Naked mole rats could help pain management research

The naked mole rat isn't a pretty creature, but it is unique

Berlin researchers show that the adaptable creatures have a surprising ability to not feel pain. The animals, which live entirely underground, are believed to have evolved with other unique abilities, such as long life.

While the naked mole rat may not be much to look at, it turns out that this subterranean critter may have a lot to teach us about pain management.

In a new paper published last month in the journal Science, German researchers have discovered why the African Naked Mole Rat is immune to feeling pain on its skin. The Berlin group's findings now bears vast implications for analgesic drug research - bringing new hope to chronic pain sufferers.

The naked mole rat has always been an object of fascination for biologists, who marvel at its low metabolic rate, resistance to cancer and its longevity. But recently, this buck-toothed, underground-dwelling, cold-blooded mammal is now being targeted for its resistance to pain, and specifically, resistance to pain inflicted by acid.

Previously it was thought that naked mole rats neurons would be missing acid receptors or that they were non-functional. However, the new research shows that the naked mole rat does have these receptors, and that they work just as in humans.

We showed that the proteins or acid was acting like a local anaesthetic because when you go to the dentist and have a local anaesthetic injected in to your teeth and everything goes numb, what that substance does is essentially shuts down the action potential from the pain fibers that innervate your teeth," explained Gary Lewin, a researcher at the Max Delbruck Center for Molecular Medicine in Berlin, and one of the paper's co-authors.

'Unique in the animal kingdom'

The team honed in on the electrical charge that passes across a neuron when excited by a stimulus - generating what's called an "action potential." They found that mole rats have two mutations in their genes, which control pain-sensing neurons to never send the sensation of pain in the first place.

"In this case, acid was shutting down the ability of these neurons to fire because they were blocked by this acid stimulus because of just these three amino acids in the naked mole rat," he told Deutsche Welle.
In other words, the researchers showed that these rats have evolved to be impervious to pain, in response to their environment and living conditions, which would otherwise be toxic to many other animals.

They seem to be unique in the animal kingdom," Lewin added. "One of the theories was that they are resistant to acid doses because they live in a very high carbon dioxide environment, their normal environment that is. So we believe this is a mechanism so the animals are not always under painful stress in this high carbon dioxide environment, so their pain receptors are basically insensitive to it."

Scientists hope to use this mechanism as a way to fine-tune pain sensitivity, without blocking out other sensations.

NAVI.7 is the name of the sodium channel responsible for acid insensitivity in mole rats, and is already a hot target for the pharmaceutical industry.

Lewin's study has proven for the first time that this channel is blocked by protons, as well as the amino acids responsible for this action, which could lead to a whole new class of drugs aimed at these three proteins.

**New research to advance naked mole rat studies**

According to Dr. Frank Berklein, a neurologist and doctor specializing in chronic pain at the University of Mainz in Germany, the potential development of a new class of anaesthetic and analgesic drugs with far fewer side effects would mean a drastic improvement in quality of life for his patients.

"This means if you could block these sodium channels, you should be able to block completely pain perception, but leave superficial feeling and sensing cold, sensing warm for instance - unchanged," he told Deutsche Welle.

Meanwhile, Lewin is excited about the next phase of mole rat research. In fact, he says, there's much more to naked mole rats than just their unique tolerance for pain.

In fact, Lewin has just been awarded a 2.5 million euro ($3.2 million) research grant that will allow his team to insert cloned mole rat genes into mice, to see if other traits unique to this odd animal are transplantable across species.

"They have a very low metabolic rate, they don't produce heat, and they live ten times longer than a mouse, so understanding those metabolic issues might lead us to understand metabolic diseases in humans," he said.

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