, researchers engineered cells to release insulin in response to specific sound waves: the music of the band Queen. Though it still has a long way to go, this new system may one day replace the insulin injection with a dose of rock 'n' roll.

What is diabetes?

Diabetes is a chronic disease that arises when the body fails to make enough insulin or respond to insulin. Insulin is a hormone the pancreas makes in response to the rise in sugar concentration in the blood when the body digests food. This crucial hormone gets those sugars out of the blood and into muscles and tissues where it is used or stored for energy.

Without insulin, blood sugar levels remain high and cause symptoms that include frequent urination, thirst, blurry vision and fatigue. Left untreated, this hyperglycemia can be life-threatening, causing organ damage and a diabetic coma. According to the U.S. Centers for Disease

Control and Prevention, diabetes is the No. 1 cause of kidney failure, lower-limb amputations and adult blindness, making it the eighth most common cause of death in the U.S.

Treating diabetes is straightforward: When the body is lacking insulin, give it more insulin. Scientists have mastered how to make the hormone, but direct injection is the only effective way to get it into the body. Diabetic patients usually have to carry insulin vials and needles wherever they go. Considering that many people fear needles, this may not be an ideal way to manage the disease.

This challenge has sparked researchers to look into new ways to deliver insulin more easily.

What is cellular engineering?

Cells are the basic unit of life. Your body is composed of hundreds of different types of cells that carry out specialized functions. In some diabetic patients, the pancreatic beta cells that make insulin have malfunctioned or died. What if there were a way to replace these defective cells with new ones that could produce insulin on demand?

That's where cellular engineering comes in. Cellular engineering involves genetically modifying a cell to perform a specific function, like producing insulin. Installing the gene that makes insulin into cells is not difficult, but controlling when the cell makes it has been a challenge. Insulin should be made only in response to high blood sugar levels following a meal, not at any other time.

Scientists have been exploring the idea of using ion channels—proteins embedded in a cell's membrane that regulate the flow of ions such as calcium or chloride—like a remote-controlled device to activate cellular activity. Cells with specific types of ion channel in their membranes can

be activated in response to certain stimuli, such as light, electricity, magnetic fields or mechanical stimulation.

Such ion channels exist naturally as sensory devices to help cells and organisms respond to light, magnetism, touch or sound. For example, hair cells in the inner ear have mechanosensitive ion channels that respond to sound waves.

Combining cellular engineering with Queen

Bioengineering professor Martin Fussenegger of ETH Zurich, a university in Basel, Switzerland, led a recent study that used a mechanosensitive ion channel as a remote control to signal cells to make insulin in response to specific sound waves.

These "MUSIC-controlled, insulin-releasing cells"—MUSIC is short for music-inducible cellular control—were cultured in the lab next to loudspeakers. His team tested a variety of musical genres of different intensities and speeds.

Among the songs they played were pop songs like Michael Jackson's "Billie Jean," Queen's "We Will Rock You" and the Eagles' "Hotel California"; classical pieces such as Beethoven's "Für Elise" and Mozart's "Alla Turca"; and movie themes such as Soundgarden's "Live To Rise," which was featured in "The Avengers," a Marvel film. They found that pop music heavy in low bass and movie soundtracks were better able to trigger insulin release compared with classical music, and cells were able to release insulin within minutes of exposure to the song.

In particular, they found that the Queen song "We Will Rock You" most faithfully mimicked the rate of insulin release in normal pancreatic beta cells.

The team then implanted the MUSIC-controlled, insulin-releasing cells into diabetic mice. Listening to the Queen song for 15 minutes once a day returned the amount of insulin in their blood to normal levels. Blood sugar levels returned to normal as well. In contrast, mice that were not exposed to the song remained hyperglycemic.

Could music make insulin in people?

Despite these promising results, much more research is needed before this musical approach to producing insulin can be considered for human use.

One concern is the possibility of making too much insulin, which can also cause health problems. Fussenegger's study found that talking and background noise such as the racket made by airplanes, lawn mowers or firetrucks did not trigger the insulin production system in mice. The music also needed to be played close to the abdomen where the MUSIC-controlled, insulin-releasing cells were implanted.

In an email, Fussenegger explained that extensive clinical trials must be performed to ensure efficacy and safety of the technique and to determine how long the cellular implants can last. As with introducing any foreign material into the body, tissue rejection is also a concern.

Cellular engineering may one day provide a much-needed alternative to frequent injections of insulin for the millions of people with diabetes around the world. In the future, different cell types could be engineered to release other drugs in the body more conveniently.

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